Review of the Efficient Funding of Chemotherapy (EFC) Funding Arrangements

Interim Report

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Acronyms

ABC	Activity-based costing
AE	Adverse event
AEMP	Approved ex-manufacturer price
AHA	Australian Healthcare Associates
AHI	Administration, Handling and Infrastructure
AIHW	Australian Institute of Health and Welfare
ARIA	Accessibility/Remoteness Index of Australia
BSA	Body surface area
CHERE	Centre for Health Economics Research and Evaluation
CI	Confidence interval
CCPS	Chemotherapy Compounding Payment Scheme
CDU	Chemotherapy day unity
CPA	(7th) Community Pharmacy Agreement
CPAP	Chemotherapy Product Access Program
CSO	Community Service Obligation
CSTD	Closed system transfer devices
CTG	Close the Gap
DAEN	Database of Adverse Event Notifications
DoH	Department of Health
DPMA	Dispensed price per maximum amount
EFC	Efficient Funding of Chemotherapy program
5-FU	5 Fluorouracil
FDA	Food and Drug Administration (United States)
FFS	Fee for service
FOLFOX	5-FU folinic acid oxaliplatin
FTE	Full-time equivalent
GI	Gastrointestinal
GST	Goods and services tax
HEPA	High efficiency particulate air (filter)
HER-2	Human epidermal growth factor receptor - 2
HTA	Health technology assessment
IHPA	Independent Hospital Pricing Authority

IT	Information technology
ICER	Incremental cost-effectiveness ratio
iu	International units
IV	Intravenous
LHD	Local health district
LSDP	Life Saving Drugs Program
MAb	Monoclonal antibody
MBS	Medicare Benefits Schedule
MeDRA	Medical Dictionary for Regulatory Activities
mg	milligram
NAb	Non-albumin bound (paclitaxel)
NHRA	National Health Reform Agreement
NSW	New South Wales
NZ	New Zealand
OIMS	Oncology information management system
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PCCA	Professional Compounding Centers of America
PD-1/PD-L1	Programmed Death-1 or Programmed Death-ligand 1
PI	Product information
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PSD	Public summary document
QALY	Quality-adjusted life year
ROR	Reporting odds ratio
RSA	Risk-sharing agreement
RPBS	Repatriation Pharmaceutical Benefits Scheme
QA/QC	Quality assurance/quality control
SHPA	Society of Hospital Pharmacists of Australia
SPA	Special Pricing Arrangements
TGA	Therapeutic Goods Administration
UK	United Kingdom
USP	United States Pharmacopeia
USA	United States of America
WHO	World Health Organization
XELOX	Capecitabine oxaliplatin

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Glossary of terms

Terms	Source
Active pharmaceutical ingredient: Any substance or mixture of substances to which the effect of a finished medicinal product is adjudged, or which acts as such.	PICS, 2014
Batch: A defined quantity of starting materials, packaging materials or products processed in one process or series of processes so that it could be expected to be homogeneous.	PICS, 2014
Batch number: A distinctive combination of numbers, symbols and/or letters which specifically identifies a batch.	PICS, 2014
Clean area: An area with defined environmental control of particulate and microbial contamination constructed and used in such a way as to reduce the introduction, generation and retention of contaminants within the area.	PICS, 2014
Closed Procedure: A procedure whereby a sterile pharmaceutical product is prepared by transferring sterile ingredients or solutions to a pre-sterilised sealed container, either directly or using a sterile transfer device, without exposing the solution to the external environment.	PICS, 2014
Compounding: The process of combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug or bulk drug substance to create a sterile medication.	USP 797
Controlled work area: An enclosed work area constructed and operated in such a manner and equipped with appropriate air handling and filtration systems to reduce to a pre-defined level the introduction, generation and retention of contaminants. A controlled work area may also be used to protect the external environment from the materials being handled in it e.g. vaccines or cytotoxics.	PICS, 2014
Critical zone: That part of the controlled work area where containers are opened and the product is exposed. Particulate and microbiological contamination should be reduced to levels appropriate to the intended use.	PICS, 2014
Cross contamination: Contamination of a material or product with another material or product.	PICS, 2014
Extemporaneous preparation: A product, which is dispensed immediately after preparation and not kept in stock.	PICS, 2014
Expiry date: The end of the shelf-life period, in non-coded form, after which the medicinal product should not be used. Also called the use before date.	PICS, 2014
Finished product: A medicinal product, which has undergone all stages of production, including packaging in its final container.	PICS, 2014
Intermediate product: A partly processed material, which should undergo further preparation steps.	PICS, 2014
Packaging: All operations, including filling and labelling, which a bulk product should undergo in order to become a finished product. Note: Sterile filling would not normally be regarded as part of packaging, the bulk product being the filled, but not finally packaged, primary containers.	PICS, 2014
Packaging material: Any material employed in the packaging of a starting material, an intermediate or finished product, excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.	PICS, 2014
Preparation: All operations of purchase of materials and products, production, quality control, release, storage, delivery of medicinal products and the related controls. Note: The simple provisioning of medicinal products according to authorised instructions and without necessitating pharmaceutical technical knowledge, where medicinal products are made ready for immediate application (e.g. dissolution of a powder for immediate application according to the instructions in the package leaflet of an authorised product), is normally not normally considered as preparation.	PICS, 2014
Processing: That part of the preparation of a medicinal product involving the dosage form.	PICS, 2014

Production: Part of preparation. It involves all processes and operations in the preparation of a medicinal product, from receipt of materials, through processing and packaging, to its completion as a finished product.	PICS, 2014
Stability: The extent to which a product or preparation retains physical and chemical properties and characteristics within specified limits throughout its expiration or beyond-use dates	USP 797
Sterililty: The absence of viable microorganisms	USP 797
Transfer Device: A fixed or removable device, which allows material to be transferred into and out of a container or a pharmaceutical isolator, without exposing it to the external environment.	PICS, 2014
Validation: The risk based, systematic, GMP compliant and documented evidence that a defined process actually leads reproducibly to the required results.	PICS, 2014
Wastage: The amount of pharmaceutical product remaining in a vial (and not pertaining to the amount that cannot be extracted due to product viscosity, vial shape or practitioner proficiency) in excess of the quantity required for a prescribed dose.	Based on definitions in the literature

Executive Summary

Overview

The Efficient Funding of Chemotherapy (EFC) program is a key component of the Pharmaceutical Benefits Scheme (PBS); in 2020-21, there were over 1.39 million PBS claims for cancer medicines in Australia, representing $1.95 billion in Government spending. A Review commenced in 2021 to consider whether the existing EFC arrangements are appropriate with respect to the production, distribution, preparation, administration and remuneration of cancer medicines, and whether the EFC arrangements may be enhanced to improve program efficiency and patient access to medicines. The Review considered input from multiple stakeholders throughout the cancer medicines supply chain—including patients, clinicians, pharmacies, hospitals, cancer medicines compounders and manufacturers, and the Commonwealth Government—as well as data and other published information on the sale and PBS reimbursement of cancer medicines.

Stakeholder submissions made clear the complexity of the cancer medicines supply chain, including the specialised nature of cancer medicines supply, the interconnectedness between existing EFC reimbursement arrangements and commercial activity, and the impact of funding and supply chain arrangements on prescriber behaviour. Enhancing patient access to cancer medicines was considered an overarching aim of supply chain interactions.

The Review found that, by and large, the EFC continues to be an appropriate policy response for the specialised nature of cancer care and to ensure access to cancer medicines via the PBS. A number of amendments to those arrangements were proposed, with a focus on reducing administrative burden, improving inefficiency in remuneration, enhancing equity of access and strengthening system accountability. Proposed amendments include: a change in the name of the program; stakeholder education on the operation of the EFC and PBS more broadly; the removal of the distinction in PBS item codes between public and private hospital providers; consideration of expanding the scope of activities captured by EFC fees; the adoption of a per-mg reimbursement model; introduction of serialised vials; the payment of compounding fees to all compliant providers; and exploring the establishment of a National Stability Testing Centre.

Long-term transition to some of the proposed arrangements (e.g., a per-mg reimbursement model) and consideration of the importance of activities affecting cancer medicines care that sit outside of the EFC require further investigation and consultation beyond the period of this Review.

Introduction

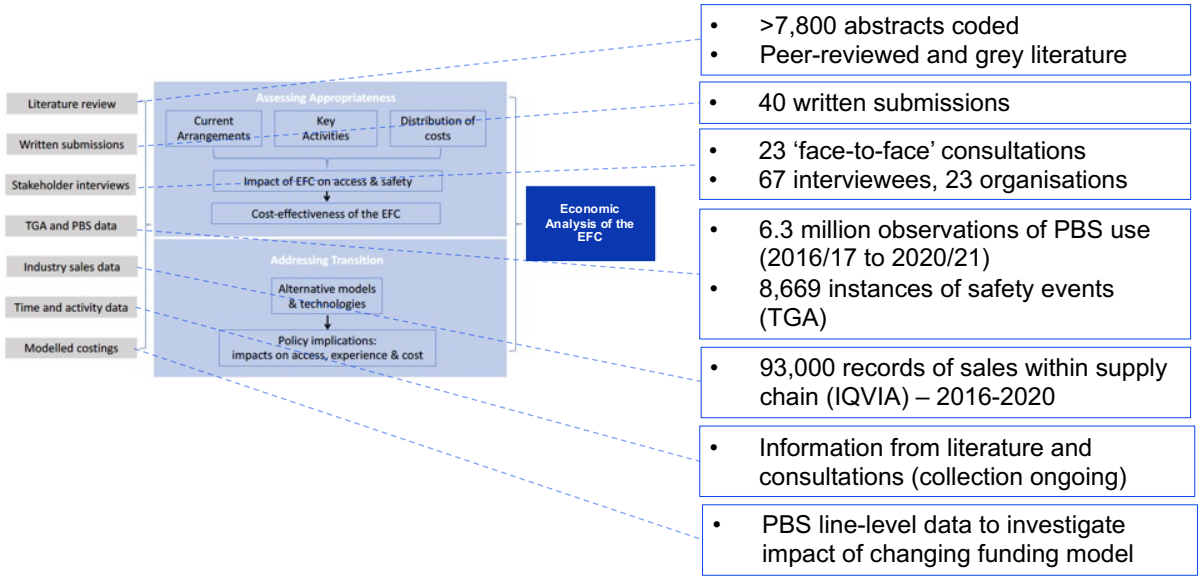
The Efficient Funding of Chemotherapy (EFC) was established to fund the supply and preparation of infusible cancer medicines that require compounding on an individual patient-basis, as well as a number of related medicines (e.g., antiemetics and immunostimulants) through the Pharmaceutical Benefits Scheme (PBS). Recognising the specialised nature of cancer care, establishment of the EFC aimed to facilitate patient access to high-quality cancer medicines while minimising costs to Government. In the 2020-2021 financial year, total Government benefits paid for medicines subsidised through the EFC were $1.95 billion for over 1.39 million PBS claims; the total PBS spend over the same period was $13.8 billion.

A Review of the EFC program was commissioned by the Commonwealth Department of Health in 2021 to investigate current processes involved in the production, distribution, preparation, administration and remuneration of cancer medicines provided through the EFC, and to identify whether the EFC arrangements may be enhanced to improve program efficiency and patient access to medicines. Professor Sanchia Aranda was appointed as Lead Reviewer, with the Centre for Health Economics Research and Evaluation (CHERE) at University of Technology Sydney commissioned to undertake the Economic Analysis component of the Review. This Interim Report details the Review's overall aim, specific objectives, research questions, methodology, findings, discussion and recommendations.

Approach

The Review was undertaken to address: (1) the appropriateness of existing EFC program arrangements with respect to achieving patient access and efficiency in the funding of cancer medicines; and (2) transition arrangements that may be required to ensure continued and appropriate access to treatment, encourage innovation and facilitate collaboration in Australia's cancer medicines supply chain. These issues have been investigated through the conduct of the Economic Analysis, which comprised extensive qualitative research and consultation, coupled with analysis of quantitative data on activities undertaken throughout the EFC supply chain (see Figure ES1).

Figure ES1. Approach to the Economic Analysis



Abbreviations: EFC, Efficient Funding of Chemotherapy; PBS, Pharmaceutical Benefits Scheme; TGA, Therapeutic Goods Administration

Importance of stakeholder views

A critical aspect of the Review was the participation and input of EFC supply chain stakeholders, including patients, clinicians, pharmacies, hospitals, cancer medicines compounders and manufacturers, and the Commonwealth Government. Information provided through written submissions to the Review and follow-up interviews revealed nine key themes with respect to the operation of the EFC (see Table ES1).

Overall, these themes revealed the complexity and interconnectedness of the EFC medicines supply chain, including the specialised nature of cancer medicines supply, regulation, the reciprocal influence of reimbursement and commercial arrangements, and the impact of funding and supply chain arrangements on prescriber behaviour. Common among all stakeholders was the stated desire to maintain/enhance patient access to cancer medicines and reduce complexity for participants in the supply chain.

Table ES1. Summary of consultation input

Theme	Overview of Input
Chemotherapy as a 'specialty service'	Provision of cancer medicines is specialised (e.g., with respect to training, equipment, regulations, safety), involving multiple stakeholders throughout the supply chain (e.g., doctors, nurses, pharmacists, compounders, logistics); the provision of cancer care should be viewed holistically. The program name 'Efficient Funding of Chemotherapy' is no longer fit for purpose, as cancer care is increasingly focused on non-cytotoxic medicines and critical supportive care. (see Section 4.1.5)

Theme	Overview of Input
Service viability	Provision of cancer medicines is costly and managing stock bears substantial financial risk. Providers increasingly rely on 'just-in-time' ordering to minimize stock holdings and associated risk exposure (e.g., cold chain storage, stability). Potential gaps between a drug's purchase price and reimbursed price (e.g., due to price disclosure or other price changes) increase providers' financial exposure. (see Sections 4.1.1; 5.1.1)
EFC fees/ remuneration	Existing fees do not cover the costs of all inputs (e.g., containers) and activities (e.g., drug repurposing) associated with the provision of cancer medicines. Fees are levied inconsistently within the EFC (e.g., public vs private) and relative to similar activities undertaken in other sections of the PBS (e.g., there is no wholesaler mark-up on EFC medicines). (see Sections 4.1.6; 6.1.2)
EFC administrative burden	Prescribing on the PBS is complicated by drugs having multiple benefit item codes (e.g., public vs private) and being available on different schedules (e.g., (s100), (s85)). Authority requirements for many EFC-listed items increase complexity and may hamper patient access. Script management, including written authorities, dual processing and paper scripts, is time consuming and inefficient. (see Sections 4.1.3; 5.1.3; 6.1.1)
Compounding	Compounding is critical to the EFC supply chain, impacting access, timing and wastage. Compounding is an expensive, specialised and manual process. The remuneration of some compounding activities is inconsistent, based on TGA-licensing status, rather than activities/standards. Product stability data are critical. Growing systemic dependence on the private sector may reduce health services' capacity to manage risk. (see Sections 4.1.1; 4.1.4; 4.1.6; 5.1.1; 6.1.2; 6.1.5)
Wastage	Vial-sharing is critical to minimise drug wastage and is fundamental to compounder viability. The practice of vial-sharing results in a disconnect between drug sales and reimbursement claims, which affect commercial contract arrangements between manufacturers and the Commonwealth. Currently, the Commonwealth pays twice for the wastage component within vials that are shared; once as part of the claim for the efficient combination of vials that resulted in that wastage amount, and once as part of the claim for the efficient combination of vials associated with shared-vials incorporating that wastage. Potential avenues to reduce drug wastage include dose-banding/rounding, incentives to re-issue/repurpose drug when the nominated patient is no longer eligible, and increased access to product stability data. (see Sections 4.1.1; 4.1.2; 5.1.1; 6.1.2; 6.1.5)
Patient access and safety	Stakeholders voiced a strong commitment throughout to maintain and enhance patient access to cancer medicines. Patients have less access in non-urban areas due to logistics, timing and limited compound stability. There are inconsistencies in co-payment arrangements for ancillary drugs (i.e., EFC Schedule 2) and between some states and settings (e.g., public vs private). The requirement that patients be treated as outpatients in public hospitals may adversely affect practice and patient care. There is a strong reliance on hospital services, particularly in private settings, rather than community pharmacy. (see Sections 4.1.5; 5.1.1; 5.1.2; 5.1.3; 6.1.1; 6.1.2; 6.1.4)

Theme	Overview of Input
Standards	Compounding operations are highly regulated; the perceived gap between TGA and USP standards is narrowing, which calls into question the disparate remuneration of TGA-licensed and non-licensed facilities. Increased standards may threaten the viability of some services, especially in rural/remote settings. Increased focus on non-cytotoxic cancer medicines (e.g., immunotherapies) may be shifting the occupational health and safety requirements for preparing cancer medicines (i.e., to be less stringent relative to the preparation of cytotoxic chemotherapies). (see Sections 4.1.4; 4.1.5; 5.1.1)
Public vs private	With respect to prescribing and availability of medicines, there is unnecessary complexity caused by the disparate PBS item codes applied in public and private settings. Differences in patient co-payments based on treatment setting (i.e., public vs private) may impact equity of patient access, particularly in non-metropolitan areas where patients tend to have less choice of treatment setting. (see Sections 4.1.5; 5.1.2; 6.1.3)

Abbreviations: EFC, Efficient Funding of Chemotherapy; PBS, Pharmaceutical Benefits Scheme; TGA, Therapeutic Goods Administration; USP, United States Pharmacopeia.

In submissions to the Review, many stakeholders identified issues that do not relate directly to the EFC, such as funding for the administration of cancer medicines to patients, clinical management, infrastructure and specialised training and education. While beyond the direct scope of the Review, these are important elements of a system that delivers safe, high-quality cancer medicines. Further consultations on these critical elements of cancer medicines care will be pursued by the Lead Reviewer, in collaboration with relevant government agencies and peak cancer care organisations.

Findings and Recommendations

The Findings and Recommendations of the Review are summarised in Table ES2. Overall, the Review finds that the EFC continues to be an appropriate policy response that recognises the specialised nature of cancer care and works to ensure access to cancer medicines via the PBS. The Review has made a number of recommendations to the ongoing operation of the EFC, including:

- changing the name of the program;
- stakeholder education on the operation of the EFC and PBS more broadly;
- removal of the PBS item code distinction between public and private hospital providers;
- consideration of expanding the scope of activities captured by EFC fees;
- adoption of a per-mg reimbursement model;
- serialisation of vials;
- equitable payment of compounding fees to all compliant providers; and
- exploring the establishment of a National Stability Testing Centre.

Long-term transition to some of the proposed arrangements (e.g., a per-mg reimbursement model) will require further investigation and consultation beyond the period of this Review to ensure ongoing timely and efficient access to high-quality medicines.

Table ES2. Summary of Findings and Recommendations

Theme	Findings	Recommendations
Chemotherapy as a 'specialty service'	Cancer care is specialised, including the complex nature of compounding, prescribing and administration of cancer medicines. Given this specialisation, it is appropriate to maintain the EFC as a separate entity within the PBS. The nature of cancer medicines themselves has changed; at its inception, the EFC was dominated by cytotoxic drugs but the overwhelming volume and value of EFC services are now associated with immunotherapies and other biological medicines.	1. Short-term: Modify the EFC legislative instrument to recognise that the program funds more than cytotoxic chemotherapy and intravenous cancer medications. Consideration should be given to the following suggestions: (1) 'Efficient Funding of Cancer Medicines'; (2) 'Cancer Medicines Funding Program' 2. System change: Investigate system changes with respect to alternative funding mechanisms for the delivery of cancer medicine services that better integrate all aspects of the care pathway (including assessment for treatment, treatment preparation and delivery, and follow-up care). (see Sections 3.1.1; 3.2.1; 4.1.5)
Service viability	PBS arrangements involve a complex interplay of multiple stakeholders in which the Commonwealth acts as a price-setter for drug reimbursement and reimburses hospitals/pharmacies for drug supplied to patients but does not take receipt of purchased stock. This creates a disconnect in the system between the decision to reimburse drug, the process by which drug is supplied and the impacts therein on subsequent volumes claimed for reimbursement from the Commonwealth.	3. System change: Consider the potential for the Commonwealth to purchase medicines directly from manufacturers as a means of increasing system efficiency and reducing pharmacy/hospital exposure to cost pressures associated with purchasing and carrying EFC-listed stock. (see Sections 3.2.2; 5.1.1; 6.3.6)
EFC fee remuneration	There was insufficient basis to support the amendment of current EFC fees. Additional fee components could be considered in the long term to address changes in the provision of cancer medicines and pharmacy practices designed to minimise waste.	4. Short-term: Maintain the EFC's existing fee structure and level as currently legislated, subject to indexing arrangements. 5. Long-term: Consider amending the EFC fee components and levels (subject to an analysis of stakeholders' empirical cost data) to add specific payments with respect to infusion devices, repurposing/reissue of compounded medicines, and the provision of cancer medicines in rural areas. 6. Long-term: Consider amending the EFC distribution fee in lieu of a specific wholesaler payment (potentially as part of future negotiations of the Community Services Obligation).

Theme	Findings	Recommendations
		(see Sections 3.2.2; 4.1.6; 4.3.1; 4.3.2; 4.3.3; 5.1.1; 5.1.2; 6.1.1; 6.1.2; 6.3.5)
EFC administrative burden	Under current arrangements, access to EFC-listed medicines is reportedly overly complex and associated with a high level of administrative burden, particularly with respect to: written and online authorities; permitted dosing regimens; disparities between restrictions on the EFC and elsewhere on the PBS; and disparities in co-payment arrangements between the EFC and other sections of the PBS.	7. Short-term: Continue operation of the Medicare Prescribing chart for online prescribing and claiming. 8. Short-term: Expand the medicines covered under the EFC to include all compounded cancer medicines listed for cancer indications on the PBS. 9. Short-term: Develop an education program targeting all system stakeholders to focus on: (1) PBAC cost-effectiveness recommendations, including the setting of PBS restrictions; (2) item coverage under extant EFC arrangements. (see Sections 3.2.2; 3.2.3; 3.2.4; 4.1.3; 5.1.3; 6.1.1)
Compounding	Compounding is a critical and complex element of the cancer medicines supply chain. The increasing use of third-party, private-sector compounders has increased the capacity of some small-scale hospitals to provide quality care in a more timely manner (particularly in regional and rural areas) but has reduced public sector capacity for the provision of compounding services. The changing nature of cancer treatment, (i.e., increasing reliance on non-cytotoxic chemotherapies) and coming-together of operational standards, has reduced the rationale to distinguish between TGA-licensed and non-licensed facilities with respect to the payment of compounding fees. Stability testing and compounding are recognised as specialised services. However, there was no clear evidence to substantiate a change in the quantum of fees paid for compounding services. Moreover, fees do not appear to vary with throughput scale.	10. Short-term: Payment of the CCPS should be: (1) expanded to all (TGA and non-TGA licensed) compounding facilities, subject to annual review of compliance with relevant regulatory guidelines and best practice (Pharmacy Board Guidelines/USP 797); (2) uncoupled from service volume and made on an annual grant basis. 11. Long-term: Investigate the requirements and feasibility of establishing a National Centre for Stability Testing to increase the shelf-life of compounded products under conditions replicable by local compounders. (see Sections 4.1.1; 4.1.5; 4.3.3; 5.1.1; 6.3.4)
Wastage	Remuneration of medicines on the basis of the most efficient combination of vials is associated with inefficiency with respect to PBS claims due to a 'double-payment' for wastage (i.e., the volume of drug contained in a vial in excess of the prescription on a per-patient basis).	12. Short-term: Continue the current system of reimbursement based on the most efficient combination of vials. 13. Medium-term: Investigate the introduction of a PBS Dose-Banding chart for cancer medicines to facilitate ease of prescribing within bands (with an aim to reduce wastage on a per-

Theme	Findings	Recommendations
	The practice of vial sharing to minimise the quantum of drug discarded is more efficient than would otherwise occur if drug was supplied and claimed on a whole-vial basis, and reflects the commercial reality of the PBS supply chain. Reimbursement of drug on a per-mg basis would reduce the extent to which there is 'double-payment' for wastage. However, adoption of a per-mg reimbursement model has systemwide implications, particularly for the flow of funds within public hospitals, necessitating that any such change be managed with careful regard to the overall arrangement of public sector hospital funding. Extant commercial arrangements between the Commonwealth and manufacturers of cancer medicines necessitate the periodic reconciliation of drugs sold by manufacturers into the supply chain with what is claimed for Government reimbursement via the PBS. Current data collection arrangements do not readily support the conduct of such reconciliations.	patient basis). Reimbursement would continue to be based on the most efficient combination of vials (ad-interim). 14. Long-term: Adopt a per-mg reimbursement model as the most efficient use of cancer medicines and to potentially support reconciliation of sales with manufacturers. This is predicated on broader system change with respect to the interface between PBS reimbursement for drug supplied and the flow of funds to states for hospital funding through the Australian Hospital Agreements. 15. Medium-term: Upgrade PBS data collection and reporting systems to ensure information on the form and strength of vials used in estimating the most efficient combination of vials can be readily extracted from the system. 16. Long-term: Serialise vials to facilitate reconciliation of drugs transacted with PBS claims. Feasibility of such an arrangement is subject to requisite infrastructure (e.g., sterility-compliant scanning devices in compounding facilities, pharmacy scanning software) and financial capital investment. 17. System change: Consider the potential for the Commonwealth to purchase medicines directly from manufacturers as a means of increasing system efficiency and more directly align the purchase and reimbursement of PBS medicines. (see Sections 4.1.1; 4.1.2; 4.2.1; 4.2.2; 4.2.3; 5.1.1; 6.1.2; 6.1.5; 6.3.2; 6.3.4; 6.3.5; 6.3.6)
Patient access and safety	There is an ongoing need to ensure that Australian cancer patients continue to have access to quality cancer medicines. Current co-payment arrangements result in some disparities for cancer patients, depending on the type and setting of care. Access to Closing the Gap co-payment subsidies is unnecessarily complex and restricts participation in that measure by some Indigenous Australians. Ensuring access to quality care for patients in non-metropolitan areas is critical; current arrangements for the funding and provision of cancer medicines may result in delays for patients in rural/remote areas and	18. Short-term: Remove the distinction between public and private hospital prescribing to rationalise co-payments. 19. Short-term: Expand the availability of Closing the Gap arrangements to all eligible Indigenous peoples accessing cancer medicines. 20. Short-term: Extend the current co-payment arrangements for EFC Schedule I medicines to Schedule II medicines to ensure patients are not differentially affected by co-payments. 21. Medium-term: Conduct a system-wide consultation (State/Territory/Commonwealth Governments and peak cancer

Theme	Findings	Recommendations
	increased 'costs' to access care. It is recognised that many of these issues relate to service provision and are beyond the scope of the Review.	care/consumer organisations) to consider initiatives that may improve access to quality cancer care. (see Sections 3.2.1; 5.2-5.4; 6.3.3)
Standards	Compliance with international and local standards for compounding, pharmacy and manufacturing practices are critical to the provision of safe and effective cancer medicines. TGA-licensed compounders currently adhere to PIC/S standards, as well as numerous state and territory-based standards, and are subject to annual audit of their practices. Non-TGA licensed compounders generally adhere to guidelines as set out by the Pharmacy Board of Australia in compliance with the USP 797 standards and are not subject to annual external audits. Over time, the gap between these sets of standards has narrowed; bringing the compliance activities of TGA-licensed and non-licensed compounders closer into alignment.	22. Short-term: The Review reiterates the findings of the King Review (2017) and recommends the application of a nationally consistent set of standards to the compounding and supply of cancer medicines. Those standards as they apply to compounding providers for the EFC should be clearly articulated. (see Sections 4.1.1; 4.1.4; 4.1.6; 4.3.3; 6.3.4)
Public vs private	The current division of PBS item numbers between (s94) public and private hospital providers results in unnecessary complexity. The associated administrative burden may adversely affect access for cancer patients, who commonly move between public and private settings. With respect to EFC fees, there is no apparent basis for public hospital providers to be paid less than (s90) community and (s94) private hospital providers.	23. Short-term: Remove the distinction between (s94) public and private hospital settings with respect to PBS item codes. 24. Short-term: Remove the distinction between (s94) public and private hospital providers with respect to the EFC fees paid for the supply of cancer medicines. (see Sections 4.1.1; 4.1.5; 5.1.2; 6.3.3)

Abbreviations: EFC, Efficient Funding of Chemotherapy; PBAC, Pharmaceutical Benefits Advisory Committee; PBS, Pharmaceutical Benefits Scheme; PIC/S, Pharmaceutical Inspection Co-operation Scheme; TGA, Therapeutic Goods Administration; USP, United States Pharmacopeia.

1 Background to the Review

The Efficient Funding of Chemotherapy (EFC) arrangements were established in 2011 through the National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011 (Cth). Recognising the specialist requirements of cancer care, the EFC program provides funding through the Pharmaceutical Benefits Scheme (PBS) for the supply and preparation of infusible cancer medicines that require compounding on an individual patient-basis, as well as for a number of related benefits, including antiemetics and immunostimulants. The EFC program aims to facilitate patient access to high-quality cancer medicines while minimising costs to Government [1].

In the 2020-21 Commonwealth budget, the Government announced a Review of the EFC program to investigate the current processes involved in the production, distribution, preparation and administration of cancer medicines provided through the EFC, and to identify whether those arrangements may be enhanced to improve program efficiency and patient access to medicines [2]. The Review was tasked to consider the:

- Appropriateness of the EFC's fee structure with respect to the cost of compounding, including operational costs in relation to compounding in facilities licensed by the Therapeutic Goods Administration (TGA);
- Administrative burden associated with the claiming and receipt of payment for EFC-listed medicines dispensed from a range of pharmacy settings; and
- The EFC's approach to ensuring all participants in the cancer medicines supply chain are reimbursed fairly and appropriately.

Prior to the Review, stakeholders to the EFC supply chain voiced concerns with the Department of Health regarding an ostensible disparity between the volume of drug sold by manufacturers and subsequently claimed by dispensing pharmacies/hospitals, and the implications therein for the manufacturers' commercial supply and reconciliation arrangements with Government. Accordingly, the remit of the Review extends to include consideration of whether the program's reimbursement framework and administrative arrangements can be adjusted to enhance stakeholder equity, patient access, innovation and collaboration across the cancer medicines supply chain.

The Department of Health named Professor Sanchia Aranda as Lead Reviewer and contracted the Centre for Health Economics Research and Evaluation (CHERE) to undertake an Economic Analysis of the EFC arrangements. This Final Report details the Review's overall aim, specific objectives, research questions, methodology, findings, discussion and recommendations.

For clarity, the Interim Report also details the correspondence between CHERE's research activities (as outlined in the Official Order/contract) and the Terms of Reference of the EFC Review (published 1 May 2021 by the Department of Health; see Appendix 1 and Appendix 2).

1.1 Overall aim of the Economic Analysis

The Economic Analysis examined the extent to which the EFC framework supports patient access to cancer medicines in an efficient and cost-effective manner, and whether changes to current arrangements are required to ensure continued and appropriate access to treatment, encourage innovation and facilitate collaboration in Australia's cancer medicines supply chain.

1.2 Objectives

The key Objectives of the Economic Analysis were to:

1. Identify the key activities (and distribution of costs and remuneration) that participants in the EFC supply chain undertake to support safe patient access to cancer medicines and related pharmaceutical benefits;

2. Assess whether current arrangements support patient access to cancer medicines in a safe and efficient manner;

3. Assess the potential impact of alternate models for the provision and remuneration of goods and services for the treatment of cancer (including the incorporation of new technologies and/or service delivery approaches) with respect to innovation, collaboration and patient access;

4. Assess the ways in which potential changes to EFC arrangements identified during the Review may affect access, safety and costs among EFC stakeholders relative to current arrangements.

1.3 Research Questions

The Economic Analysis was structured to address two overarching themes:

1. Appropriateness: Are the EFC funding arrangements still the right policy response?

2. Transition: What are the implications of changing the current EFC funding arrangements?

The specific research questions investigated under these themes of Appropriateness and Transition were as follows:

Appropriateness

1. What activities are undertaken by EFC supply chain participants?

2. What are the costs and remuneration arrangements associated with EFC supply chain activities?

Appropriateness

3. Are current arrangements appropriate for actual EFC supply chain activities and associated costs?

4. Do current EFC arrangements support patient access to chemotherapy medicines in a safe and efficient manner?

Transition

5. Are there alternative remuneration models, technologies or service delivery approaches that could drive innovation, collaboration or otherwise improve upon current EFC arrangements?

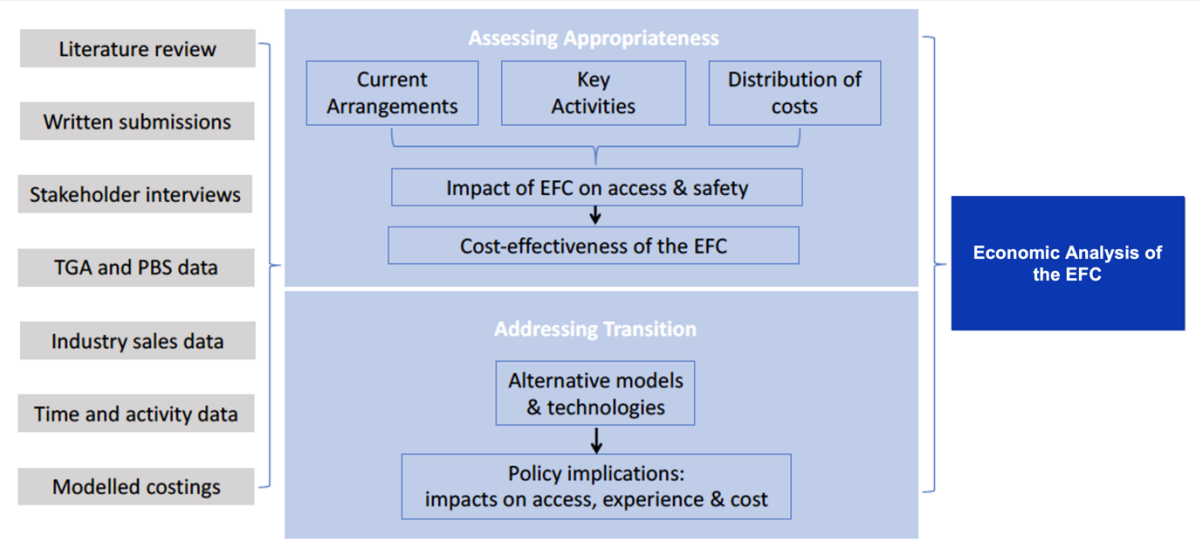
6. How could changes to EFC arrangements improve access, safety, efficiency and reduce cost burdens for key stakeholders compared to current arrangements?

Transition

2 Methods

An overview of the approach applied in the Economic Analysis is outlined in Figure 1.

Figure 1. Overview of the approach



Abbreviations: EFC, Efficient Funding of Chemotherapy; TGA, Therapeutic Goods Administration; PBS, Pharmaceutical Benefits Scheme.

Inputs to the Economic Analysis are shown in grey. Core components of the analysis and their correspondence are shown in the central element of the figure, with the (final) output on the right. The following subsections elaborate the ways in which the research questions have been informed by the various components of the approach.

2.1 Research questions and activities

2.1.1 What activities are undertaken by EFC supply chain participants?

Activity 1a. Peer-reviewed and grey literature concerning the manufacture, compounding, administration and remuneration of compounded chemotherapy medicines in Australia and comparable international contexts were reviewed. A narrative synthesis of that literature according to the key themes emerging from the stakeholder consultations is presented in Sections 4-6 of this Final Report. Details of the methods applied in the search for the literature and subsequent data extraction process are provided in Appendix 3.

Activity 1b. The Department of Health released Terms of Reference and a Discussion Paper inviting submissions by stakeholders to the EFC supply chain. A thematic analysis of these written

submissions was conducted to formulate an understanding of EFC supply chain activities, costs and remuneration, and stakeholders' concerns in these areas. This analysis, conducted in collaboration with the Department of Health and Lead Reviewer, also informed the development of interview protocols for the subsequent, in-depth consultation of identified stakeholders.

Activity 1c. Semi-structured interviews with stakeholders involved in the supply, delivery and administration of EFC-funded medicines, including manufacturers, wholesalers and compounders; State and Territory public health services; hospital pharmacists and administrators; health-sector peak bodies; health care professionals involved in cancer treatment and care; and patients were conducted. The list of individuals interviewed was developed in consultation with the Lead Reviewer and Department of Health, informed by stakeholders' previous participation in the development of the Review's Terms of Reference, as follow-up to written submissions received in the review's public consultation phase and on a 'snow-ball' basis following prior consultations. Details of consultations undertaken for the Review may be found in Appendix 4.

Interviews were guided by structured protocols, adapted for individual stakeholder engagements to reflect specific points of reference and relevant lines of inquiry, audio-recorded (with participant consent) and transcribed. Conduct of interviews and thematic analysis of findings was undertaken jointly by the Lead Reviewer and CHERE's nominated senior investigators. All findings were de-identified, noting only the sector from which respondents were sourced. Where there were fewer than three contributors within a given sector, responses were aggregated across multiple sectors to ensure that individual stakeholders cannot be identified. Data were analysed individually on an ongoing basis using an 'abductive' approach—i.e., the researchers examined the extent to which the data support the underlying rationale of the EFC framework, as well as how the data may call for modifications to these arrangements—until thematic saturation was reached.

Activity 1d. Throughout the interviewing period, CHERE's nominated senior investigators met with the Lead Reviewer to share findings, identify emergent themes in the research data, consolidate these themes within a cohesive analytical framework, discuss the policy implications of initial findings and coordinate subsequent coding and write-up. At the conclusion of the interviewing period, the research team coded all interview data in accordance with the identified themes and agreed analytical framework using Nvivo [3]. The research team collated all coded materials for final integration and reporting. The results of those consultations are reported throughout Sections 3-6 of this Final Report, based on a thematic presentation of the evidence.

2.1.2 *What costs and remuneration arrangements are associated with EFC supply chain activities?*

Activity 2a. The research team compared the registered and reimbursed indications of each of the infusible medicines supplied via the EFC to inform an understanding of EFC institutional arrangements, and the extent to which the empirical utilisation of listed medicines is consistent with the underlying intent of the EFC.

Activity 2b. Interviewees (see Activity 1c) described their roles and activities in the delivery of chemotherapy, and the costs and remuneration associated with those activities. These descriptions were used to further understand EFC institutional arrangements and to discern the practical correspondence between the EFC's intended and actualised outcomes.

Activity 2c. Under pre-EFC funding arrangements, cancer drugs were reimbursed on the basis of the full pack quantity, rather than the minimum combination of vials required to provide the prescribed dose. To assess the impact of shifting to remuneration on the basis of the efficient combination of vials, an historical analysis of aggregate PBS services volumes and benefit value was conducted. Results of this analysis are presented in Appendix 5.

Activity 2d. The costs and remuneration of EFC supply chain activities were enumerated and mapped through an analysis of: 1) drug manufacturers' sales data (purchased through third-party data supplier, IQVIA); and 2) PBS claims data (provided by the Department of Health). This component of the analysis considered the extent to which industry and PBS data correspond, whether differences are evident by jurisdiction or product, and the extent to which stakeholders' descriptions of their roles and activities are reflected in the available industry sales and PBS claims data.

The IQVIA sales data reflect the totality of sales for EFC-listed products and are therefore broader than the corresponding PBS remuneration data in many instances. However, reconciliation of these data is an important element of the Economic Analysis, particularly as it pertains to the capacity of program stakeholders to utilise disparate datasets to address supply, reimbursement and rebate issues throughout the supply chain.

IQVIA industry sales data were provided on a mg per-molecule basis, allowing a like-for-like comparison with PBS remuneration data. Industry sales data were aggregated at the level of State/Territory and do not include information at the levels of individual institution, professional or patient. All data have been fully de-identified by the research team.

Together, these data—i.e., a comparison of therapies' registered and reimbursed indications (see

Activity 2a), stakeholders' descriptions of their roles and activities (Activity 2b), historical utilisation data (Activity 2c), and manufacturers' sales data and PBS claims data (Activity 2d)—informed a detailed exposition of the EFC's institutional arrangements, the extent to which stakeholder activities correspond with the system's intended function, and implications for policy, including potential incentives for vial-sharing. Results from these activities are reported in Sections 3-6, with details of the underlying analyses of the PBS claims data and IQVIA sales data in Appendix 6 and Appendix 7, respectively.

2.1.3 Are current arrangements appropriate for EFC supply chain activities and costs?

Activity 3a. Information from interviews and informants' documentation of operational costs was used to assess the time-and-activity required for the provision of cancer medicines via the EFC supply chain. The resulting cost estimates were compared against EFC fee components to determine the appropriateness of current remuneration arrangements. The analysis also considered the extent to which EFC arrangements may contribute to patient costs. Results from these activities are reported in Sections 3-6.

2.1.4 Do current arrangements support safe and efficient patient access to medicines?

Activity 4a. PBS data on EFC drug utilisation were combined with data from the TGA Database of Adverse Event Notifications (DAEN) to assess the extent to which the incidence of safety events related to the administration of select EFC items reflects safe and efficient provision of cancer medicines. Results from this analysis are reported in Section 5, with details of the safety analysis provided in Appendix 8.

Activity 4b. CHERE also analysed stakeholders' written submissions and interview responses to assess the potential impact of EFC arrangements on patient access (e.g., via patient 'batching'). In addition, the research team engaged with a number of cancer patients to explore issues of access, cost and quality from the consumer perspective.

2.1.5 Are there alternative remuneration models, technologies or service delivery approaches that could drive innovation, collaboration or otherwise improve upon current EFC arrangements?

Activity 5a. The research team reviewed peer-reviewed and grey literature on the EFC and alternative reimbursement approaches in relevant international contexts (e.g., Canada, UK, NZ)—including reviews of chemotherapy funding arrangements preceding the EFC—to identify relevant potential alternatives to EFC arrangements (see Activity 1a). The analysis identified how chemotherapy drugs

are funded internationally and considered how elements from these models may be applied in Australia, including potential impacts on service delivery, access and cost-effectiveness. Results from this analysis are reported in Sections 6 and 7.

2.1.6 How might changes to EFC arrangements improve access, safety, efficiency and cost burdens for key stakeholders compared to current arrangements?

Activity 6a. CHERE conducted a desktop-modelled analysis to compare the impact on Government costs of alternative models for the efficient provision of chemotherapeutics against current EFC arrangements. This analysis follows the structure of a standard 'Section-4' workbook for three demonstration medicines: avelumab, bortezomib and cabazitaxel. Results from this analysis are reported in Section 6.3 with details provided in Appendix 9.

3 Provision of cancer medicines in Australia

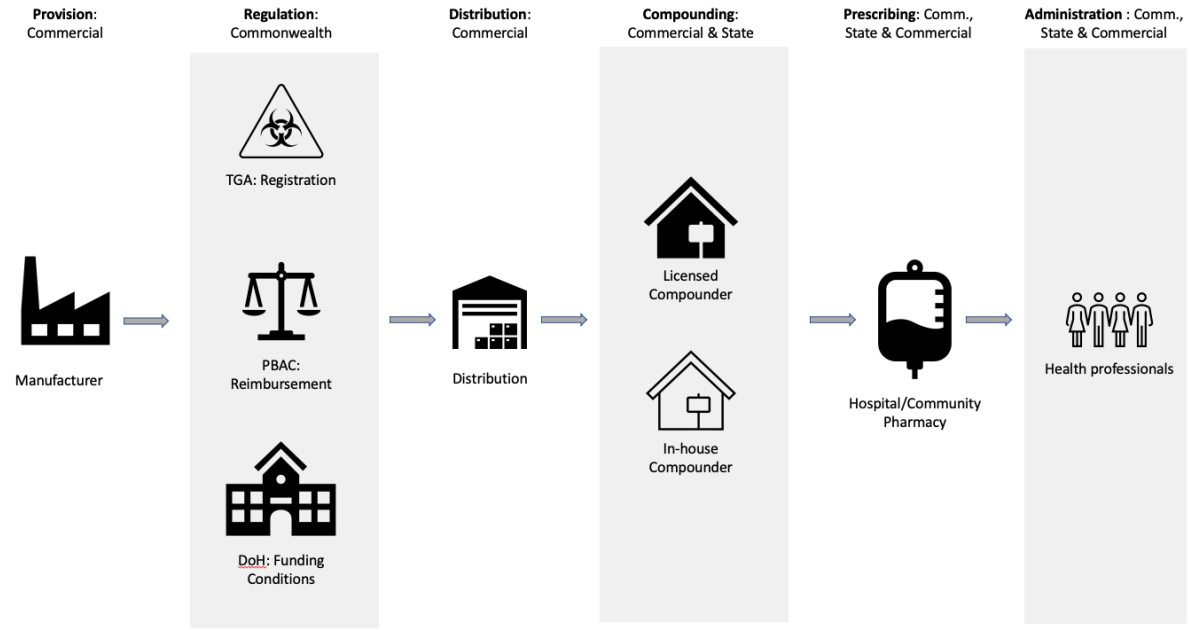
3.1 Background to the EFC

The PBS is a critical pillar of Medicare, subsidising the provision and supply of medicines to Australian patients in private community, public hospital outpatient and private hospital settings. Under the umbrella of Section 100 of the National Health Act 1953 (Cth), most infusible medicines for the treatment of cancer are subsidised under the National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011 [4]. Among its aims, the EFC seeks to enhance patient access to injectable and infusible cancer medicines at the lowest cost to Government.

To date, the term 'chemotherapy' has been used broadly to refer to the use of medicines in the treatment of cancer. More precisely, however, 'chemotherapy' refers to a class of typically cytotoxic medicines used to inhibit cancer cell reproduction. Modern cancer treatment has seen an increasing role for emergent biologics—including monoclonal antibodies, proteasome inhibitors and check-point inhibitors—that target specific cellular pathways. While cytotoxic chemotherapies continue to account for the majority of services via the EFC, they now comprise less than 10% of the overall benefits paid through this program (financial year 2020-21; see Appendix 6).

Establishment of the EFC recognised what were at the time considered unique challenges associated with the provision of cancer care, including a complex, inter-dependent network of stakeholders involved in the manufacture, supply, administration and remuneration of specialised medicines. As can be observed in Figure 2, the supply of cancer medicines via the EFC involves multiple participants—in various stages and settings—including: drug manufacturers; Government and its agencies (including, inter alia, the TGA, the Pharmaceutical Benefits Advisory Committee (PBAC) and the Department of Health), who regulate and manage the reimbursement of medicines via the PBS; commercial wholesalers and distributors; State and Territory and private compounders who prepare medicines for dispensing; and State and Territory and private hospitals and pharmacy providers who prescribe, dispense and administer medicines to patients. Facilitating equitable and efficient interaction among these participants, to enable equitable access to medicines for patients, is a key consideration of the EFC arrangements.

Figure 2. Participants to the EFC supply chain



Abbreviations: DoH, Department of Health; EFC, Efficient Funding of Chemotherapy; PBAC, Pharmaceutical Benefits Advisory Committee; TGA, Therapeutic Goods Administration.

As with all reimbursement under the PBS, the EFC provides compensation for drug preparation. Yet, for EFC medicines—cytotoxic chemotherapies, in particular—that preparation is complex and may involve risks to operators that are not present with other medicines. The administration of EFC medicines also bears risks to patients (e.g., extravasation, complications associated with flow rate errors) and is therefore considered a specialised medical service. While the increased utilisation of biologics has mitigated some of these risks, particularly with regards to preparation, all EFC medicines maintain strict preparation and administration requirements to ensure product safety and sterility.

A core differentiator of EFC medicines relative to many other medicines supplied via the PBS is the role of compounding in drug preparation. By and large, EFC medicines are not supplied by manufacturers in a form that is ready for administration to patients but require compounding into an infusible form and device. For cancer medicines, each infusion is made either to a specific dose, which varies by patient size (i.e., weight or body surface area, BSA), or a flat dose (i.e., independent of patient size) by indication. Drug is provided for compounding by manufacturers in vials whose sizes—beyond a limited number of flat-dosed products—do not correspond directly with the prescribed dosage. Thus, in most cases, the compounding of cancer medicines involves some level of wastage—i.e., a quantum of drug that is supplied but not used in the compounding of the prescribed dosage. Depending on the shelf-life of the medicine and other concurrent prescriptions to be compounded,

wastage may be combined across vials to produce additional infusions. In principle, the utilisation of wastage represents an efficient use of drug as it reduces the volume of unused product that would otherwise be discarded.

The EFC reimburses cancer medicines on the basis of the cheapest possible combination of vials required to produce a given dosage, thereby minimising the cost of each infusion to taxpayers and contributing to the sustainability of cancer treatment in Australia. At its inception, there were 37 molecules funded via the EFC. There are currently 54 infusible cancer medicines funded through Schedule 1, in addition to 13 'related benefit' items via Schedule 2 of the EFC (see Table 1). This includes 19 biologics via Schedule 1 and four via Schedule 2.

Table 1. EFC molecules by schedule

Schedule 1		
Arsenic	Atezolizumab†	Avelumab†
Bendamustine	Bevacizumab†	Bleomycin
Blinatumomab†	Bortezomib†	Brentuximab vedotin
Cabazitaxel	Carboplatin	Carfilzomib†
Cetuximab†	Cisplatin	Cladribine
Cyclophosphamide	Cytarabine	Daratumumab†
Docetaxel	Doxorubicin	Doxorubicin hydrochloride (pegylated)
Durvalumab†	Epirubicin	Eribulin
Etoposide	Fludarabine	Fluorouracil
Fotemustine	Gemcitabine	Idarubicin
Ifosfamide	Inotuzumab ozogamicin†	Ipilimumab†
Irinotecan	Methotrexate	Mitozantrone
Nanoparticle Albumin-Bound Paclitaxel	Nivolumab†	Obinutuzumab†
Oxaliplatin	Paclitaxel	Panitumumab†
Pembrolizumab†	Pemetrexed	Pertuzumab†
Pralatrexate	Raltitrexed	Rituximab†
Topotecan	Trastuzumab†	Trastuzumab Emtansine†
Vinblastine	Vincristine	Vinorelbine

Schedule 2 'Related Benefits'		
Aprepitant	Folinic Acid	Fosaprepitant
Granisetron	Interferon Alfa-2a†	Mesna
Mycobacterium Bovis (BCG)†	Netupitant + Palonosetron	Ondansetron
Palonosetron	Rituximab†	Trastuzumab†
Tropisetron		

Note: †Denotes biologic (including monoclonal antibodies, proteasome inhibitors and/or check-point inhibitors)

Proportionally, EFC spending has doubled in the seven years since the previous review in 2013 [5]. In the 2019-20 financial year, total Government benefits paid for EFC items totalled just over $1.65 billion, or approximately 13% of total PBS spend ($12.6 billion), of which just over $6 million was for EFC Schedule 2 medicines. In comparison, EFC spend in 2012-13 was $570 million, comprising 6.3%

of total PBS spending ($9.0 billion) [6].

3.1.1 Chemotherapy Product Access Program

Prior to commencement of the EFC in 2011, extant drugs subsequently listed on the EFC were supplied on the PBS via the Chemotherapy Product Access Program (CPAP) for public hospitals, with parallel listings under s100 and the General Benefits section of the PBS for private hospital access. Under pre-EFC funding arrangements, drugs were reimbursed on the basis of the full-pack quantity, rather than the minimum combination of vials required to provide a prescribed dose. To assess the impact of shifting to remuneration on the basis of the efficient combination of vials, an historical analysis of aggregate PBS services volumes and benefit value was conducted.

The molecules used as the basis for this comparison and their corresponding PBS indications are listed in Table 2. Molecules were included if previously funded via the CPAP, with at least two years of PBS service and benefit value data prior to the commencement of the EFC. To mitigate likely confounding, the molecules rituximab, trastuzumab, doxorubicin and methotrexate were excluded, as these drugs have PBS-approved intravenous (IV) formulations for non-EFC indications. All non-IV formulations (i.e., tablets) were excluded from the analysis. Full details of the analysis are provided in Appendix 5.

Table 2. Select CPAP-listed drugs by PBS indication

Molecule	*PBS indication (IV formulations only)*
Bleomycin	Germ cell neoplasm
Bortezomib	Multiple myeloma
Carboplatin	NR
Cetuximab	Stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx
Cisplatin	NR
Cladribine	Hairy cell leukaemia
Cyclophosphamide	NR
Cytarabine	NR
Docetaxel	NR
Epirubicin	NR
Etoposide	NR
Fludarabine	NR
Fluorouracil	NR
Fotemustine	Metastatic malignant melanoma
Gemcitabine	NR
Idarubicin	Acute myelogenous leukaemia
Ifosfamide	NR
Irinotecan	NR
Oxaliplatin	NR
Paclitaxel	NR
Raltitrexed	Advanced colorectal cancer
Topotecan	NR
Vinblastine	NR

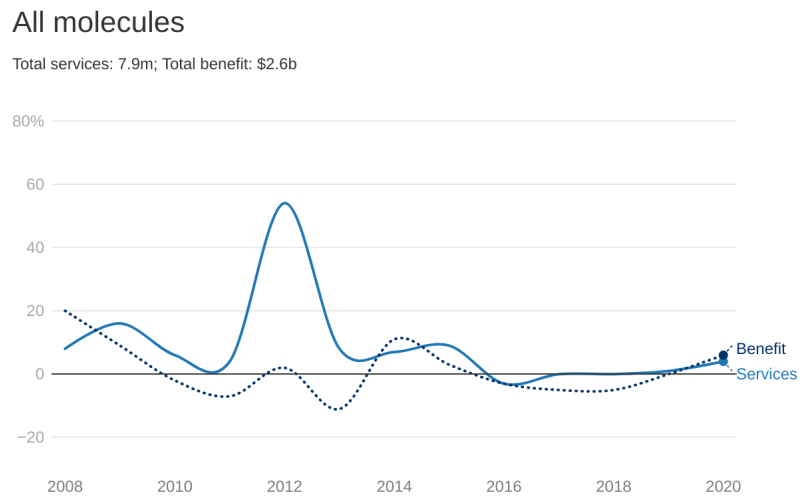
Vincristine	NR
Vinorelbine	NR

Abbreviation: IV, intravenous; NR, not restricted.

Each drug's corresponding PBS item codes active under the CPAP and EFC periods were used to derive historical PBS service volumes and benefit values for the periods immediately before (2008-2011) and after the introduction of the EFC (2012-2020) [7]. For each molecule, the year-on-year growth rate (i.e., percent change) in PBS service volume and benefit value was calculated and plotted to assess whether the introduction of the EFC corresponded with an apparent change in utilisation.

Across all molecules analysed, aggregated annual service volumes increased 54% in the year following the introduction of the EFC (i.e., in the calendar year ending December 2012) (see Figure 3). In the same period, aggregated benefit values increased by only 2%, representing greater overall service provision at reduced per-unit cost to government over the previous year (i.e., percent growth in service volume was greater than percent growth in benefit value in 2012).

Figure 3. Annual % change, services and benefit value, select CPAP-listed molecules (2008-2020)

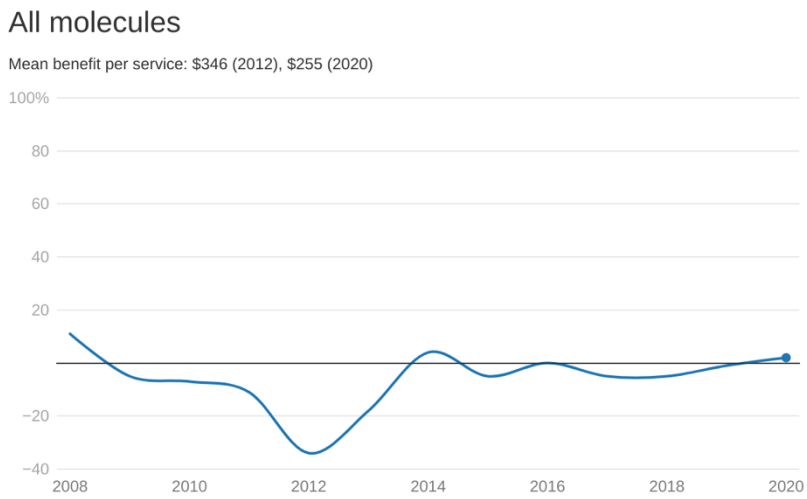


Abbreviations: CPAP, Chemotherapy Product Access Program.
Note: Solid line=Services, Dotted line=Benefit
Source: Produced for this Review using aggregate PBS data.

For the majority of molecules (88%), introduction of the EFC coincided with a year-on-year increase in PBS service volume in the year ending December 2012, with only docetaxel, fotemustine and raltitrexed experiencing a decline in the number of services relative to 2011 (-12%, -14% and -16%, respectively). Across all drugs previously funded under CPAP arrangements, mean benefit value-per-service fell 34% in the year immediately following the introduction of the EFC (see Figure 4). Over

the full period of this analysis, the mean overall cost-per-service to Government for EFC drugs previously funded under CPAP arrangements fell 62%, from $666 (2008) to $255 (2020).

Figure 4. Annual % change, mean benefit per service, select CPAP-listed molecules (2008-2020)



Abbreviations: CPAP, Chemotherapy Product Access Program; PBS, Pharmaceutical Benefits Scheme.
Source: Produced for the Review using aggregate PBS data.

Overall, transition to the EFC was associated with an increase in PBS service volumes and benefit values for drugs previously available under the CPAP. While the analysis undertaken here has not determined this relationship to be causal—both service volumes and benefit values are a function of multiple inter-related factors, including underlying clinical demand and relative prices—evidence suggests that reimbursement of infusible cancer medicines based on the efficient combination of vials has generally promoted access to these drugs at a reduced per-unit cost to Government relative to previous arrangements under the CPAP.

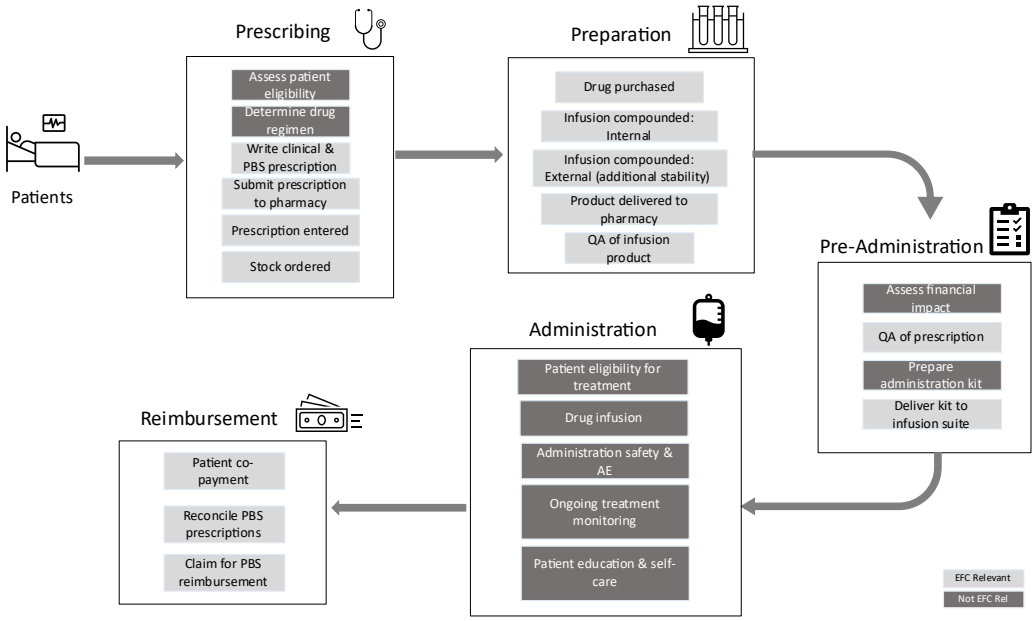
3.2 The EFC supply chain

3.2.1 Flow of activities

The provision of cancer medicines via the EFC is multi-faceted, comprising a number of core activities, as depicted in Figure 5. For the purpose of this exposition, the supply of cancer medicines begins with the relevant prescription (Prescribing). That prescription must be clinically appropriate (as per TGA registration) and satisfy requirements for EFC reimbursement (as per PBS indication). Once prescribed, cancer medicines for parenteral administration must be prepared for infusion/injection into patients. The relevant pharmaceutical preparation is purchased from the manufacturer to be compounded (combined) into the required dose and form for patient administration (Preparation).

Once prepared, medicines undergo stringent quality assurance processes to ensure product safety and compliance with the originating prescription (Pre-Administration). Immediately prior to administration, the patient's eligibility must be confirmed (particularly with respect to safety). Upon administration, patients are monitored for adverse effects and clinical outcomes, and informed of post-care expectations (Administration). Finally, financial reconciliations occur between multiple system stakeholders, including the payment of patient co-payments (where applicable), and the submission of claims to Services Australia for reimbursement of PBS benefits on EFC-listed medicines (Reimbursement).

Figure 5. Flow of activities



Abbreviations: AE, adverse event; PBS, Pharmaceutical Benefits Scheme; QA, quality assurance.

The specific activities underpinning the supply of cancer medicines are elaborated in Table 3, including a brief description of each activity, relevant actors (by occupational role, patient or institutional type), funding source(s), and whether support for the activity falls with the remit of the EFC legislation. Activities considered within-scope of the EFC Review relate to the purchase, compounding and supply of cancer medicines up to the point of administration to patients. Other activities may indeed be relevant to the supply of cancer medicines but were considered beyond the remit of the EFC legislative instrument.

Table 3. Activities in the provision of cancer medicines

Activity	*Actors*	*Funding Pool*	*Within scope of EFC*

Activity	*Actors*	*Funding Pool*	*Within scope of EFC*
	Prescribing		
Assess patient eligibility			
Patient's clinical, medication and family history assessed to design a pharmacotherapeutic plan	Medical oncology Pharmacy Nursing Patient	MBS Hospital Pharmacy	No
Pre-treatment chart revision: body surface area, dosages, pre-treatment and take-home medications checked	Pharmacy	Hospital Pharmacy	No
Patient vitals and blood-levels checked	Medical oncology Nursing	MBS Hospital	No
Determine drug regimen			
Determine relevant drug (regimen) and dose	Medical oncology Pharmacy Nursing Patient	MBS (for specialty consultation) Hospital Funding	No
Prescribing			
Prescription for infusion/injection written on a PBS prescription form/chemotherapy chart.	Medical oncology	MBS Hospital	Yes
All treatment orders documented on the patient's hospital medication chart	Medical oncology	MBS Hospital	Yes
Prescription and/or copy of treatment orders submitted to pharmacy	Medical oncology Pharmacy	MBS Hospital	No
Patient and prescription details entered into dispensing system; software returns the vial combination to be dispensed Patient eligibility and claim details confirmed via PBS Online.	Pharmacy	PBS	Yes
Ordering			
Pharmacist orders required medications	Pharmacy	PBS	Yes
	Preparation/Supply		
Purchasing			
Pharmaceutical product (uncompounded) purchased by compounder (internal or third-party)	Compounding pharmacy Manufacturer Logistics	PBS	Yes
Compounding			
Infusion compounded (includes delivery container) per named patient under conditions that ensure sterility and stability (with indicated expiry)	Compounding pharmacy	PBS Compounders Hospital	Yes
Internal—Product delivered to infusion suite is labelled with patient name and 24-hour expiry	Hospital Pharmacy	Hospital Pharmacy	Yes
External—Product delivered to infusion suite is labelled with patient name and (extended) expiry consistent with relevant stability data	Independent compounder Logistics	Hospital Pharmacy	Yes
Quality assurance—compounding			
Compounded products checked upon for dose, container, compatibility, expiry and safety	Pharmacy	Hospital Pharmacy	Yes
	Pre-Administration		
Financial assessment			
Financial impact of the selected treatment assessed for hospital/clinic, pharmacy and patient	Pharmacy	Hospital Pharmacy	No
Patient eligibility			

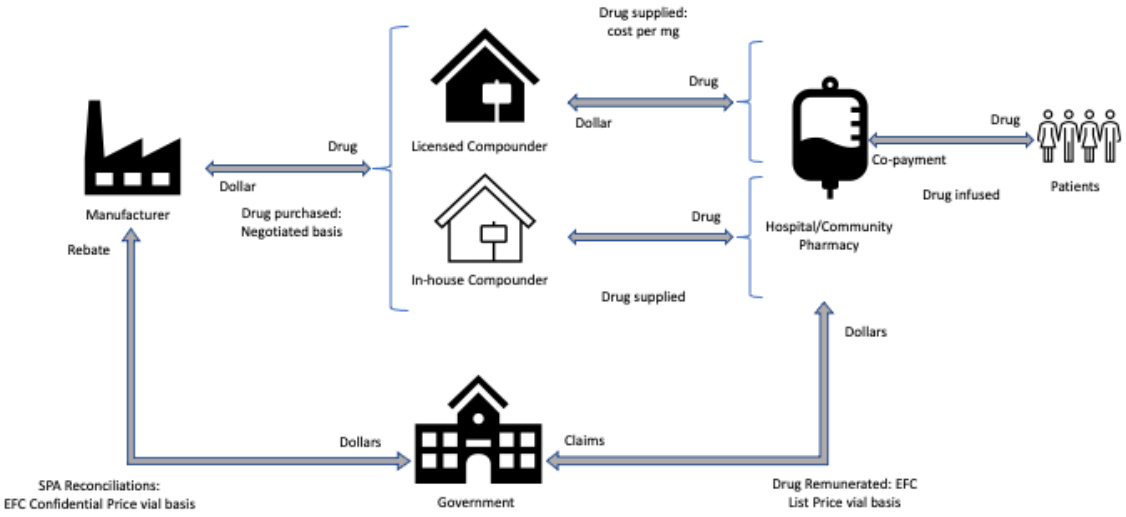
Activity	*Actors*	*Funding Pool*	*Within scope of EFC*
Determine whether additional pathology tests are required prior to the patient commencing treatment	Pharmacy Medical oncology	Hospital Pharmacy	No
Quality assurance—prescription			
Dispensing checked (labelling, medication selection, PBS claim status)	Pharmacy	Hospital Pharmacy	Yes
Kit preparation			
Individualised patient medication kits packed (include treatment, pre-med and supportive medications)	Pharmacy	Hospital Pharmacy	No
Delivery			
Infusion delivered to delivery centre/suite	Pharmacy Logistics	Hospital Pharmacy	Yes
Administration			
Patient eligibility			
Patient vitals and blood-levels checked (this step determines if the remainder of nominated activities occur	Nursing Medical oncology Pharmacy	MBS Hospital	No
Infusion			
Drug administered to patient	Nursing Pharmacists	MBS Hospital	No
Safety and ongoing monitoring			
Holistic assessment of patients' wellbeing and any non-chemotherapy related adverse effects that may require referral	Nursing Pharmacy	MBS Hospital	No
Monitor adherence with medications, diet, sleep, nausea, constipation, lifestyle and medication interactions; respond to medication information requests; liaise with nursing staff about medication issues; liaise with family members	Nursing Pharmacy Medical oncology	MBS Hospital	No
Patient education on ongoing treatment requirements, side effects and self-care	Nursing Pharmacy	MBS Hospital	No
Reimbursement			
Co-payment			
Patient contribution paid (where applicable)	Patient	Out-of-pocket NSW Health	Yes
Reconciliation			
Follow up with prescriber for prescription validation if necessary (may be delays)	Pharmacy	Hospital Pharmacy	Yes
PBS Claiming			
Claim submitted via PBS Online; all prescriptions submitted to Medicare in support of claim	Pharmacist Hospital	PBS	Yes

Abbreviations: EFC, Efficient Funding of Chemotherapy; MBS, Medicare Benefits Schedule; NSW, New South Wales; PBS, Pharmaceutical Benefits Scheme.

3.2.2 Flow of funds

The flow of funds as it relates to the purchase and reimbursement of cancer medicines via the EFC is provided in Figure 6.

Figure 6. Flow of funds



Abbreviations: EFC, Efficient Funding of Chemotherapy; SPA, special pricing arrangement.

Broadly, the stakeholders involved and their roles in the EFC supply chain are summarised as follows:

- Cancer therapeutics manufacturers: Register drugs for sale in Australia and seek listing of those drugs for subsidy on the EFC via the PBS. Any drug can be sold in Australia once registered with the TGA (regardless of PBS listing), but subsequent claims for reimbursement via the EFC require prescription for a valid PBS indication. Drugs are made available for sale to compounders/wholesalers (the latter not shown on the schematic due to limited engagement with EFC).
- TGA-licensed compounders: Purchase product from manufacturers. Drugs are compounded to meet external orders from third-party dispensing pharmacies/hospitals; compounded product is supplied in ready-to-infuse form.
- In-house compounders: Purchase drug from manufacturers (either directly or via jurisdictional purchasing mechanisms) to meet in-house orders (prescriptions) for compounded products.
- Hospital/community pharmacy: Receive compounded products in ready-to-infuse form for administration to patients.
- Patients: Receive infusions from hospitals/treatment centres and make co-payments on drugs as required by relevant jurisdictional arrangements.
- Government: Responsible for the listing of reimbursed products, regulation of the supply chain, reimbursement of claims and reconciliation of rebate agreements with manufacturers.

Understanding the interactions of these stakeholders requires some exposition of the flow of funds throughout the EFC supply chain, namely:

- Compounders pay manufacturers for the acquisition of drug. It is understood that drug is sold by manufacturers according to the dispensed price per maximum amount (DPMA) as listed on the PBS. However, those purchases are not defined by PBS use insofar as compounders purchase drug without specifying how it is to be on-sold for administration to patients; the quantum of PBS and non-PBS supply cannot currently be discerned (for an analysis of manufacturers' sales and PBS reimbursement data, see Section 4.3).
- Pharmacists/hospitals pay compounders for drug that has been compounded for infusion. Consultations indicated that the sale of drugs from compounders to hospitals/pharmacists occurs without direct regard to the PBS fees/prices associated with those drugs and is enacted on a price-per-mg basis (rather than the DPMA basis on which the drugs are listed on the PBS). A comparison of EFC drugs' average prices per mg—as observed from industry sales data and corresponding PBS list prices—shows that PBS prices are generally higher than ex-manufacturer prices on a per-mg basis (see Section 4.3).
- Pharmacists/hospitals submit claims to Services Australia for reimbursement of the PBS list price for each infusion administered. Claims are lodged per-patient based on the most efficient combination of vials required to deliver the prescribed dose. Approved claims are paid by Government to the pharmacist/hospital.
- Patients contribute a co-payment for each initial prescription of an EFC-subsidised drug; there are no co-payments levied on repeat prescriptions. Within NSW, co-payments for public patients are met by NSW Health.
- Government collects rebates from manufacturers to reconcile differences between an EFC product's publicly visible list price and any special pricing arrangements in place. Rebate arrangements are applied on the basis of the quantum of vials for which reimbursement claims were approved, where the number of vials is calculated according to the most efficient combination of vials required on a per-dosage basis.

The flow of funds highlights that while, subsequent to recommendations of the PBAC, Government is responsible for negotiating the initial list price of EFC-listed drugs, it is not directly involved in the purchase of drug from manufacturers (noting that purchasing undertaken independently by hospital providers may be subsidised by Government). Rather, drug purchasing is enacted via two key intermediaries—compounders and hospitals/pharmacists. At a minimum, the supply and reimbursement of drugs via the EFC necessitates transactions between four stakeholders

(manufacturers, hospitals, patients and Government), but in the majority of cases, five stakeholders are involved in that process (manufacturers, compounders, hospitals, patients and Government).

The most efficient combination of vials minimises wastage and cost

Under current arrangements, the particular combination of vials used to constitute a prescribed dose would impact the cost to Government if the price per mg differed across a given molecule's various formulations. As observed in Table 4, with the exception of atezolizumab and ipilimumab, a given molecule's mean dispensed price per mg does not differ between its formulations. Thus (for all but atezolizumab and ipilimumab), the principle of the most efficient combination of vial sizes reflects the combination that minimises the excess quantum of drug in a vial not required in the constitution of a given prescribed dose. This is because the difference in the quantity wasted—rather than the price per mg—drives the efficiency of using particular formulations as the basis for determining the most efficient combination of vials.

Table 4. Weighted mean price per mg by molecule and formulation

Drug	*Formulation*	*Number of presentations*	*Weighted mean price per mg*
Arsenic	Injection concentrate containing arsenic trioxide 10 mg in 10 mL	8	$33.14
Atezolizumab	Solution concentrate for I.V. infusion 1200 mg in 20 mL	18	$6.05
	Solution concentrate for I.V. infusion 840 mg in 14 mL	12	$6.02
Avelumab	Solution concentrate for I.V. infusion 200 mg in 10 mL	4	$6.92
Bendamustine	Powder for injection containing bendamustine hydrochloride 100 mg	2	$8.66
	Powder for injection containing bendamustine hydrochloride 25 mg	2	
Bevacizumab	Solution for I.V. infusion 100 mg in 4 mL	18	$3.14
	Solution for I.V. infusion 400 mg in 16 mL	18	
Bleomycin	Powder for injection containing bleomycin sulfate 15,000 I.U.	4	$0.01
	Powder for injection containing bleomycin sulfate 15,000 I.U. in 1 vial	2	
Blinatumomab	Powder for I.V. infusion 38.5 micrograms	10	$105.96
Bortezomib	Powder for injection 1 mg	6	$0.46
	Powder for injection 3 mg	14	
	Powder for injection 3.5 mg	8	
Brentuximab vedotin	Powder for I.V. infusion 50 mg	16	$96.90
Cabazitaxel	Concentrated injection 60 mg (as acetone solvate) in 1.5 mL, with diluent	2	$54.11
Carboplatin	Solution for I.V. injection 150 mg in 15 mL	2	$0.20
	Solution for I.V. injection 450 mg in 45 mL	4	
Carfilzomib	Powder for injection 10 mg	2	$22.18
	Powder for injection 30 mg	2	
	Powder for injection 60 mg	2	
Cetuximab	Solution for I.V. infusion 100 mg in 20 mL	10	$3.29
	Solution for I.V. infusion 500 mg in 100 mL	10	
Cisplatin	I.V. injection 100 mg in 100 mL	2	$0.71

Drug	*Formulation*	*Number of presentations*	*Weighted mean price per mg*
	I.V. injection 50 mg in 50 mL	2	
Cladribine	Injection 10 mg in 5 mL	2	$67.87
	Solution for I.V. infusion 10 mg in 10 mL single use vial	2	
Cyclophosphamide	Powder for injection 1 g (anhydrous)	2	$0.06
	Powder for injection 2 g (anhydrous)	2	
	Powder for injection 500 mg (anhydrous)	2	
Cytarabine	Injection 100 mg in 5 mL vial	2	$0.13
Docetaxel	Solution concentrate for I.V. infusion 160 mg in 16 mL	2	$0.81
	Solution concentrate for I.V. infusion 160 mg in 8 mL	2	
	Solution concentrate for I.V. infusion 80 mg in 4 mL	2	
	Solution concentrate for I.V. infusion 80 mg in 8 mL	2	
Doxorubicin	Solution for I.V. injection or intravesical administration containing doxorubicin hydrochloride 200 mg in 100 mL single dose vial	4	$1.17
	Solution for I.V. injection or intravesical administration containing doxorubicin hydrochloride 50 mg in 25 mL single dose vial	2	
Doxorubicin p.l.	Suspension for I.V. infusion containing pegylated liposomal doxorubicin hydrochloride 20 mg in 10 mL	4	$11.78
	Suspension for I.V. infusion containing pegylated liposomal doxorubicin hydrochloride 50 mg in 25 mL	4	
Durvalumab	Solution concentrate for I.V. infusion 120 mg in 2.4 mL	2	$8.09
	Solution concentrate for I.V. infusion 500 mg in 10 mL	2	
Epirubicin	Solution for injection containing epirubicin hydrochloride 100 mg in 50 mL	2	$0.85
	Solution for injection containing epirubicin hydrochloride 200 mg in 100 mL	6	
	Solution for injection containing epirubicin hydrochloride 50 mg in 25 mL	4	
Eribulin	Solution for I.V. injection containing eribulin mesilate 1 mg in 2 mL	4	$264.96
Etoposide	Powder for I.V. infusion 1 g (as phosphate)	2	$0.68
Etoposide	Solution for I.V. infusion 100 mg in 5 mL	4	
Fludarabine	Powder for I.V. injection containing fludarabine phosphate 50 mg	4	$3.10
	Solution for I.V. injection 50 mg fludarabine phosphate in 2 mL	2	
Fluorouracil	Injection 1000 mg in 20 mL	8	$0.07
	Injection 2500 mg in 50 mL	8	
	Injection 500 mg in 10 mL	8	
	Injection 5000 mg in 100 mL	8	
Fotemustine	Powder for injection 208 mg with solvent	2	$8.55
Gemcitabine	Solution for injection 1 g (as hydrochloride) in 26.3 mL	2	$0.06
	Solution for injection 2 g (as hydrochloride) in 52.6 mL	2	
Idarubicin	Solution for I.V. injection containing idarubicin hydrochloride 10 mg in 10 mL	2	$7.97
	Solution for I.V. injection containing idarubicin hydrochloride 5 mg in 5 mL	2	
Ifosfamide	Powder for I.V. injection 1 g	2	$0.08
	Powder for I.V. injection 2 g	2	
Inotuzumab ozogamicin	Powder for I.V. infusion 1 mg	4	$14.86
Ipilimumab	Injection concentrate for I.V. infusion 200 mg in 40 mL	2	$126.19
	Injection concentrate for I.V. infusion 50 mg in 10 mL	4	$134.3
Irinotecan	I.V. injection containing irinotecan hydrochloride	10	$0.21

Drug	*Formulation*	*Number of presentations*	*Weighted mean price per mg*
	trihydrate 100 mg in 5 mL		
	I.V. injection containing irinotecan hydrochloride trihydrate 40 mg in 2 mL	4	
	I.V. injection containing irinotecan hydrochloride trihydrate 500 mg in 25 mL	2	
Methotrexate	Injection 5 mg in 2 mL vial	4	$0.29
	Injection 50 mg in 2 mL vial	8	
	Solution concentrate for I.V. infusion 1000 mg in 10 mL vial	16	
	Solution concentrate for I.V. infusion 500 mg in 20 mL vial	4	
	Solution concentrate for I.V. infusion 5000 mg in 50 mL vial	4	
Mitozantrone	Injection 20 mg (as hydrochloride) in 10 mL	4	$6.64
	Injection 25 mg (as hydrochloride) in 12.5 mL	2	
Nivolumab	Injection concentrate for I.V. infusion 100 mg in 10 mL	24	$21.20
	Injection concentrate for I.V. infusion 40 mg in 4 mL	24	
Obinutuzumab	Solution for I.V. infusion 1000 mg in 40 mL	12	$5.44
Oxaliplatin	Solution concentrate for I.V. infusion 100 mg in 20 mL	6	$0.55
	Solution concentrate for I.V. infusion 200 mg in 40 mL	2	
Paclitaxel	Solution concentrate for I.V. infusion 100 mg in 16.7 mL	4	$0.40
	Solution concentrate for I.V. infusion 150 mg in 25 mL	4	
	Solution concentrate for I.V. infusion 30 mg in 5 mL	4	
	Solution concentrate for I.V. infusion 300 mg in 50 mL	10	
Paclitaxel, n.a.b.	Powder for I.V. injection containing 100 mg paclitaxel, nanoparticle albumin-bound	4	$3.96
Panitumumab	Solution concentrate for I.V. infusion 100 mg in 5 mL	4	$5.45
	Solution concentrate for I.V. infusion 400 mg in 20 mL	4	
Pembrolizumab	Solution concentrate for I.V. infusion 100 mg in 4 mL	22	$40.97
Pemetrexed	Powder for I.V. infusion 1 g (as disodium)	4	$0.19
Pemetrexed	Powder for I.V. infusion 100 mg (as disodium)	10	
	Powder for I.V. infusion 500 mg (as disodium)	12	
Pertuzumab	Solution for I.V. infusion 420 mg in 14 mL	4	$7.56
Pralatrexate	Solution for I.V. infusion 20 mg in 1 mL	4	$56.21
Raltitrexed	Powder for I.V. infusion 2 mg in single use vial	2	$165.18
Rituximab	Solution for I.V. infusion 100 mg in 10 mL	30	$2.09
	Solution for I.V. infusion 500 mg in 50 mL	30	
Topotecan	Powder for I.V. infusion 4 mg (as hydrochloride)	2	$0.04
Topotecan	Solution concentrate for I.V. infusion 4 mg in 4 mL (as hydrochloride)	2	
Trastuzumab	Powder for I.V. infusion 150 mg	96	$3.37
	Powder for I.V. infusion 420 mg	16	
	Powder for I.V. infusion 60 mg	32	
Trastuzumab emtansine	Powder for I.V. infusion 100 mg	4	$17.15
	Powder for I.V. infusion 160 mg	4	
Vinblastine	Solution for I.V. injection containing vinblastine sulfate 10 mg in 10 mL	2	$9.00
Vincristine	I.V. injection containing vincristine sulfate 1 mg in 1 mL	2	$62.03
Vinorelbine	Solution for I.V. infusion 10 mg (as tartrate) in 1 mL	4	$2.54
	Solution for I.V. infusion 50 mg (as tartrate) in 5 mL	4	

Abbreviation: I.V., intravenous.

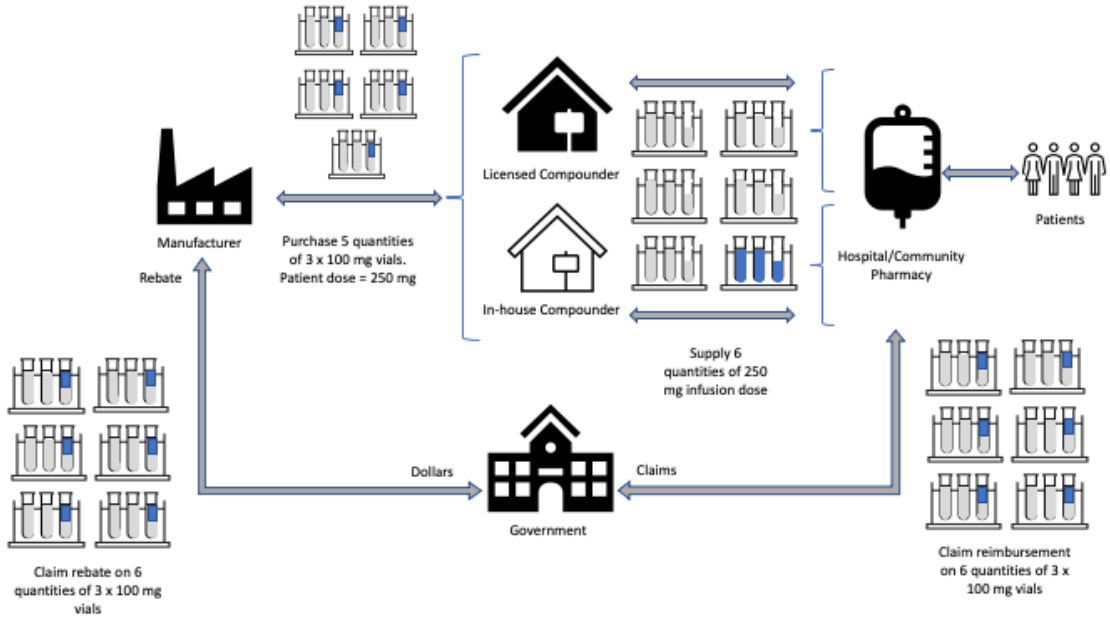
Vial optimisation

Currently, the prices at which drugs are purchased at the various stages of the EFC supply chain are not directly visible to stakeholders (but may be inferred from industry sales data; see Section 4.3). This lack of visibility may facilitate the ability of larger purchasers to benefit from scale by increasing the margin between the price at which a drug is purchased from manufacturers and subsequently reimbursed by the PBS. It is believed that the recently announced Strategic Agreement between the Commonwealth and Medicines Australia (2022-2027) contains a provision for the prices of drugs purchased at the hospital-level to be made available for calculations of price adjustments in accordance with PBS price disclosure requirements; this provision is likely to reduce the discounting of drug prices at the hospital level, as discounts would likely flow on to PBS-subsidised prices [8].

A key implication of the disconnect between the purchase, on-selling and reimbursement of EFC-listed drugs is that stakeholders within the system have the capacity to vary the basis upon which drug is transacted (i.e., compounders and hospitals/pharmacists may transact on a per-mg basis, rather than on the basis of the most efficient combination of vials). This disjunction allows for the practice of vial-optimisation or vial-sharing, in which compounders utilise the contents of supplied vials to provide as many compounded infusions as possible.

The practice of vial optimisation is illustrated in Figure 7. In this hypothetical scenario, a compounder purchases five quantities of a product dosed at 250 mg per patient. Each dose is supplied in three vials of 100 mg, so that each prescription is associated with an excess (i.e., 'wastage') of 50 mg. By aggregating the wastage across five patients (five x 50 mg), the compounder may produce an additional 250 mg dose to be sold to the hospital/community pharmacy for administration to a sixth patient. When lodging PBS claims for reimbursement, the hospital/pharmacy submits a claim for each of the six patients. Under EFC pricing rules, claimants are reimbursed for three x 100 mg vials per patient (despite each patient only having received 250 mg), which represents the efficient combination of vials required to deliver the prescribed doses.

Figure 7. Vial optimisation



For ease of exposition, Figure 7 depicts a situation in which the full volume of drug contained within each vial is extracted for the purposes of patient administration. In reality, the extent to which the full contents of a vial may be extracted depends upon the drug being compounded (e.g., its viscosity), vial type and skill of the compounding operator. Within-vial residuals are therefore variable and influence the volume of 'overage' (i.e., the quantity of drug remaining in the vial once the required dose is extracted) that may be utilised for additional patients. In the example above, even a one mg residual in each vial would necessitate a sixth initial prescription to accumulate sufficient overage for an additional 250 mg dose.

The extent to which stakeholders may engage in vial optimisation is impacted by the interplay between:

- The shelf-life of the uncompounded product once a vial has been opened—Products with a shorter shelf-life are less amenable to combination across preparations if there is any time lag between the initial preparation and subsequent utilisation of overage.
- Throughput—For a given shelf-life, vials of drug with lower throughput have less potential to be combined across infusions.
- Inventory management infrastructure—For drug overage to be utilised, excess volumes must be immediately and accurately identified, and (re)introduced to the compounding process without compromising the product's safety or stability.

In theory, the practice of vial optimisation should result in the efficient use of drug, as it minimises

waste due to the discarding of overage. However, because of the disconnect between the sale of drug (by manufacturers) and the reimbursement of drug (by Government), such efficiencies may not be realised for the payer. That is, the PBS list price of an EFC-listed drug is based on the most efficient combination of vials required to supply the prescribed dose on a per-patient basis. These price calculations therefore already incorporate a payment for overage associated with every infusion supplied. Thus, in the example above, PBS reimbursement of each 250 mg infusion would cover three x 100 mg vials—the efficient combination of the available vials needed to produce a 250 mg dose—inclusive of the 50 mg overage. A payment for overage would be included in all six infusions claimed, essentially comprising a double-payment for overage—once as a component of each original infusion and again in the reimbursement of a sixth infusion comprised entirely of overage.

Manufacturers consulted in the Review voiced concerns that current practice associated with vial-optimisation results in:

- An inefficiency in the payment for drugs on the EFC (as described above); and
- Claims from Government to manufacturers for payment of rebates on a higher number of infusions than have been supplied by manufacturers. The use of overage to construct 'phantom' vials for administration to patients results in the volume of drug claimed on the PBS exceeding the volume of drug sold by manufactures (on a per-vial basis). This is problematic for manufacturers where rebate arrangements exist between manufacturers and the Commonwealth.

In general, rebates on PBS subsidised drugs arise where a drug has been listed with: (1) a Special Pricing Arrangement (SPA) which requires manufacturers rebate the difference between a product's published dispensed price and agreed confidential price; or (2) risk-sharing arrangements (RSAs) enacted on the volume of sales (threshold) which require manufacturers rebate a proportion of sales above an agreed threshold. In both cases, the existence of phantom vials was perceived as problematic for manufacturers. Where rebates are triggered by an SPA, it implies the payment of a rebate on sale which they dispute, while in the case of RSAs, it may mean that volume at which a rebate is to be enacted is reached sooner than estimated.

In addition, payment for drug on the basis of the efficient combination of vials is premised on minimising the cost to Government (as per the EFC legislation). However, this does not recognise the underlying variable costs associated with the compounding process, which depend on the number of vials handled in a given compounding session. Consider the example of bortezomib, which is available in 1 mg, 3 mg and 3.5 mg vials. If a patient requires a dose of 2.5 mg, the 'cost' with respect to drug

wastage (in terms of mg not utilised) is the same, irrespective of whether the 1 mg or 3 mg vial is used as the basis to estimate the efficient combination of vials. Similarly, on the basis that the price per mg (on a dispensed price basis) is the same across the strengths, there is no impact on the cost to Government. For the compounder, however, there will be more time, risk and effort required to compound a 2.5 mg infusion from three x 1 mg vials than from one x 3 mg vial.

3.2.3 Establishing PBS prices

PBS subsidies for pharmaceuticals provided via (s90) community and (s94) hospital pharmacies for outpatient (public and private hospitals) or inpatient use (private hospitals) are a key feature of the Australian health care system. Under the National Health Act 1953 (Cth), the PBAC is charged with considering the comparative effectiveness and costs of each drug for which an application is lodged, and to make recommendations to the Minister for Health of the conditions under which a product may be listed on the PBS to achieve cost-effective use in clinical practice. In reviewing applications for drug subsidy, the PBAC considers, inter alia, the cost-effectiveness of the proposed drug for each indication for which PBS listing is sought (see Text Box 1).

Text Box 1. Factors affecting PBAC decision-making

The following is an excerpt from the PBAC Guidelines (2016, p.4):

PBAC decision making is influenced by five quantitative factors:

- Comparative health gain. Assessed in terms of both the magnitude of effect and clinical importance of effect. Presented as both effectiveness and safety (discussed in Section 2), and the denominator of the incremental cost-effectiveness ratio or incremental cost-utility ratio (discussed in Section 3A).
- Comparative cost-effectiveness. Presented as incremental cost-effectiveness ratios (including incremental cost-utility ratios) or a cost-minimisation approach. Includes a consideration of comparative costs, including the full spectrum of health care resources (discussed in Section 3).
- Patient affordability in the absence of PBS subsidy. Presented as cost per patient per course for acute or self-limited therapy, or cost per patient per year for chronic or continuing therapy (discussed in Section 3A).
- Predicted use in practice and financial implications for the PBS. Presented as the projected annual net cost to the PBS/RPBS or the National Immunisation Program (discussed in Subsection 4.4).
- Predicted use in practice and financial implications for the Australian Government health budget. Presented as the projected annual net cost per year (discussed in Subsection 4.5).

Other less-readily quantifiable factors that also influence PBAC decision making include:

- Overall confidence in the evidence and assumptions relied on in the submission.

- Equity. Implicit equity and ethical assumptions, such as age, or socioeconomic and geographical status, may vary for different submissions and need to be re-evaluated case by case.
- Presence of effective therapeutic alternatives. This helps to determine the clinical need for the proposed medicine.
- Severity of the medical condition treated. Relates to any restrictions requested in Subsection 1.4. The emphasis is on the nature and extent of disease as it is currently managed (see Subsection 1.2).
- Ability to target therapy with the proposed medicine precisely and effectively to patients likely to benefit most. The cost-effectiveness of the proposed medicine may be greatest in patients likely to benefit the most. Claims of benefits that are greater than the average result from an intention-to-treat analysis should be supported by appropriate trial evidence.
- Public health issues; for example, development of resistance (for antimicrobial agents; see Subsection 5.3).
- Any other relevant factor that may affect the suitability of the medicine for listing on the PBS.

Source: [9]

Cost-effectiveness is assessed as the ratio of the incremental cost of a drug to its incremental benefit (most often expressed in quality-adjusted life years, QALY), relative to a comparator in a proposed indication. For the purposes of the Review, two elements of cost-effectiveness are of particular interest: the inputs to the assessment of costs, and the proposed indication(s) to which those costs apply.

Assessment of cost: Incorporating wastage

The PBAC Guidelines note that the estimation of cost-effectiveness should account for all resource use associated with the utilisation of a drug in its proposed indication. This includes wastage, which is considered "consumption, and therefore an incurred cost" (p. 81). For any given price, wastage increases the resulting cost of a drug relative to its comparator. For a drug to be recommended as cost-effective, its proposed price may need to be lower (i.e., to compensate for wastage). Price adjustments incorporating wastage may be observed in PBAC recommendations for a number of EFC-listed medicines between 2017 and 2020, particularly the immunotherapy, pembrolizumab, for which the PBAC noted incorporation of wastage required a price reduction to achieve an acceptable cost-effectiveness ratio (see Appendix 10).

Beyond the assessment of cost-effectiveness and its impact on a product's PBS list price,

consideration of wastage also impacts the assessment of the overall cost to Government associated with a proposed drug. That is, all applications to the PBAC must consider the impact on the cost to Government of the proposed listing in terms of the anticipated volume of drug utilisation (i.e., units dispensed) and value (i.e., cost), relative to that of the product(s) for which it is substituted. When lodging an application to list an EFC medicine on the PBS, a sponsor will propose an applicable authority level (see Text Box 2). The proposed level of restriction reflects the population for which the sponsor believes they can demonstrate the drug's efficacy, safety and cost-effectiveness.

Text Box 2. PBS restriction levels

Medicines on the PBS are supplied as an Unrestricted (General Benefit), Restricted or Authority Required item:

- *Unrestricted* medicines under the PBS Schedule may be prescribed by a prescriber within their scope of practice at their discretion.
- *Restricted* medicines listed in the schedule, are only prescribed if a condition meets the stated restrictions.
- *Authority Required (STREAMLINED)* medicines are prescribed for specific conditions and do not need prior approval from Services Australia or the Department of Veterans' Affairs. Instead, the process is streamlined by providing a four-digit streamlined authority code on an authority prescription.
- *Authority Required* medicines are medicines that can only be prescribed by if prior approval is obtained from Services Australia or the Department of Veterans' Affairs as appropriate.

See https://www.pbs.gov.au/info/general/faq

In assessing the proposed listing type, the PBAC considers whether there the possibility that the proposed drug will be used in a patient group for which it is not cost-effective or its cost-effectiveness has not been determined. In addition, the PBAC considers whether there is the potential for there to be a high unit cost per patient—or high total opportunity cost (with respect to the total cost to the PBS)—associated with subsidy under the proposed listing type [9]. In addition, restriction types are also considered with respect to product safety and quality use of medicines issues, particularly as they may relate to new medicines for which little is known about in-market use. Similarly, the maximum quantities proposed are those which are likely to be associated with the proposed use of the drug for the average patient and as associated with the estimate of cost-effectiveness.

In proposing restrictions, sponsors are asked to consider "trade-offs between the clinical preference for a simple restriction and a complex restriction to limit the use of the proposed medicine to the target population" [9] (p 21). The clearest of these trade-offs is price. For example, if suggesting that

a product be given a broad, unrestricted listing based on evidence from a more tightly defined population, the sponsor may anticipate that a lower price would be required in order to achieve an acceptable cost-effectiveness ratio across the broader population (particularly if evidence of efficacy in the broader population is uncertain) and where an expanded population would be associated with a higher cost to government.

Inter alia, for a given product, the number of units to be dispensed per service, per patient is a function of the prescribed dose and the quantity supplied per pack. Where per-mg prescribing is based on patient size, inclusion of wastage will increase the estimated number of units to be dispensed via the PBS. Thus, inclusion of wastage increases the overall estimated cost to Government (by increasing the volume dispensed), which may have implications for financial caps included in risk sharing arrangements (RSAs) between Government and sponsors (i.e., where caps trigger volume-based rebate arrangements, as distinct from rebates for special pricing arrangements, which are levied irrespective of the number of units sold).

The incorporation of wastage in PBAC deliberations is an important consideration with respect to the Review. A key factor raised during consultations for the EFC Review is that the remuneration of drugs based on the efficient combination of vials allows product compounders to utilise wastage for the preparation of additional doses. As noted elsewhere, efficiencies associated with the practice of vial optimisation (i.e., utilisation of overage that would otherwise be discarded) may not be actualised, as there may be 'double payment' for wastage (see Section 3.2.2, Vial optimisation). Vial optimisation may therefore result in the number of vials claimed for PBS reimbursement exceeding estimates, with financial caps underpinning RSAs being reached sooner than anticipated by sponsors and Government.

3.2.4 Elements of PBS prices on the EFC

Products supplied via the EFC arrangements on the PBS are reimbursed (priced) on the basis of a DPMA, comprising:

- the approved ex-manufacturer price (AEMP) per unit of supply (vial), multiplied by the number of vials required to achieve the maximum amount per supply.
- the addition of allowable fees and wholesaler mark-ups, which vary based on whether supply of the pharmaceutical product is via an (s90) community pharmacy or (s94) public or private hospital pharmacy, and whether it includes supply of trastuzumab (or its analogues). The allowable fees and mark-ups for EFC products are summarised in Figure 8.

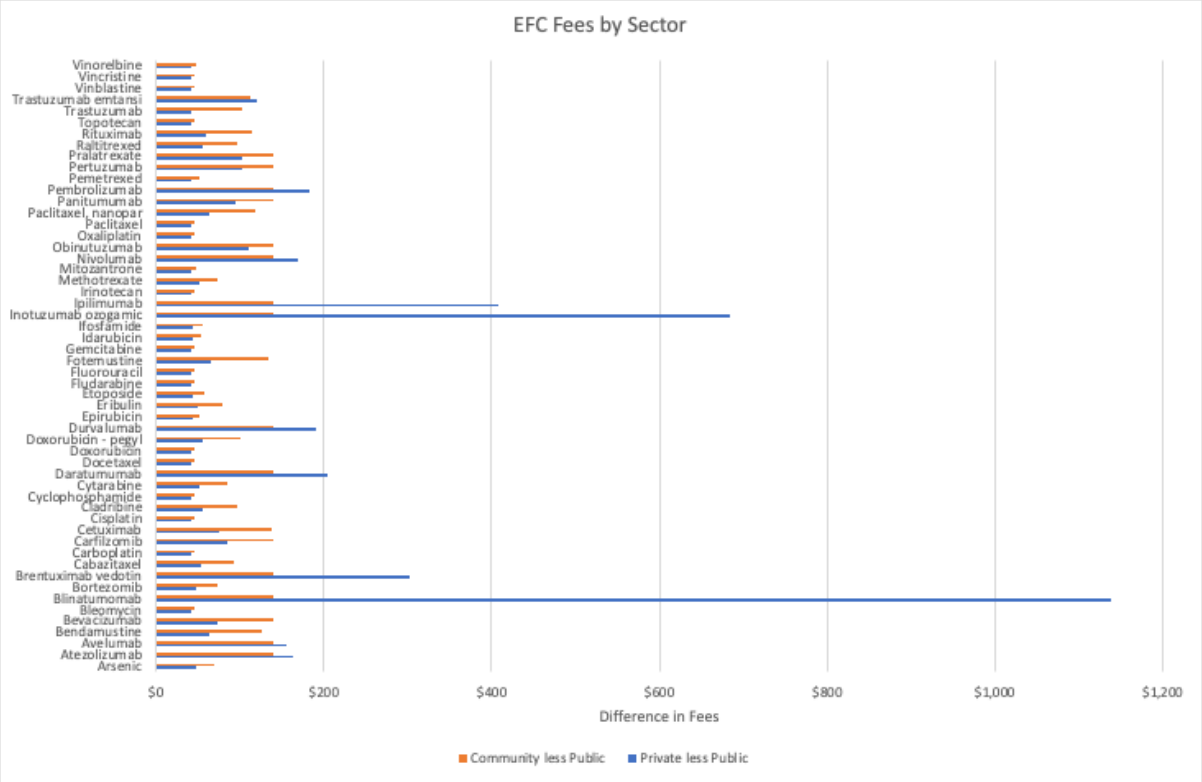
Figure 8. EFC fees

Efficient Funding of Chemotherapy								
Price								
s90			**PRIVATE HOSPITAL**			**PUBLIC HOSPITAL**		
Pharmacy mark-up			Pharmacy mark-up	1.40%		applicable fees for all drugs except trastuzumab		
Tier 1	PTP < $100	$4.30	applicable fees for all drugs except trastuzumab			Preparation fee	$86.28 (+ further $20 for TGA-licensed compounder)	
Tier 2	PTP $100 - $2000	$4.30 + 5% of the amount which the PTP for max qty exceeds $100	Distribution fee	$27.75		applicable fees for trastuzumab where prescribed for HER-2 positive early breast cancer		
Tier 3	PTP > $2000	$99.30	Diluent fee	$5.50		Preparation fee	$86.28 (+ further $20 for TGA-licensed compounder)	
applicable fees for all drugs except trastuzumab			Preparation fee	$86.28 (+ further $20 for TGA-licensed compounder)		Other Fees		
Distribution fee		$27.75	Ready Prepared Dispensing fee	$7.78				
Diluent fee		$5.50	applicable fees for trastuzumab where prescribed for HER-2 positive early breast cancer					
Preparation fee		$86.28 (+ further $20 for TGA-licensed compounder)	Diluent Fee	$5.50				
Ready Prepared Dispensing fee		$7.78	Preparation Fee	$86.28 (+ further $20 for TGA-licensed compounder)				
applicable fees for trastuzumab where prescribed for HER-2 positive early breast cancer			Ready Prepared Dispensing fee	$7.78				
Distribution Fee		$27.75	Other Fees					
Diluent Fee		$5.50						
Preparation Fee		$86.28 (+ further $20 for TGA-licensed compounder)						
Ready Prepared Dispensing fee		$7.78						
Other Fees								

Source: Australian Government [10]. See https://www.servicesaustralia.gov.au/about-pbs-for-pharmacists?context=22861

Under the existing fee structure, reimbursement fees differ depending on the setting from which a PBS claim is lodged. Under EFC arrangements (s94) public hospital facilities receive payment for the preparation fee only (currently $86.28), in addition to drug reimbursement, while (s94) private and (s90) community pharmacy facilities also receive ready-prepared dispensing fees, mark-ups, and distribution and diluent fees. The differences in fees across sectors by molecule can be observed in Figure 9. The largest numerical differences (over $200 per item) all occur in the newer MAbs (prices shown are the mean (s94) private hospital DPMA across all presentations of a molecule): blinatumomab ($79,654); inotuzumab ($46,652); ipilimumab ($26,749); brentuximab vedotin ($19,008); and daratumumab ($11,975).

Figure 9. EFC fees by molecule and sector



Abbreviations: EFC, Efficient Funding of Chemotherapy.
Source: Developed for this Review based on the DPMA for all EFC listed items as at 1 August 2021 as obtained from the DoH website (https://www.pbs.gov.au/pbs/industry/pricing/ex-manufacturer-price).

For (s94) private hospitals, mark-ups (1.4% of the AEMP) range from just under $0.10 per maximum amount of fluorouracil to $1,138.67 per maximum amount of blinatumomab. Adjusting by the per molecule service volume observed for (s94) private hospitals in 2021, the mean mark-up across molecules was $25.63. When added to the remaining EFC fee components, this results in a mean fee per item of $152.94. For (s90) community pharmacies, the payment of mark-ups is tiered as per the Administration, Handling and Infrastructure (AHI) fee, with a minimum of $4.30, up to $99.30 per maximum amount. Weighted by the 2021 service volume for (s90) community pharmacies, the mean mark-up was $40.67. When added to the remaining EFC fee components, this results in a mean fee per item of $167.98. Higher per unit mark-ups for some items dispensed by (s94) private hospitals do not appear to result in those higher cost items representing a greater proportion of services in that setting. The comparison across sectors, with the overall fee for which costs were included in the 2013 Review (inflated to 2021 prices) is summarised in Table 5.

Table 5. EFC fees across settings

Component of PBS reimbursement	*Fee per service*
Current mean EFC Fees	
(s94) Private Hospitals	$152.94
(s94) Public Hospitals	$86.28
(s90) Community (AHI) (3-tiered)	$167.98
Supporting cost as in 2013 Review[1]	$143.18

Abbreviations: AHI, administration handling and infrastructure; EFC, Efficient Funding of Chemotherapy.
Notes: 1. Inflated to 2020/21 prices.

The Chemotherapy Compounding Payment Scheme

Currently, under the EFC Program, TGA-licensed compounders are paid a $20 fee per eligible PBS reimbursed EFC item. Payment of the fee is facilitated via the Chemotherapy Compounding Payment Scheme (CCPS), via the Australian Healthcare Associates (the administrators of the scheme). It is understood that the fee was initially introduced in recognition of the additional regulatory requirements faced by TGA-licensed compounders with respect to the provision of compounded medicines.

A compounded item is deemed eligible for payment of the fee if it is an EFC subsidised product for which the claiming pharmacy has correctly included the TGA compounder's identification code as part of the PBS reimbursement claim. Claims for payment of the CCPS fee are not lodged by TGA-licensed compounders, but rather are generated by reimbursement claims being lodged into the system by claiming pharmacists.

Distribution of EFC Fees

Noting the differences in fees paid across settings, it is pertinent to examine the impact of those differences across molecules. For each PBS item, the relevant fees (taking into account the respective settings) were expressed as a proportion of its DPMA and averaged across all brands within a molecule.

There are a total of 298 unique PBS item numbers on the EFC (noting that this represents 149 unique listings as each listing on the EFC is associated with two unique PBS items—for public and private hospital settings), with a total of 96 brands (with the maximum for any one molecule being for trastuzumab; see Table 6). Mean DPMA and the price per mg for each molecule (both averaged over all brands and strength presentations in that molecule) are shown in Table 6.

Table 6. PBS item codes, unique brands, mean DPMA and price per mg by molecule

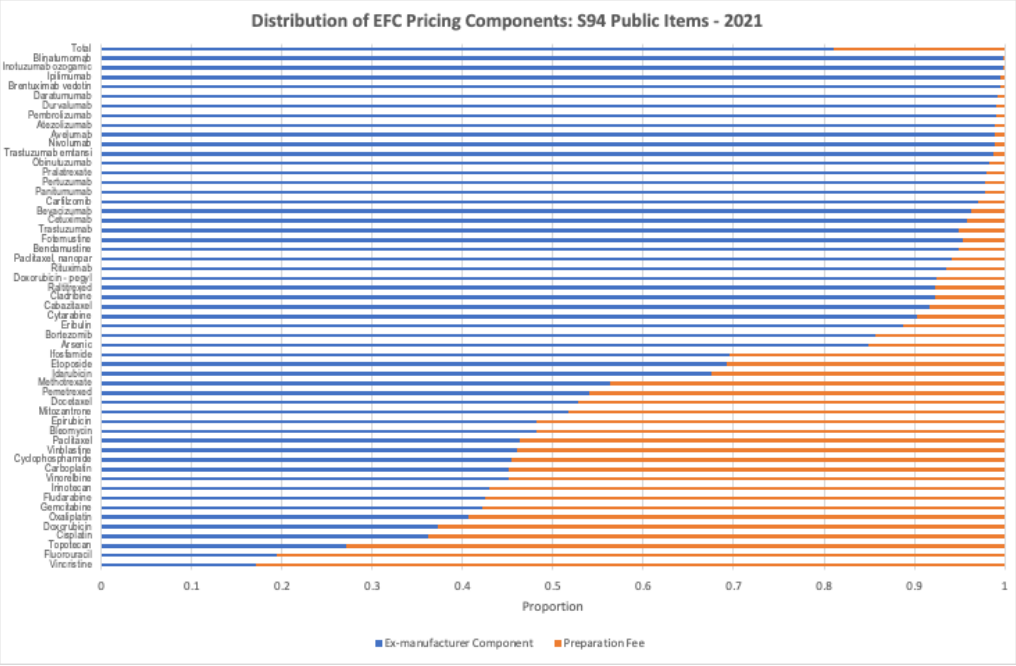
Molecule	*PBS Item Codes*	*Unique Brands*	*Mean DPMA*	*Price per mg*
Arsenic	4	3	$597.21	$33.18
Atezolizumab	28	1	$8,594.08	$6.04
Avelumab	4	1	$8,307.96	$6.92
Bendamustine	2	1	$1,732.74	$8.66
Bevacizumab	2	1	$2,318.17	$1.29
Bleomycin	4	3	$187.36	$0.01
Blinatumomab	8	1	$79,084.63	$105.45
Bortezomib	16	2	$629.15	$0.21
Brentuximab vedotin	16	1	$18,857.14	$96.90
Cabazitaxel	2	3	$1,059.58	$19.27
Carboplatin	2	2	$178.28	$0.20
Carfilzomib	4	1	$3,088.38	$22.08
Cetuximab	10	1	$2,220.70	$3.29
Cisplatin	2	1	$156.11	$0.71
Cladribine	2	2	$1,154.52	$67.91
Cyclophosphamide	2	1	$178.99	$0.06
Cytarabine[1]	2	1	$910.40	$0.13
Daratumumab	8	1	$11,872.37	$6.18
Docetaxel	2	2	$203.96	$0.82
Doxorubicin	2	2	$158.31	$1.17
Doxorubicin – pegyl	2	2	$1,178.23	$11.78
Durvalumab	2	1	$9,713.60	$8.09
Epirubicin	2	2	$187.60	$0.85
Eribulin	4	1	$795.58	$265.19
Etoposide	2	3	$301.65	$0.69
Fludarabine	2	2	$170.93	$3.11
Fluorouracil	4	3	$130.00	$0.07
Fotemustine	2	1	$1,880.63	$8.55
Gemcitabine	2	1	$170.29	$0.06
Idarubicin	2	1	$287.52	$9.58
Ifosfamide	2	1	$304.82	$0.08
Inotuzumab ozogamic	4	1	$46,310.31	$14.86
Ipilimumab	10	1	$26,544.86	$137.08
Irinotecan	2	5	$172.30	$0.22
Methotrexate	4	4	$498.97	$0.29
Mitozantrone	2	2	$200.05	$6.67
Nivolumab	30	1	$8,973.85	$21.20
Obinutuzumab	12	1	$5,170.35	$5.17
Oxaliplatin	2	3	$166.43	$0.55
Paclitaxel	2	4	$181.80	$0.40
Paclitaxel, nanopar	4	1	$1662.33	$3.96
Panitumumab	4	1	$3,926.33	$5.45
Pembrolizumab	24	1	$10,374.84	$38.95
Pemetrexed	2	5	$208.66	$0.19
Pertuzumab	4	1	$4,515.57	$7.19
Pralatrexate	4	1	$4,497.32	$56.22
Raltitrexed	2	1	$1,156.94	$165.28
Rituximab	10	2	$1,357.62	$1.70
Topotecan	2	2	$139.10	$0.04
Trastuzumab	16	6	$2,011.37	$2.72
Trastuzumab emtansine	4	1	$7,337.04	$16.30
Vinblastine	2	1	$180.65	$9.03
Vincristine	2	1	$124.76	$62.38
Vinorelbine	2	2	$178.19	$2.55

Molecule	*PBS Item Codes*	*Unique Brands*	*Mean DPMA*	*Price per mg*
Total	*298*	*96*	*$4,786.34*	*$14.48*

Abbreviations: DPMA, dispensed price per maximum amount; PBS, Pharmaceutical Benefits Scheme.
Notes: 1. There is only one brand of cytarabine, the generic provided by Pfizer Australia Pty Ltd, listed with the company name as the brand. This brand name appears across 8 PBS items and thus is not unique to cytarabine (but is shown here to ensure completeness of information).
2. These 298 items appear across 730 observations due to multiple vial sizes being listed per item number.

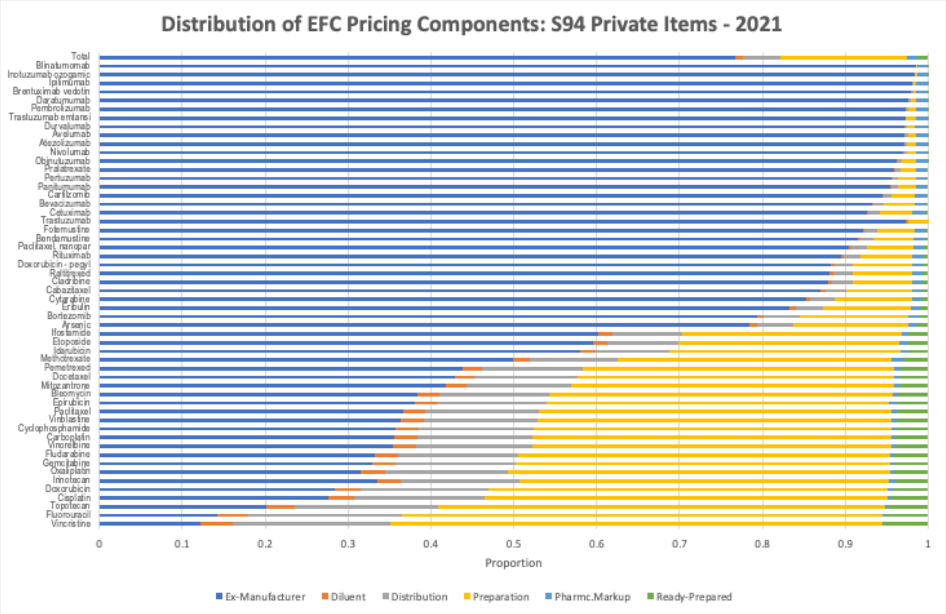
There is considerable variability across the prices of PBS listed items with respect to the proportion of the DPMA allocated to the manufacturer (reimbursement for the product) and others in the supply chain. For items listed for use in the private hospital setting, the proportion of the DPMA attributed to manufacturer prices ranges from a minimum of 12.2% for vincristine (an off-patent, older product supplied by a generic manufacturer) to 98.5% for blinatumomab (an on patent, innovator brand), with the average across all products (not weighted by sales) being 77.4% (see Figure 10). The next major component of the DPMA is that associated with the preparation fee, ranging from 59.3% of the DPMA for vincristine to 0.1% for blinatumomab, with an average across all products of 14.8%. The same pattern of fee components within the DPMA is observed for (s94) private hospital items (noting that only a preparation fee is applied; see Figure 11) and (s90) community pharmacy items (see Figure 12).

Figure 10. EFC pricing components, (s94) public items (2021)



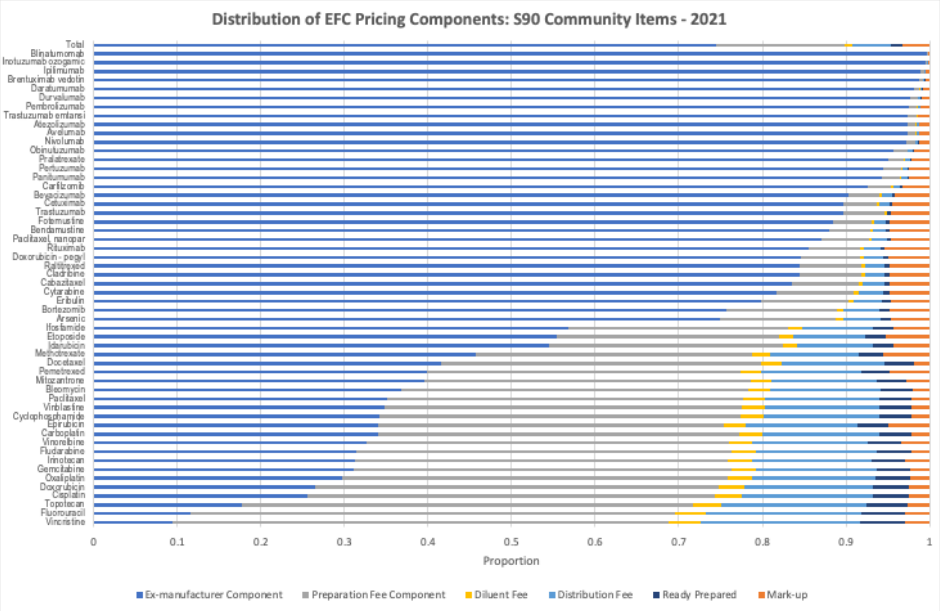
Abbreviations: EFC, Efficient Funding of Chemotherapy.
Source: Developed for this Review based on PBS list prices as at August 2021.

Figure 11. EFC pricing components, (s94) private items (2021)



Abbreviations: EFC, Efficient Funding of Chemotherapy.
Source: Developed for this Review based on PBS list prices as at August 2021.

Figure 12. EFC pricing components, (s90) community items (2021)



Abbreviations: EFC, Efficient Funding of Chemotherapy.
Source: Developed for this Review based on PBS list prices as at August 2021.

As noted, TGA-licensed compounders receive a $20 fee (CCPS Fee) per compounded EFC item claimed. Payment of the CCPS fee is not included as part of the DPMA for EFC listed products (in either estimating the cost-effectiveness of drugs for which a CCPS fee might be claimed, or in

reporting Government PBS spending on EFC medicines). For the majority of medicines (34/54), the CCPS fee represents less than 5% of the cost to Government on a per-molecule basis (when added to the DPMA; see Appendix 11). For those medicines with lower DPMAs (e.g. vincristine), the CCPS accounts for approximately 10% of the cost on a per molecule basis.

4 EFC costs and reimbursement

4.1 Stakeholder views

Feedback from stakeholder submissions to the Review and subsequent targeted interviews on the current structure of the EFC program, its associated costs and the implications for the delivery of chemotherapy services for Australian patients are presented below. Presentation of stakeholders' views has been organised thematically, informed by the questions that framed the Review (see Appendix 1).

4.1.1 Service viability

Issues around supply chain activities affecting service viability were raised by member organisations, community pharmacy, logistics companies, and the Department of Health. Hospital and community pharmacies undertaking in-house compounding keep a range of non-compounded stock 'on-hand' for both routine and emergency use. However, increases in drug prices, particularly related to MAbs and emergent immunotherapies, have caused significant increases in the cost of holding stock related to:

- Physical space required for storage;
- Interruption of cash flow linked to the delay between the purchase of expensive stock and (uncertain) lodgment of claims for reimbursement;
- 'Stranded' stock purchased but not used before its expiry date;
- Increased insurance costs and financial exposure related to potential stock loss (e.g., due to refrigerator failure);
- Changes in PBS list prices after stock is purchased but before it is used, resulting in declining margins on the cost of goods sold. In addition, a number of submissions reported instances of suppliers setting prices higher than the PBS reimbursement amount (PBS list price), meaning the cost to pharmacy to purchase EFC medications may be greater than its associated sales revenue (see Section 4.3 for a quantitative analysis and discussion of supplier and PBS reimbursement prices); and
- De-listing of medications after purchase of stock but before a claim is submitted for PBS reimbursement. This is of particular concern for small-volume pharmacies and hospitals with limited capacity to absorb such costs.

These costs are borne by pharmacies and are exacerbated by the higher costs of emergent cancer medicines and the requirement to maintain sufficient stock of a large range of medicines.

> *The most significant cost is that of holding higher inventory levels. Our inventory is purposefully at a level higher than industry standard to enable same-day treatment and to mitigate anticipated delays in transportation. On the day this discussion paper was released, (21st May 2021) [we] had $375,009 of chemotherapy inventory on hand in the oncology fridge. These high inventory levels are kept at significant cost to the business. The PBS funding model assumes 'just in time' supply, which is ineffective in […] country areas where many drugs are delivered 2-3 business days (in some cases up to 5 days) after placing an order. In other industries, the cost of holding higher inventories is generally offset by higher margins, which is not possible with established Commonwealth fees for compounding EFC medicines.*
>
> *-Commercial pharmacy*

Additionally, due to the gaps between when medications are compounded, administered and claimed, cancer medicines may be compounded and/or administered but ineligible for PBS reimbursement. A cancer medicine is compounded, either in-house or externally once an order is written by a physician. Claiming, on the other hand, cannot occur until the medicine is administered to the patient, which may be several days later. In some settings, the submission of claims was reportedly 'batched' on a monthly basis. Processing of claims may therefore occur weeks after a drug has been administered. Further, PBS claims may be rejected or reversed under audit for minor administrative and technical issues related to the prescription as received by the pharmacy. Where a corrected script cannot be obtained, the associated reimbursement is generally foregone.

Stakeholder interviews with community pharmacists, as well as representatives of a pharmacy member organisation, confirmed these issues, highlighting the challenges of holding expensive inventory and the risks associated with stranded and spoiled stock.

> *The difference is the cost of stock-holding—these things are expensive, the risk is large. Being in a rural regional site, we have to maintain our inventory at a greater level than in the city—those things take time to get to us. Yes, the majority of drugs are overnight, or depending, if it's a weekend can be two days. There are some instances with specialised drugs that come from individual manufacturers that take longer. For example, NAb paclitaxel—that can take three to four days to get to us.*

> *Pfizer is another one, or DHL, that can take an extra couple of days.*
>
> *You need to have stock on hand to cover your basics and stock up again when needed. You run the risk of 1) not using drugs, for some reason, they fall out of favour, and you're left with stock; 2) fridge failure and the insurance risks associated with that.*
>
> *-Commercial pharmacy*

A representative of a pharmacy member organisation confirmed that as a result of the substantial costs associated with high-quality compounding of cancer medicines—from facility and product logistics to skilled labour and insurance—very few community pharmacies are in a position to offer these services.

> *While most pharmacies do compounding of some sort—you know, making up a cream or an ointment, or a mixture—there are really only specialty pharmacies now that are doing any sterile compounding. Because again, you're needing specialty equipment, you need to have trained personnel, you need very strict protocols and processes in place. […] Even with non-chemo compounding, you're seeing pharmacies […] having to refer that on to the specialty ones.*
>
> *A lot of the pharmacies [undertaking in-house compounding] tended to have a very small, local service to be able to respond to last minute dose changes. […] The problem with that, of course, is you really need the trained staff and the equipment to even be able to do that.*
>
> *-Pharmacy member organisation*

A non-metropolitan hospital pharmacist underscored the challenges of identifying, recruiting and retaining suitably qualified staff as additional barriers to service viability in rural areas. The stakeholder noted, however, that despite these challenges, maintaining local capacity in small-volume settings was critical to the retention of specialised skills in the public sector.

Members of a commercial pharmacy group posited that in-house compounding could potentially save

hospitals money by avoiding price mark-ups charged by third-party compounders. However, specific data were not provided with respect to potential financial differences between in-house and third-party compounding.

TGA-licensed compounders and an independent compounding consultant discussed in detail the differences between in-house and third-party compounding in relation to auditing requirements and their associated costs. It was noted by one TGA-licensed compounder that changes to TGA requirements can have significant impacts on their business model. This was confirmed by a number of small volume, non-TGA licensed compounders, for whom TGA compliance costs were deemed prohibitive.

> *The Pharmaceutical Society of Australia has the compounding guidelines, and the professional practice standards. And then the board recommends that you adhere to either PICS or to USP 797, if you're doing sterile compounding. That's self-regulated, though.*
>
> *In [community pharmacy], the pharmacy board doesn't audit sites for compliance to either of those two standards. […] We consider ourselves to be 797 compliant—that's the standard we work to. PICS really is for TGA-licensed compounders. Knowing what is required for TGA-licensed compounders, if any community pharmacy said that they were compliant to PICS, I think that would be a stretch, because it is another level.*
>
> *TGA-licensed compounders are inspected every 12 months by the TGA. […] So there's an entire quality team. I could go on and on about the additional costs involved.*
>
> *-Commercial pharmacy*
>
> *Right up through that whole transport process, that is also audited under the TGA component as well. Again, as they sort of zoom in and change different requirements—sometimes it's not even necessarily a requirement change, but how they interpret the change—so too, does our testing requirements and the cost to go back and revalidate and do all those pieces. There's a very complex matrices*

> *involved in all of that.*
>
> *-TGA-licensed compounder*

Members of a commercial pharmacy group highlighted the disparate reimbursement for like services based on providers' registration status (i.e., (s90) community pharmacies vs (s94) private hospital pharmacies). A provider also maintained that hospital-owned pharmacies have greater capacity to offer supporting clinical services covered by their hospital's cost centre, whereas private pharmacies providing chemotherapy services to hospitals must cover costs through PBS reimbursement alone.

> *We operate a mixture of [(s90) and (s94) pharmacies] throughout the country, depending on the size of the hospital facility. The (s94), just because of the way that it's set out, attracts less funding for these medications. So not only are you in a smaller, less busy facility, but you're getting less remuneration as well. […] The community pharmacy gets access to the AHI—the three level markup—whereas the (s94) has a 1.4% flat markup fee, and that can be quite a significant difference between the two.*
>
> *Our main source of revenue is from the prescriptions in the private hospital setting, so if we don't dispense the prescription, usually we're not paid. Some hospitals do pay for above-and-beyond clinical services, but, usually, not in the oncology setting. We usually provide that ourselves.*
>
> *[…] I think it's fair to say [hospital-based pharmacies] are more of a cost centre. You know, they don't need to stand up as a business—they can just keep incurring costs up to a point. They've obviously got a budget, but there's a key difference there.*
>
> *-Commercial pharmacy group*

Representatives of pharmacy member organisation underscored that financial risks associated with clinical errors are often borne by pharmacy.

> *Not all of them are expensive, but some are and this can be a very expensive*

> *process and the pharmacy is so reliant on claims. We're seeing, you know, the Department undertaking some compliance activities, and they come in a couple of years after and ping the pharmacy on a claim because of an administrative error, rather than an eligibility error.*
>
> *In some instances, the doctor has just reprinted a prescription from their dispense history and the pharmacist has dispensed that. And then the pharmacy is the one that gets pinged and loses thousands of dollars. At that stage, the doctor can't do anything—even if they want to help—because it's too late to get a new prescription and an authority or whatever. There's so many administrative issues within this PBS system as a whole. There are so many risks involved with [chemotherapy]. I think administration of the PBS needs to be improved for the whole system, including for the specialty programs.*
>
> *-Pharmacy member organisation*

4.1.2 Wastage

Representatives of community and hospital pharmacies, pharmacy and medical member organisations, industry, and Government reported a range of concerns pertaining to wastage stemming from the operation of the EFC supply chain. Issues raised included how wastage occurs, a lack of system incentives to reduce wastage, and the financial impact on industry related to practices such as vial-sharing (for a detailed discussion about vial-sharing and related reimbursement issues, see Section 3.2.2).

In this context, interviewees used the term 'wastage' broadly to refer variously to the amount of pharmaceutical product contained within a vial as provided by the manufacturer that is in excess of the amount required to formulate a dose for a given patient, product that has been prepared but not administered to a nominated patient, and product that has expired or whose sterility has been compromised and must be discarded. Wastage may arise from a number of sources:

- When doses are compounded, there is typically some level of 'overage,' i.e., product left in the vial that cannot be accessed due to the size or shape of the vial, viscosity of the drug, needle used to aspirate the drug, or proficiency of the technician compounding the product.
- Accidental loss through operator error at the time of compounding, resulting in drug being

discarded.

- A prescribed dose may require less product than the quantity provided in its comprising vial(s), e.g., a prescribed dose of 160 mg drawn from a vial containing 200 mg will produce 40 mg of excess product, less overage. PBS remuneration based on the most efficient combination of vials assumes this excess product is discarded.
- A dose may be ordered and compounded, but not administered, e.g., due to the patient's health status, pathology results or death.
- Product stock may expire before it can be used. This issue may be particularly challenging for low-volume providers who need to keep stock on hand for 'just-in-time' compounding, but who lack regular throughput of various medicines.

> *Gilbar et al. [evaluated] the proportion of compounded cancer medicines that could not be administered to the patient as planned. The researchers concluded that over 12% of compounded cancer drug products used in the Toowoomba Hospital became orphaned for a variety of reasons. Where these cancer treatments could be used for the same patient or another patient at a later stage there would be significant cost reductions where compounded medicines were compounded by a TGA-licensed compounder that could allocate extended stability to their products.*
>
> *Likewise, King et al. found in a study at the Princess Alexandra Hospital in Brisbane that 1,847 doses of parenteral cancer medicines were reassigned over a 12-month period in 2018 and 2019, resulting in a saving of $2.4 m to the PBS. In addition to the financial benefits, the ability of hospitals to store chemotherapy medicines with extended stability has a positive impact on those patients who might experience a treatment disruption and are able to recommence their treatment immediately when they are assessed as being in a state of readiness.*
>
> *-TGA-licensed compounder*
>
> *If a patient cancels or reschedules, pharmacies aim to keep and reuse chemotherapy for their next treatment wherever possible by cancelling the initial dispensing and PBS claim, then reallocating the treatment to another patient where appropriate.*
>
> *This saves taxpayers' money and prevents unnecessary discarding and remaking.*

> *As referenced elsewhere in this submission, independent studies have demonstrated the benefits of these practices to the PBS. However, it is important to recognise that when pharmacies orphan a chemotherapy product and re-use it for another patient, there is a significant administrative/unfunded burden for the pharmacy in terms of cancelling and re-issuing PBS scripts, and monitoring risk of expiry, as well as the additional work in manipulating the dose.*
>
> *-Pharmacy member organisation*

Strategies reported by stakeholders to mitigate wastage included:

- Repurposing prepared doses for other patients—Where a patient is unable to receive a compounded dose, the drug needs to be discarded unless it can be repurposed or relabeled for another patient within the product's expiry date. This repurposing may occur for both PBS indications, as well as non-PBS indications (e.g., compassionate use). It was noted that extended drug expiry (such as allocated by TGA-licensed compounders) is critical to facilitate dose repurposing.
- 'Just-in-time' compounding, i.e., the preparation of a dose only once patient eligibility is confirmed and awaiting administration.
- Informal networks of proximate providers so that medications approaching their expiry may be put to use where needed.
- Extended expiry dates—Stability studies, typically undertaken by TGA-licensed compounders, mitigate wastage by allowing pharmacies to maintain ageing stock that would otherwise need to be discarded.
- Vial-sharing—Compounders frequently combine the excess product left over in vials to compound additional prescribed doses. Excess product may be combined across vials within a single compounding session or, under suitable conditions, re-labeled and stored for later use. Discrepancies arising from vial-sharing concerning manufacturers' recorded unit sales and service volumes claimed via those dispensing PBS items are discussed in detail in Section 3.2.2.

Some low-volume compounders, including private and hospital pharmacies, expressed frustration that TGA-licensed compounders typically do not publish the results of their product stability research. Smaller compounders, who cannot afford to undertake their own stability studies, therefore remain

unable to apply extended expiry dates to their own compounded products, exacerbating the issue of wastage. However, an independent compounding consultant suggested to the Review that even if product stability results were made available, smaller pharmacies are typically not capable of replicating these studies' strict conditions.

> *Older agents tend to have published stability studies that we can lean on. Of course, then you've got to be confident in your sterile production facilities. We don't think that in our facilities we will be looking to put 28, 30, up to 60 days shelf-life on products—that is what particular licensed compounders do. They feel confident doing that because of the way that they validate their operators, validate equipment, that continuous air particle monitoring, things like that, that feed them that confidence on the sterility.*
>
> *[…] In the UK, for instance, NICE has taken a more active role in encouraging the sponsors to perform those studies themselves. […] But I don't think [facilities like ours] would ever be looking to put the amount of time on products that the TGA-licensed can.*
>
> *-Commercial pharmacy group*
>
> > *Interviewer: If you test something for stability under certain conditions at the laboratories here in Australia—assuming the same laboratory conditions—your colleagues can use that data internationally, correct?*
>
> *Yep. Whereas hospitals can't replicate the study, because often they don't have the same level of some conditions that we did.*
>
> *-TGA-licensed compounder*

4.1.3 Administrative burden of EFC claiming

Several respondents reported challenges with the administrative burden related to EFC claiming (see Section 6.1.3 for a discussion of strategies to mitigate this administrative burden). Issues raised by physicians included time spent seeking authority approvals and insufficient maximum quantities for obese patients. In addition, respondents highlighted the complexity of PBS item codes, with

molecules ascribed multiple codes across various conditions and treatment settings.

4.1.4 Standards

Stakeholders outlined disparate regulatory standards and enforcement regimens applied to compounders, with TGA-licensed compounders adhering to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) standards, and non-TGA licenced compounders typically following United States Pharmacopeia (USP) 797 standards. A comparison of these standards as they pertain to the sterile compounding of (cytotoxic) drugs for administration to single patients by injection or infusion is provided in Appendix 14. Only TGA-licensed compounders are audited by the TGA, with apparently diverse auditing of non-TGA licenced facilities, depending on jurisdiction.

> *The Pharmacy Board of Australia allows compounding to take place under three scenarios. The first scenario is to comply with the full code of good manufacturing practice, which is the PIC/S document, 090, which has very little relevance in hospital or compounding. Then there is the PIC/S document, 010, Compounding in Healthcare Establishments—and that's a critical document. But they have also determined that we can work within the United States Pharmacopeia (USP), 797, Compounding of Sterile Products. That's a very detailed set of instructions prepared in conjunction with the FDA.*
>
> *The reason why the pharmacy board chose that as a standard, was that a lot of the retail pharmacists had joined up with an American compounding organisation called PCCA (Professional Compounding Centers of America) that sells a heck of a lot of raw materials and provides training and all that sort of stuff. And that is all, of course, compliant with the [USP] 797. So, a very large swathe of the community pharmacies know and realise the importance of 797.*
>
> *These documents are not contradictory—they can't be. […] The difference is the extent of regulation and surveillance that the industry people have to ensure that they comply. […] But in the end, all the practitioners are fully aware of this set of standards and they work to that very well. […] By and large, self-regulation in that area is very good.*
>
> *-Independent compounding consultant*
>
> *You have the Pharmaceutical Society of Australia with the compounding guidelines,*

and the professional practice standards. And then the board recommends that you adhere to either PIC/S or to USP 797 if you're doing sterile compounding. […] The pharmacy board doesn't audit [Hospital pharmacy] for compliance to either of those two standards—it's largely self-regulated. We consider ourselves to be 797-compliant. […] PIC/S really is for TGA-licensed compounders. […] Knowing what is required for TGA-licensed compounders, if any community pharmacy said that they were compliant to PIC/S, I think that'd be a stretch.

-Hospital pharmacy

But in the private hospital setting, there is also the hospital that has oversight as well. Usually when they're going through the hospital accreditation process, they'll investigate the compounding facility.

-Commercial pharmacy group

4.1.5 Complexity of service delivery

Representatives of the Department of Health provided insight into practical aspects of program delivery. The EFC is governed by the relevant legislative instrument (see Section 3.1). Any changes to the PBS legislation impacting the cost of implementation require approval of the Federal Cabinet. Some newly listed drugs—including subcutaneous medications—were reportedly difficult to place within the service delivery framework, as they do not fit readily within the Schedule 1 of the EFC's legislative framework. Such medicines have been placed on Schedule 2, despite not actually being considered 'related benefits' (i.e., they are alternative presentations of molecules that can be infused, e.g., trastuzumab, but are not intended as supportive therapies of Schedule 1 molecules, e.g., ondansetron). A government representative who is also a clinician mentioned that a drug's product information dictates how reimbursement will be made.

From a service-delivery point-of-view, decisions made elsewhere in the Department of Health, such as item coding, impact EFC implementation. For example, ascribing separate PBS item numbers for molecules in public and private settings has led to patient access issues (e.g., when patients begin cancer treatment in the public system and are subsequently moved to the private system, or vice versa). As a workaround, and to maximise patient access, Government administrators at the 'back-end' allocate all scripts to 'private' status to allow patients seamless access to prescribed medications

in private hospital, public hospital and community pharmacy settings.

> *When patients are in a public hospital and it's been claimed for the public hospital pharmacy—but they're expecting to get their medicines from a community pharmacy that can do compounding—then the 'private' item code is the correct one to use in that setting. Where they started in a public hospital […] it gets a bit more complicated when they go home and try to take that script to a community pharmacy. And there's actually been the reverse, where they started in a private hospital and there's a publicly funded clinic in their home town that they can use.*
>
> *-Government program administrator*

TGA-licensed compounders and hospital pharmacists outlined that provision of compounded cancer medicines is governed by contracts between providers and hospitals/pharmacies. These contracts are negotiated at the hospital/pharmacy-level and may be subject to different rates depending on the volume of services, among other factors. As these contracts are not necessarily negotiated with reference to PBS reimbursement amounts, there is a systemic disconnect between what is paid to external providers and what is reimbursed by the PBS.

Stakeholders had differing opinions on the effect of distributing cancer medicines to rural areas. One TGA-licensed compounder maintained that rural distribution was not necessarily more expensive than metropolitan distribution—rural distribution was often planned well in advance, whereas metropolitan distribution was frequently on short notice or after-hours, leading to additional costs to accommodate rapid turnaround. Representatives from a third-party logistics provider noted that the volume of goods is often more impactful than cost of goods or distance travelled, as there are economies-of-scale associated with the delivery of larger quantities. Distributors reportedly cross-subsidise costs between regions to ensure a more affordable service to rural customers. However, it was noted that rural supply was often more challenging due to having only one 'run' per day. Further, (third-party) delivery drivers and receiving personnel may not be aware of medicines' critical cold-chain requirements, leaving stock to spoil or expire on loading docks. While the majority of costs for lost stock are borne by the delivery company or purchaser, limited liability agreements may pass some costs on to distributors.

> *Interviewer: What about drug fees? Do you negotiate per item? Like, do*

> *you have a standard list of items you provide for chemotherapy compounding and how much you charge for them?*
>
> *Correct. We charge them an individual price per drug, negotiated by individual customers. […] The commercial terms can be different for different customers.*
>
> *Interviewer: So that allows larger customers to negotiate a better price for the drugs based on volume?*
>
> *Based on a whole lot of factors, but absolutely right. Based on efficiencies, cost to serve, all those pieces.*
>
> *Interviewer: Beyond the cost of the drug itself, would that also cover things like the logistics of getting the drug from your door to their door in a form that they can inject into the patient—that's all captured?*
>
> *Sometimes it's a standard fee. Sometimes it'll be broken up into multiple parts, and that'll depend on the particular customer, the particular devices that they want to use. Yeah, logistics, that sort of stuff will get in there.*
>
> *-TGA-licensed compounder*

Hospital pharmacists noted different levels of funding for pharmacies, determined by location. Two TGA-licensed compounders and a clinician added that additional fees include a wholesaler fee, which is paid by sponsors. A TGA-licensed compounder stated that as a third-party compounder, they can only claim the $20 compounding fee from the PBS. Any other money is claimed from the hospital or pharmacy that procured their services. TGA-licensed compounders added that the $20 CCPS fee is a non-indexed amount (introduced in 2012/2013), calculated on a per-item basis prepared in accordance with PIC/S guidelines.

Representatives from a community pharmacy member organisation, a clinician and a hospital pharmacist likewise mentioned the disparate reimbursement structure for private and public hospitals, and for different payers at various points in the treatment pathway. All of which potentially impact patient access to care, since treatment may involve multiple settings, payers and reimbursement systems (see Section 5.1.2 for further discussion of patient access).

> *The one thing on my mind is the issue around infusional drugs for public hospital inpatients—inpatients becoming outpatients and outpatients becoming inpatients. This is an issue in the clinical haematology space for a couple of drugs, but the big one at the moment is blinatumomab. […] The problem is this issue about reduced access for patients—the hospital feels it's paying for drugs that if the person was an outpatient, the Commonwealth would be paying for, and if they're an inpatient, the Commonwealth's view is that the hospital should be paying for it.*
>
> *It makes no sense at the patient or physician-level. And it leads to game-playing and to use of drugs not strictly per protocol. I think there are a lot of adverse consequences from that and I would wonder, particularly for a patient who might start as an inpatient but continues an infusional drug as an outpatient, which is the PBS bit and which isn't?*
>
> *-Clinician*

4.1.6 Challenges with EFC remuneration

Representatives from federal and state Departments of Health, community and hospital pharmacies, pharmacy and physician member organisations, logistics providers, and TGA-licensed compounders all claimed that extant EFC remuneration arrangements were inadequate for current activities undertaken throughout the EFC supply chain. Although the areas of concern were outlined by stakeholders, scant quantitative data to support these claims were presented as part of the consultation process. The limited data that were presented typically related to case studies of specific scenarios, rather than a systematic accounting of the costs of the activies involved in EFC activities that would have illuminated any discrepancies between those costs and the associated EFC reimbursement.

Issues raised with respect to EFC reimbursement included:

- A lack of specific coverage of various components directly required for EFC compounding, such as the cost of the device/container into which a cancer medicine is compounded;
- A lack of wholesaler and logistics provider fees (which is inconsistent with the fees paid for items reimbursed under other PBS sections);
- The reimbursement of logistics costs associated with delivery to rural areas;

- Payment for specialised staff training to undertake compounding;
- High costs associated with maintaining the sterile production environment required for the compounding of cancer medicines; and
- Costs associated with potential defects in the compounded product (e.g., particulates, discolouration), which require discarding of the dose. With emerging immunotherapies, in particular, such costs can be substantial and were anecdotally estimated (but not substantiated) to be in the millions of dollars each year for some compounding services.

> *The current remuneration arrangements are not commensurate with the increased costs incurred in the compounding and dispensing of EFC medicines, including the higher average cost of the medications, the additional investments required in extended stability studies, increased operating costs, and the resultant costs when compounded EFC medicines cannot be administered to patients.*
>
> *-Pharmacy member organisation*

Stakeholders noted service viability risks associated with the provision of cancer medicines services in rural areas, particularly with respect to higher risk of damaged goods, wastage due to dose changes, and non-payment of claims due to changes in treatment. Additionally, Close the Gap (CTG) concessions are not available in public hospital pharmacies, with potential impact on patient access.

> *CTG co-payment concessions are available in private hospital and community pharmacies, but not public hospital pharmacies. This does not align with community expectations of continual/consistent care across services.*
>
> *-Hospital pharmacy*

Exclusion of wholesaler costs

Stakeholders noted that chemotherapy drugs are not covered under the existing Community Service Obligation (CSO) that applies to other areas of the PBS. The CSO requires that participating wholesalers adhere to prescribed timeframes for medication delivery, for which they are remunerated under the PBS fee structure. The CSO ensures that pharmacies have access to the full

range of PBS medications regardless of their location. However, there is no equivalent to the CSO for cancer medicines, even though these drugs are as time-critical, if not more so, than many (s85) general schedule drugs.

> *As a Section 100 PBS program, unless dual-listed, EFC medicines are not covered by the CSO. This means there are no formal controls to manage either the timeliness of delivery or to ensure the chemotherapy medicines are delivered at the agreed price to pharmacy.*
>
> *-Pharmacy peak body*
>
> *EFC medicines supplied to [TGA-licensed compounder] by wholesalers are excluded from the pool of funding that is made available to full-line wholesalers under the CSO. Many new EFC medicines are high-cost, and this has a flow-on impact in terms of the costs of their safe storage, distribution, and supply, as well as the potentially increased financial risk in terms of their purchase and sale through the supply chain. It is vital that wholesalers are appropriately funded to ensure timely access of EFC medicines to patients throughout Australia.*
>
> *-TGA-licensed compounder*

As cancer medicines are not covered under the CSO, wholesalers do not receive payment to stock these drugs. As previously noted, AHI fees are inconsistent between EFC and non-EFC drugs, despite similar administrative and labour costs in ordering and dispensing, and fees differ according to dispensing setting.

> *The 6th CPA introduced the AHI Fee which recognises the administration, handling and storage costs entailed in dispensing medicines by the pharmacy, including associated infrastructure. The AHI is a three-tiered fee based on the AEMP of the allowable maximum quantity of the PBS medicine. While this works well for most PBS medicines, which are dispensed in packs, it results in significant reductions in the AHI that is paid to chemotherapy pharmacies. The AHI for chemotherapy infusions is paid on the proportion of the allowable maximum quantity, rather than*

the AEMP of the actual prescribed dose.

Depending on the volume of the prescribed dose and the AEMP of the maximum quantity of the EFC medicine being supplied, the 'proportion of the maximum quantity' approach can mean that chemotherapy pharmacies receive an AHI fee that is a fraction of the AHI fee that is paid for non-EFC items with the same AEMP. The AHI fees that are payable for two EFC items with the same or similar AEMPs can be significantly different because of the 'proportion of the maximum quantity' approach.

In addition, if there is an upward change to the allowable maximum quantity, the AHI fee that is paid under the 'proportion of the maximum quantity' approach reduces accordingly, although the cost of the medicine, and the risk, cost and work entailed remain unchanged. This issue should be addressed in the review by basing the level of AHI that is paid on the AEMP of the actual dose prescribed.

-Compounder member organisation

Pharmacy services

It was noted that additional pharmacy services occur 'around' the compounding itself, which are important to the delivery of chemotherapy but are not specifically reimbursed (e.g., costs associated with checking the compounded product, providing clinical advice at the point of dispensing).

A hospital pharmacist also noted additional costs associated with dispensing compounded medications, such as clinical quality services that are not directly reimbursed by the EFC (although it must be noted that in the case of hospital pharmacies, these may be covered under a pharmacy cost centre as part of routine clinical services). Representatives of a pharmacy member organisation additionally noted that costs specifically associated with the disposal of cytotoxics can be a significant burden to community pharmacies but are not covered under the EFC.

Pharmacies that supply chemotherapy, that are part of the hospital, they're more likely to have an advanced clinical waste disposal arrangement in place for everything—you know, biological, cytotoxic, the whole works. The smaller pharmacies don't have those arrangements in place. […] I probably have the

normal drum disposal, but that doesn't allow cytotoxics.

[…] If they're doing vaccinations, they would have sharps disposal, but they don't have the special cytotoxic disposal arrangements. Now, that is well and good if you're buying [compounded medicines] from a third-party provider, […] but again, if for some reason the dose changes and you're stuck with this infusion, what do you do with it? I even know from prior experience of patients trying to return cytotoxic medicines to a pharmacy that they got from a hospital—you know, they've gone to the major centre and they come back. I think pharmacies may be putting those sorts of things into the drum bin when they shouldn't because they have no other means of disposing them.

-Pharmacy member organisation

Hospital pharmacists and a TGA-licensed compounder added that it was a challenge to estimate the exact cost of providing cancer services, especially with regards to dispensing EFC medicines, as there is an overlap of these and other services provided by health facilities.

Stability studies

Multiple stakeholders discussed the issue of stability studies. TGA-licensed compounders argued that it was imperative to undertake rigorous stability studies to extend the expiry of compounded products from the default 24 hours, to several days or even weeks, which is critical to maintaining access to cancer medicines in rural areas. However, stability studies—which are expensive—are not explicitly reimbursed by the EFC (though may be captured within the CCPS fee).

Reducing the level of wastage of chemotherapy medicines with longer shelf lives is highly relevant to regional locations where usage levels are, on average, likely to be lower. Providing regional chemotherapy providers with access to medicines that have been compounded to a quality standard that allows an extended stability, can enhance patient access, lowers the cost of supply, and reduces wastage. Several Australian and overseas studies have demonstrated the benefits of extended stability, including studies in regional hospitals. It is in the interests of all stakeholders for valid stability data to be available to compounders, including data

> *held by manufacturers, and that the additional costs incurred by TGA-licensed compounders in conducting extended stability studies, including for newly listed high-cost medicines, are recognised in the EFC arrangements.*
>
> *-Compounder member organisation*

All compounders reiterated that stability testing—and resulting extension of product expiry dates—is critical in enabling access to compounded cancer medicines in rural locations. TGA-licensed compounders and an independent compounding consultant reported that as stability studies are expensive (variously reported between $50,000 to $100,000 per study) and not explicitly reimbursed, studies are mostly undertaken for drugs with high demand and a robust anticipated return on investment.

> *A typical stability study will take at least six months and the companies […] have to try to estimate what the value of compounding that drug would be. Bearing in mind, the typical stability study is about $40,000, probably $50,000 by now. You have to make a value judgment about whether or not you're interested in providing that drug at all. And you need a fair volume of work before you can justify it.*
>
> *-Independent compounding consultant*

Notwithstanding concerns expressed by several drug manufacturers concerning the application of extended expiry to their products (i.e., beyond manufacturers' own product information), regulatory experts confirmed that once compounded, a given infusion preparation is considered to be a 'new' product (i.e., just manufactured) by the TGA and is therefore eligible to receive an extended expiry date (given stability studies are conducted to exacting standards). The potential to attach extended expiry dates to compounded products subject to stability testing thus affords TGA-licensed compounders a competitive advantage in the supply of cancer medicines.

Exclusion of some compounded items

Stakeholders noted that compounding of some products for non-IV and/or non-cancer use (e.g., rituximab) was not funded by the EFC despite the preparation being very similar in some cases. In the

specific case of azacitadine, which requires daily preparation over seven days due to its extremely short expiry timeframe, only a single compounding fee is reimbursed.

> *There are several chemotherapy or cancer medicines that remain outside the EFC although their preparation, dispensing and administering involves a similar level of complex work and oversight in a safe and sterile environment. All these medicines, such as azacitadine, should attract fees for dispensing, reviewing, preparing, and distributing, which reflect their complexity and high-risk nature.*
>
> *Similarly, there should be recognition of the costs entailed in safely dispensing highly toxic oral therapies. Finally, there is a need to recognise the additional costs when a dose cannot be given in one infusion and is split due to dosing requirements into two or three components, which should all be reimbursed.*
>
> *-Compounder member organisation*
>
> *The main challenge is that non-EFC infusible medications are still required to be compounded in the same manner as the EFC items (for example azacitadine, sub-cutaneous rituximab and trastuzumab). However, the current level of remuneration does not support this service. This results in the preparation being provided at an unrecoverable cost to the pharmacy or at the safety risk of the nurse if prepared on the ward/infusion centre.*
>
> *-Commercial pharmacy*

One TGA-licensed compounder suggested that infusions prepared for the Life Saving Drugs Program (LSDP) be captured under the EFC. Interviews with community pharmacies confirmed issues related to the lack of funding for azacitadine, subcutaneous rituximab and subcutaneous trastuzumab, which all require similar preparation to IV cytotoxics but are not reimbursed for compounding.

> *I think that with some of the newer MAbs, they probably don't recognise that with the funding and whether they sit on the EFC or not. There's a bit of a gap. […] You'll get the subcut trastuzamab and rituximab—which are now being probably phased out in the next couple of months—but they came out and the nurses straightaway*

wanted us to compound them. And we wanted to compound them, but there was no funding to support that. […] Azacitadine's another one, where it's not funded, but who would compound that without having it in a proper facility. It puts us in an awkward situation. But we would always recommend that they're compounded within that sterile facility—for both user protection and to protect the product itself.

-Commercial pharmacy

The Efficient Funding of Chemotherapy is basically dispensing fees to recognise the specialist nature of preparing chemotherapy. Azacitadine is not a drug that's included on that formulary. However, it's required to be specially prepared. It is cytotoxic, special handling is required, and that is stated in the product information from the company. We have to reconstitute vials with water for injection, we have to calculate individual patient dosages, and put it into two syringes for subcutaneous administration. It has a very short expiry—eight hours, up to 22 hours if you use refrigerated water for injections. And it needs to be compounded every day for a seven-day cycle.

The current rate of reimbursement from the PBS as it stands in the general schedule under Section 100 is $2,240 for 14 vials. So that's a standard seven-day treatment—two vials a day, seven days. The cost of the originator brand Vidaza is $156 a vial and that equates to a total wholesale cost of $2,192 [sic]. After the cost of goods, you have $47 that remains that doesn't even cover the cost of compounding day-one of the cycle, let alone the remaining six days.

So, the pharmacy makes the remaining six days of treatment with no reimbursement and, therefore, we compound at a loss for these patients. Considering the specialist nature of it, it should attract that EFC funding. So that's $127 per day we should be reimbursed on top of the cost of the drug.

-Commercial pharmacy

Compounding facilities and fees

Stakeholders noted that the $20 CCPS fee available to TGA-licensed compounders is not available to non-TGA licensed compounding pharmacies (seen as unfair by hospital pharmacies) and is not indexed (raised by TGA-licensed compounders). Stakeholders felt that fees should be consistent between providers and indexed. When asked about the composition of the compounding process, a group of TGA-licensed compounders enumerated the following considerations:

- Costing the processes and resources involved in compounding should be the same for all drugs;
- Costing should start from when the medicine is prescribed, through to compounding and administration to the patient;
- Costs attributed to labour should specify the type of labour and level (i.e., technical qualification) of that individual; and
- Costing should incorporate the yearly reviews of PIC/S, which serve to expand safety guidelines and require additional work.

Representatives from three hospital pharmacies mentioned that setting up and running a compounding facility was resource (i.e., labour and financially) intensive. There are capital costs involved in setting up and managing such a facility and in training people to do the work. Representatives from a TGA-licensed compounder, industry, clinical, and community pharmacy groups added that logistics for compounding included, inter alia, leasing the space, facility setup, validation processes and disposal of cytotoxic waste. One TGA-licensed compounder added that TGA-licensed compounders spend money to maintain strict quality standards to which hospital and community pharmacists are not audited.

> *In general, over the years, we have seen the cost of adhering to TGA-level quality goes up—and I am not overcooking it—in almost every review, there's a significant cost increase to adhere to TGA-level standards. […] The newest particle monitoring that I showed you—that was over a million dollars across the network. The prepping with hydrogen peroxide, that's $600,000 in materials, nearly $2 million in labour. These additional steps of the process and additional requirements certainly add to the cost of the operation.*
>
> *-TGA-licensed compounder*

Representatives of a commercial pharmacy group elaborated on the role of (s90) community pharmacies vs (s94) hospital pharmacies, and differences between fees for TGA-licensed and non-licensed facilities (see Section 3.2.4). Privately owned pharmacies receive revenue from PBS claims, rather than from a hospital's overall budget (see Section 3.2.2), hence different claim values can have significant impact.

> *We've got [more than 20] pharmacies, I'd say more than half of that would be (s94) and the remaining will be (s90). […] They are mainly in private hospitals. It's just how they're licensed. A large hospital facility—150 beds or more—you can usually get an s90 license. Or it may be the case that a community pharmacy license was purchased and moved into the hospital historically, versus a smaller facility where you can only get access to an (s94).*
>
> *[…] For example, we've got a service […] that's an (s90) license. So, technically, it's a community pharmacy. But we know it's really a hospital pharmacy, and it's there predominately for the hospital. It's there for the community, but we don't really get people coming in just off the street—they tend to come as outpatients for specific medicines. In that sort of environment, where there's a lot of choices, they usually go to outside pharmacies […]. We sort of think about community pharmacies more like hospital pharmacies, just licensed differently. […] In some of these [s90] settings, we actually service smaller hospital facilities that don't justify having a pharmacy on site.*
>
> *-Commercial pharmacy group*

Alternatively, a public hospital representative noted some third-party providers offer a full suite of services on a contract—from processing of PBS scripts to provision of compounded drug—negotiated directly with each health service and with no standardised pricing.

> *The other workaround is to get a private pharmacy to process your PBS scripts for you. There's a couple of big players in this field. As well as the compounding/manufacturing side, they offer a PBS scripting and processing functionality as well. They also have a registered pharmacy as part of their business. And they offer this all-in-one model as part of your contract with them.*

> *They coordinate getting the scripts from the doctors, processing them, ordering the drugs. They facilitate that and coordinate with the doctors on site, the pharmacist on site if there are any. It's a very good model in that they provide this all in one service, but it's really down to each individual hospital or LHD, to negotiate their own terms and conditions of those contracts.*
>
> *There isn't, you know, for example, a state-wide contract, where you notice a certain level of services agreed across the board. I know from talking to colleagues across the state, there are very different levels of service negotiated in those contracts and provided and therefore the rebate that is negotiated as part of that contract is very different as well.*
>
> *From a private pharmacy perspective, it's a very lucrative business for them, getting all those scripts, because cancer treatments are quite expensive. […] They do agree to a certain percentage of rebate with whomever that contract is negotiated, but it's down to your own negotiating skills as to what you get.*
>
> *-Public health service*

Several written submissions to the Review implied that the compounding of emergent immunotherapies was more technically challenging and EFC fees should take complex, high-cost immunotherapies specifically into account. However, it was unclear from that input how the compounding of immunotherapies or its associated costs differed from that of small molecule chemotherapies. When queried in interviews, TGA-licensed compounders, community pharmacists and representatives of a commercial pharmacy group agreed that there is no difference in how the newer MAbs are compounded relative to the older cytotoxic drugs and may be safer from an operator perspective.

> *We basically treat MAbs in the same way as the older cytotoxics in terms of safety, and sterility so we will still compound them in the sterile suite. There are some hospitals that have nurses doing some of the MAbs themselves, maybe with a closed system-type design. But we don't recommend that anywhere because of the unknowns with MAbs. Theoretically, they may be safer to handle, but I don't think*

it's clear cut enough to recommend that to anyone; we just treat them all the same.

-Commercial pharmacy group

The macromolecules, or the proteins really, of the newer agents, they do not pass skin barriers or GI tract barriers. Except for the one or two which are conjugated with an existing cytotoxic drug, they pose no hazard. And all that causes a bit of a problem for people in hospital pharmacy, who initially treated them as though they were cytotoxic agents and became used to compounding them in their cytotoxic drug safety cabinets. That was fine until it was recognised that they were not an occupational hazard.

-Independent compounding consultant

4.2 Evidence from the literature on approaches to the efficient funding of cancer medicines

A systematic literature review was undertaken to explore current and alternative models for the provision and funding of cancer medicines (for a discussion of the literature review methodology, see Appendix 3). Included studies discuss the minimisation of costs and wastage associated with the practices of:

- Prescribing cancer medicines, including dose-rounding and dose-banding
- Optimisation of vial contents in the preparation of multiple doses (i.e., vial-sharing)
- Administrative and technological practices associated with the preparation and use of cancer medicines

In addition, the literature review included evidence from time-and-motion studies that explore the costs associated with the acquisition, preparation and delivery of cancer medicines.

4.2.1 Efficiency in prescribing cancer medicines

Dose-rounding

Nine publications addressed the potential for dose-rounding as a measure to reduce the costs of cancer medicine use. In short, these studies—reflecting practice in Australia and abroad—note that

the practice of dose-rounding can be used to reduce the costs associated with cancer medicine prescribing (for a given funding model). Importantly, the studies do not necessarily address the impact on treatment efficacy or safety, making the implicit assumption that dose-rounding (within a margin of 5-10% of the prescribed dose) can be done safely and without adversely impacting patient outcomes (for further discussion of patient safety issues, see Section 5.2.2).

International publications: Chillari et al. looked at the potential for dose-rounding of BSA-dosed anti-neoplastic agents as an effective cost-containment strategy for a small volume oncology clinic [11]. Results showed a 3.8% theoretical reduction of drug cost if the calculated drug doses were rounded down by 5% compared with unrounded doses. Assuming 10% of total doses were rounded, the study reported an estimated theoretical cost saving of 5.2% compared with no dose-rounding. The authors concluded that a dose-rounding protocol for anti-neoplastic agents is associated with significant savings even for a small volume clinic.

Similar results were reported by other retrospective chart review studies estimating potential cost savings by hypothetical down-rounding of MAb doses. Assuming theoretical dose-reduction to the nearest vial size of a maximum 5%, Copur et al. estimated an average actual reduction in costs of 2.4% and 4.8% [12]. Francis et al. estimated the cost saving associated with dose-rounding protocols for three MAbs (cetuximab, bevacizumab and trastuzumab) at a single tertiary care institution for low-income patients [13]. The total annual monetary savings were estimated at US$181,944 or US$337,755, depending on the rounding limit used, accounting for between 1.5% to 2% of the institution's cancer medicines budget. In a three-month retrospective review of chemotherapy checklist and medication orders, Winger et al. estimated cost savings related to dose-rounding for adult biologic anticancer drugs [14]. Results showed that dose-rounding within a value of 10% of the biologic anticancer drugs aldesleukin, bevacizumab, cetuximab, denileukin diftitox, gemtuzumab, rituximab, and trastuzumab could reduce wastage (defined as the unused volume of drug not utilised for another dose prior to its expiration) for 42% of the orders, with associated potential savings in drug expenditure.

Jarkowski et al. estimated cost savings with dose-rounding of ipilimumab in patients with metastatic melanoma [15]. Dose-rounding of ipilimumab to the nearest 50 mg demonstrated potential to reduce overall wastage by 8% and costs by US$155,400 for the 63 doses of ipilimumab administered during the study period (March 2011 to February 2012).

In a retrospective chart review, Patel and Le compared the potential deviation from the prescribed dose to the rounded dose for rituximab over a two-year period [16]. The study reported 99% of all

rituximab doses fell within a 10% dose-deviation if rounded to the nearest 100 mg vial size and 66.1% of all rituximab orders fell within a 5% dose deviation. On balance, rounding doses down would have generated a yearly saving of approximately US$37,000, while rounding up would entail an additional cost of approximately US$43,000.

Australian publications: Results consistent with international literature were reported in an Australian study conducted by Dooley et al., who explored the potential impact of dose-rounding in five cytotoxic agents (docetaxel, liposomal doxorubicin, gemcitabine, oxaliplatin and vinorelbine) [17]. Results showed a statistically significant cost saving between the rounded and calculated acquisition cost for each agent.

In a review of cost saving initiatives, Gilbar and Davis compared flat and BSA-based dosing strategies for PD-1 and PD-L1 inhibitors [18]. The study concluded that flat or set dosing of PD-1 and PD-L1 inhibitors was not suitable for a 'one-size-fits-all' model due to significant variation in mean body weight between men and women and across countries. Instead, the author's preferred dosing strategy entailed using a range of pre-determined dosing levels up to a capped maximum. The study advocated greater use of vial-sharing and for the pharmaceutical industry to provide a range of vial sizes that more closely aligned with dosing requirements [18].

In a prospective analysis of oxaliplatin utilisation data from four Australian hospitals (Australian Comprehensive Cancer Outcomes Research Database), Field et al. estimated theoretical cost savings with dose-rounding within 10% of a 150 mg dose of oxaliplatin [19]. The dose-rounding protocol was applicable to 66 stage III or IV colorectal cancer patients between 2003 to 2008. Assuming oxaliplatin doses were rounded down to 150 mg, the authors estimated potential cost saving of AU$51,898 for the four hospitals over one year. Extrapolated to the Australian population, the estimated drug cost savings would be some AU$2.5 million per year. In addition, the study investigated attitudes to chemotherapy dose-rounding among medical oncologists employed at the four hospitals. Survey results showed three of nine (33%) oncologists were comfortable with an initial dose reduction of up to 10% in the adjuvant disease setting, and seven of nine (77.8%) in the metastatic disease setting.

Dose-banding

Five publications reflected international practice reported on mechanisms for the introduction of dose-banding and its potential impact on the costs of cancer medicines. These studies demonstrate that the introduction of dose-banding has the potential to reduce discarded drug wastage and other costs associated with the preparation of cancer medicines. However, as each of these studies pertain to practices at the clinical/pharmacy level—rather than a system-wide adoption of such strategies— the

extent to which these practices could be adopted uniformly remains unclear.

International publications: Chiumente et al. compared three scenarios of IV chemotherapy preparation [20]. Daily preparation of 13,490 individualised bags at the hospital pharmacy (Scenario 1) was compared with dose-banding (weekly preparation at the hospital pharmacy of non-individualised bags containing discrete, predefined doses covering an adequate range of doses) (Scenario 2) and the use of commercially ready to use bags based on the same approach as dose-banding (Scenario 3). The results of the analysis were presented as cost per patient for the selected drugs included in the analysis (gemcitabine, oxaliplatin, paclitaxel, trastuzumab, and 5-fluorouracil). The estimated cost per patient was based on cost of professional time involved in drug compounding (nurse and specialised laboratory technician), ex-factory cost of drugs per mg in 2019, cost of medical devices required for drug compounding (EUR5 per therapy) and administrative costs including depreciation and maintenance of premises and equipment and cost of disposal of cytotoxic waste (EUR4 per therapy). The analysis of time needed for compounding was based on the operational steps according to an activity-based costing (ABC) method. The following operational steps were included in the analysis of the individual drug preparation: pharmacy validation and laboratory entry, preparation of laboratory materials, internal laboratory (laminar flow cabinet) entry and exit followed by packaging. The authors estimated the average (min, max) time needed at each step [20].

The results reported by Chiumente et al. identified 10 dose bands for gemcitabine, 6 for oxaliplatin and trastuzumab, 9 for paclitaxel and 8 for 5-FU, with feasibility values ranging from 46% to 94% [20]. The estimated mean time needed for compounding a single dose varied by drug and dose preparing scenario: 21 minutes for gemcitabine to 40 minutes for 5-FU and trastuzumab in Scenario 1; 2.7 minutes for gemcitabine to 4.7 min for trastuzumab in Scenario 2; and times were not reported for Scenario 3 which involved commercial purchases. Given the difference in associated times, the study reported total savings associated with dose-banding according to Scenario 2 of €281,058 or €402,468 for Scenario 3, both compared with Scenario 1 [20].

Claus et al. estimated the impact of logarithmic dose-banding of anticancer drugs on pharmacy compounding efficiency [21]. The study collected data on lead time of preparation (defined as time between receipt of prescription and readiness for transfer) spanning over 2 weeks, followed by a simulation analysis of future storage possibilities for the selected anticancer drugs that could be batch produced in advance. The analysis was conducted assuming two scenarios: (1) a maximum storage scenario where all preparations in 2015 were rearranged per band and only physiochemically stable dose-banding preparations (mid-band-doses) with relative incidence of at least 2% recurrent monthly prescription were retained; (2) a 'safe' storage scenario using the conditions of maximum storage

scenario but further corrected for the lowest prescribing amount within the documented shelf-life and calculated per month. The results were presented as a difference in pharmacy working hours (full time equivalent - FTE) between the actual situation and the future forecast. The mean lead times for dose-banding storage and just-in-time preparations respectively were 17.3 min (95% CI: 13.5 – 21.0) and 26.5 min (23.3 – 29.8). A total of 15 drugs had stability data of at least 7 days and monthly prescriptions (bevacizumab, carboplatin, cisplatin, docetaxel, epirubicin, 5-fluorouracil, gemcitabine, irinotecan, methotrexate, oxaliplatin, paclitaxel, pemetrexed, rituximab, IV trastuzumab and vincristine) across 21,164 prescriptions in 2015 [21]. Claus et al. reported that of the medicines included in the analysis, 85 different strengths could be stored with a stability varying between 7 days (vincristine) and 6 months (trastuzumab) [21]. There was a mean preparation time with dose-banding of 0.99 min for one infusion bag and 2.56 min for one infusion pump. The study concluded that the existing pharmacy FTE in 2015 of 5.41 could be reduced to 4.91 under the safe storage scenario and 5.27 under the maximum storage scenario [21].

Baker and Jones conducted a prospective audit on the use of cyclophosphamide, methotrexate, and 5FU at two outpatient cancer clinics in the UK from April to September 1994 [22]. Subsequently, the authors performed two audits: the first on the capacity to reissue drug, the second to develop a system for the rationalisation of chemotherapy prescribing using dose-banding. The results of the re-issue audit showed that 13.5% of treatment courses were deferred (i.e., the drug had not expired, the integrity of the containers was intact and it could be reissued safely to another patient). All deferred chemotherapy was reissued, amounting to a saving of GB681 over the 6-month period of the study. The results of the second audit showed that allowing a 5% variance from the dose prescribed enabled prefilled chemotherapy syringes to be supplied, with no more than two syringes being used per dose. The authors concluded that the use of prefilled syringes according to dose-banding improved patient waiting times, reduced drug wastage, and has enabled rationalisation of chemotherapy services in this health district [22].

O'Leary et al. conducted an analysis of the impact of dose-banding for parenteral chemotherapy on haematology-oncology day ward practices [23]. The study applied Kotter's 8-step change management model to structure the implementation of dose-banding of 5-FU 46-h infusers on the haematology–oncology day ward. The impact of dose-banding on local practice was assessed through pre-and post-implementation surveys of stakeholders. The results showed a generally favourable attitude towards implementing changes in the parenteral chemotherapy supply system, albeit focused on 5-FU within one centre, with some resistance to change evident. That resistance appeared to reflect concerns at that institution over the practice of outsourcing for the supply of

dose-banding product and whether the benefits of dose-banding would necessarily apply to all products for which it could be carried out.

4.2.2 Efficiency in preparing cancer medicines

Vial-sharing

The Review examined 10 international publications on the practice of vial-sharing—either as a means of reducing wastage, or how vial-sharing has impacted costs associated with the preparation of cancer medicines. Overwhelmingly, these studies indicated that the practice of vial-sharing reduces discarded drug, resulting in lower costs. However, the capacity to vial share is influenced, inter alia, by the vial sizes in which cancer medicines are provided and product stability. Thus, approaches to vial-sharing with respect to workflow processes may need to be flexible across different cancer medicines.

International publications: Gopisankar et al. investigated drug loss (i.e., discarded wastage) and associated drug cost savings with chemotherapy drugs (predominantly generic products) at an oncology day-care unit in India [24]. During a 3-month period, an estimated 19.72% (95% CI: 14.5% – 24.9%) of dispensed drug was discarded solely due to vial size, with an average amount discarded over one year of 17.14% (95% CI: 14.69% – 19.58%) of total drug used. The authors concluded that the most important factor affecting drug loss was the availability of different vial sizes; drugs with only one vial size were more frequently mismatched with prescribed doses, resulting in higher wastage costs. Vial size was positively correlated with drug loss, while BSA and weight were negatively correlated with drug loss. The authors estimated that if vial-sharing had been implemented, there would be a 9% reduction in wastage [24].

Hyeda and da Costa investigated the use of centralised drug preparation units as a strategy to reduce chemotherapy waste [25]. The study defined wastage as the volume of discarded drug in excess of the prescribed dose, resulting in toxic waste. The potential of a centralised model to reduce wastage was evaluated through an hypothetical model assuming all chemotherapies were administered in the same clinic on the same day. Prescription data at seven oncology clinics in Brazil were used to estimate the amount of discarded wastage as the difference between the prescribed dose and commercially available vial sizes, assuming vial-sharing. Results showed a 65-fold potential reduction in the volume of waste and a 35-fold reduction in the cost of discarded drug based on a centralised chemotherapy preparation model. Additional benefits of centralisation included improved management of chemotherapy waste and medical prescriptions, standardisation of medications with more convenient commercial presentations, early planning of the week's anticipated treatments and improved process quality control. Several other benefits of centralised chemotherapy preparation

were noted, such as mitigating expenses related to the management of high-cost medication stocks, product expiry, improving safety, and avoiding delay to the start of treatment due to the lack of prepared infusions. Factors enabling the implementation of the centralised model included having logistical support and efficient communication, proximity of the chemotherapy preparation unit to the clinic, and defining the minimum coverage of the centralised chemotherapy unit [25].

Jang et al. estimated the amount of drug wastage (defined as the volume of unused drug leftover in vials after preparation) based on real-world utilisation data for pembrolizumab [26]. The authors estimated that adopting vial-sharing using 100 mg vials would reduce wastage by 15.25%. These findings were supported by other studies assessing the volume of pembrolizumab wastage, ranging from 11.89% (Bach et al.) to 24% (Hess et al.) for 100 mg vials and 13.2% with both 50 mg and 100 mg vials available (Hatswell & Porter) [27]. However, the variation in the calculated reduction of wastage reported in these studies may be contingent upon the underlying indications for use (i.e. non-small cell lung cancer and melanoma).

Combining data from clinical trials and the general population, Hatswell and Porter estimated the optimal vial sizes to reduce wastage for pembrolizumab and cabazitaxel [27b]. The results showed the optimal estimated combination of vials for pembrolizumab was 70 mg and 100 mg (compared with 50 mg and 100 mg vials), reducing projected wastage from 13.2% to 8.7%. Adding a smaller vial size (12.5 mg) to the existing cabazitaxel vials (60 mg) had the potential to reduce wastage dramatically from 19.4% to 6.5%. The study noted that where the larger vial was perfectly divisible by the smaller vial, wastage was higher. Therefore, having vial sizes that are not divisible can create more combinations with less wastage. The study concluded that wastage of pembrolizumab and cabazitaxel could be substantially reduced without increasing the mean number of vials administered.

Liran et al. conducted a real-world analysis of the costs of drug wastage, which reflected vial-sharing among some patients, at an Israeli hospital pharmacy [28]. The authors estimated that the total cost of drug use for the period of observation (March 2016) was US$2,763,016, of which US$141,196 (5.11%) was due to wastage. Extrapolating, this resulted in an annual wastage of US$1,694,352. Five drugs accounted for the highest cost associated with wastage (68% of the total)—bortezomib, trastuzumab, azacitidine, pemetrexed and carfilzomib. Cabazitaxel accounted for 42% of wastage volume, followed by methotrexate (40%) and trabectedin (27%).

Matsuo et at. conducted a retrospective hospital chart review to estimate the effect of optimising cancer drug vials (through vial-sharing) on medical costs in Japan [29]. The authors calculated the total quantities and costs of each drug used on a daily basis, along with the minimum cost for

specified individual drugs prepared using vial-sharing for patients treated in December 2017. The results showed that drug costs for individual vials and vial-sharing preparation were US$3,305,595 and US$3,092,955, respectively. This represents a difference of US$212,640 for the 1-month study period and an annual difference of US$2,551,680. The authors concluded that the annual spending on all cancer drugs in Japan could be reduced by 6.4% if vial-sharing was implemented [29].

Smith conducted a retrospective review to estimate the cost savings associated with vial-sharing options for the compounding of cytotoxic drugs [30]. Based on cytotoxic drug use over two years (2012-2013), four scenarios were compared: no vial-sharing or batching, vial-sharing or batching on a single day (wastage discarded at the end of the day), vial-sharing per week and vial-sharing on a rolling 7-day schedule (wastage carried over for six days, as permitted by stability). The results showed that the pattern of wastage was the same in both years. Vial-sharing with a single vial size being kept on a Monday to Friday was the most costly option, closely followed by the option of no vial-sharing or batching, using the full range of vial sizes. The option to vial-share or batch all doses on the same day led to a decrease in wastage of nearly 40% in 2012 but only a 30% wastage reduction in 2013 compared with the no vial-sharing option. Results for the number of vials showed that no vial-sharing used the largest number of vials and vial-sharing on a rolling 7 days used the least number of vials. The author noted that switching from one uniform compounding method to another for everything would not result in the best wastage outcome for all preparations. In both 2012 and 2013, trastuzumab, infliximab and 5-FU preparations would benefit from vial-sharing on a 7-day rolling basis. However, cetuximab, dacarbazine and bevacizumab preparations would be more cost-effectively compounded by having the full range of vial sizes and batching on a single day [30].

Rustemi et al. conducted a retrospective review of hospital prescription data to estimate cost savings associated with bortezomib vial-sharing at the University Hospital Center 'Mother Teresa' Tirana, Albania [31]. The study compared drug utilisation using individualised preparation (January 2015 to June 2015) with vial-sharing (January 2016 to June 2016), showing a reduction in per-cycle costs per patient of €226.81 (25.96%). This was associated with drug wastage for individualised drug preparation of 162.89 mg across 179 patients. The estimated total cost of bortezomib wastage for individualised preparation was €40,646.17. The estimated total cost of drug wastage under a vial-sharing model was €2,541.47, a difference of €38,104.0, or 46.63 vials of 3.5 mg bortezomib. The authors concluded that vial-sharing resulted in cost savings allowing the administration of 62 additional individualised preparations of bortezomib (January 2016 to June 2016) for the same initial budget [31].

General Approaches to Minimise Wastage

The Review included two international and two Australian publications that focus on general approaches to minimising wastage associated with the preparation of cancer medicines. Strategies include better aligning vial sizes with anticipated prescribed doses, making dosages less dependent on patient-specific factors, centralisation of compounding and dose preparation, re-issue of drug that would otherwise be discarded, and organisation of stock ordering systems to align drug stocks with patient needs.

International publications: Nass and colleagues from the Centers for Medicare & Medicaid Services (CMS) and the National Academies of Sciences and Engineering conducted a review of federal health care costs, safety and quality concerns associated with discarded drugs resulting from weight-based dosing of medicines contained in single-dose vials [32]. The review presented the following overarching recommendations:

- Drug developers, health care providers and payers should reduce inefficiencies in drug development, delivery and payment systems that lead to excess costs for both the health care system and for patients, rather than trying to recoup payment associated with discarded drugs. Efforts should focus on the goals of promoting the effective, efficient and safe use of infused or injectable drugs, and implementing an efficient and effective reimbursement system for the clinical administration of infused or injected drugs. This includes encouraging manufacturers to develop trials that present evidence on the use of fixed-dose formulations, and potentially introducing technologies that allow single-dose vials to be used safely across multiple patients.
- Drug manufacturers should be required to produce injectable and infused drugs in multi-dose vials when it is safe to do so.
- Uncouple add-on payments to clinicians for infused and injected drugs (currently a feature of the reimbursement system in the USA). The focus should be to design and evaluate new payment models that reimburse health care providers by treatment episode, rather than by the volume or cost of a drug vial.
- The use of a 'justified-wastage' modifier should be discontinued due to issues related to inconsistent and fragmented use across the practices, which compromises estimates of discarded drug amounts and their associated payments.
- Potential rebates occurring in the system as a result of legislation or regulatory action should be directed first to cover patients' out-of-pocket expenses for discarded drug and thereafter to health care providers and payers. [32]

Fasola et al. showed that the financial loss due to wastage of six drugs (cetuximab, docetaxel,

gemcitabine, oxaliplatin, pemetrexed and trastuzumab) accounted for about 5% of annual expenditure at a centre in Brazil [33]. Drug wastage was minimised by four corrective measures: a rational, by-disease organisation of chemotherapy sessions over the course of the week; the use of multi-dose vials; reasonable rounding of drug dosages; and selection of the most appropriate vial size, depending on drug-unit pricing. The authors demonstrated that the management of waste in a centralised medication preparation unit may reduce chemotherapy costs by 45% in two years of monitoring.

Gilbar et al. identified numerous injectable cancer drugs that are amenable to strategies for reducing expenditure and avoiding drug wastage [34]. The study used a survey, as well as available regulatory documents, to collect data from pharmacists from 20 countries on drug form, availability and stability. The study observed the following:

- The availability of cancer drugs was highest in Australia and Germany (97.8%) and lowest in Kenya (37.8%) where only 14 of 29 cytotoxic agents and 3 of 16 cancer-indicated MAbs could be obtained.
- Only 10 drugs (bleomycin, bortezomib, cyclophosphamide, docetaxel, doxorubicin liposomal, gemcitabine, ifosfamide, irinotecan, oxaliplatin, vinorelbine) were available in all 20 countries. Eight drugs (azacitidine, cabazitaxel, dactinomycin, daunorubicin, fludarabine, fotemustine, raltitrexed, romidepsin) had only a single vial size available in all countries where they were marketed. Two drugs (dacarbazine and docetaxel) were identified with multiple vial sizes available in all countries. The presence of overage (excess product) was reported in 31% of drugs. Stability data for cytotoxic drugs were inconsistent, with 24-hour expiry in the majority of countries.
- Only three MAbs with cancer indications (bevacizumab, rituximab and trastuzumab) were available in all 20 countries. Five MAbs (alemtuzumab, blinatumomab, brentuximab vedotin, obinutuzumab, pertuzumab) were only available in a single vial size. The presence of overage was reported in 63% of drugs. Stability of MAbs varied from immediate use to 36 hours.

The authors recommended strategies to achieve considerable monetary savings, not from a reduction in drug prices, but by minimising wastage (including unused portion of vials and unadministered prepared doses), as well as time spent on preparation and improved occupational safety. Strategies included increasing the available range of drug vial strengths; ensuring vials contain overage (an excess of drug available in a vial above that stated on the label); provision of reliable extended stability data; and manufacture of products in the most suitable form for administration.

Australian publications: Gilbar and Chambers presented several strategies to reduce expenditure associated with cancer drugs, including minimisation of wastage, provision of a range of vial sizes in countries, extended cancer drug expiry, and use of pre-filled syringes and subcutaneous administration, rather than preparation from a vial [35].

In a six-month prospective study, Gilbar, Sung et al. evaluated the impact of an electronic stock management system on the amount of drug wastage at a regional cancer centre in Australia [36]. The centre's oncology information system (CHARM) was monitored regularly for stock, doses and expiry dates, in order to ensure orphaned doses (i.e., prepared but not administered) were either administered at the patient's next appointment (within expiry) or given to another suitable patient. The main reasons for unutilised preparations were the patient being unwell on the day of the scheduled infusion leading to treatment delay (20.4%), disease progression (8%), delayed treatment start (6.3%) and toxicity reactions. Through the stock management system, a large proportion of orphaned infusions could be re-used (86.7%), of which 63% could be used in the same patient. The total estimated savings from recycling orphaned cancer drugs by oncology pharmacy staff were estimated at AU$300,000 over the 6-month study period, projected to exceed AU$600,000 over a year.

4.2.3 Evidence on the time and costs of preparing cancer medicines

The Review summarised two international publications highlighting the processes and costs associated with the preparation and administration of cancer medicines. These studies make clear the importance of compounding time in the resource utilisation associated with preparation of cancer medicines. Similarly, the availability of non-IV administration routes (either subcutaneous in the case of trastuzumab or oral in the case of capecitabine as a 5-FU analogue) result in substantial cost reductions associated with drug preparation.

North et al. conducted an observational study at the outpatient oncology centres at Auckland City and Tauranga Hospitals in New Zealand, comparing the medical resource utilisation associated with administration of trastuzumab subcutaneous injection vs IV infusion in women with HER2-positive breast cancer [37]. It was observed that trastuzumab subcutaneous injection reduced trastuzumab-related tasks, drug preparation time, chair time and the volume and cost of consumables in the outpatient treatment setting. The authors concluded that trastuzumab subcutaneous injection could reduce overall resource utilisation, help address oncology centres' capacity issues, and inform future HER2-positive breast cancer treatment delivery options.

Shinder et al. conducted a time-and-motion study to assess the efficiency of the treatment pathway

and workflow during administration of chemotherapy treatment for colorectal cancer [38]. The study identified the direct work steps (prescription validation, preparation, verification and premedication) and time worked by employees delivering cancer care. The average total duration of physician visits was 129.2 minutes (95% CI: 114.2 – 144.2), whereas the mean duration of the timed work steps was 51.6 minutes (95% CI: 46.3 – 57.1). For treatment visits, the average total duration was 393.0 minutes (95% CI: 374.9 – 411.1), with timed work steps taking up 343.5 minutes (95% CI: 328.1 – 358.7).

For treatment visits, employee time was longer for patients treated with FOLFOX/bevacizumab, at 70.0 minutes (95% CI:67.1–72.7) compared with 43.7 minutes (95% CI: 41.2 – 46.0) for XELOX/bevacizumab. Preparation of FOLFOX took 39.6 minutes (95% CI: 35.9 – 43.3) of employee time, whereas the preparation of XELOX took 13.3 minutes—capecitabine pre-counts: 2.0 minutes (95% CI: 2.0 – 2.0); capecitabine preparation: 3.4 minutes (95% CI: 2.3 – 4.5); oxaliplatin preparation: 7.9 minutes (95% CI: 7.2 – 8.5). The study reported total pharmacy staff time for the preparation of FOLFOX/bevacizumab was longer than for XELOX/ bevacizumab (61.4 minutes vs 35.1 minutes) and was more expensive with respect to personnel costs: C$36.97 versus C$20.85.

4.3 Quantitative analysis (including IQVIA/PBS data)

4.3.1 Tracking EFC medicines reimbursement

Total EFC expenditure

Line-level data on the PBS claims data for EFC medicines (Schedule 1 and 2) for the period 1st July 2016 to 30th June 2021 were obtained from the Department of Health. A total of 6,303,730 dispensing records were provided which pertained to 270,676 unique patient records. This provided data on all 54 medicines listed under Schedule 1 of the EFC and 14 medicines listed under Schedule 2 (see Appendix 6 for a full listing of all medicines, the relevant PBS item codes and formulations available on the PBS).

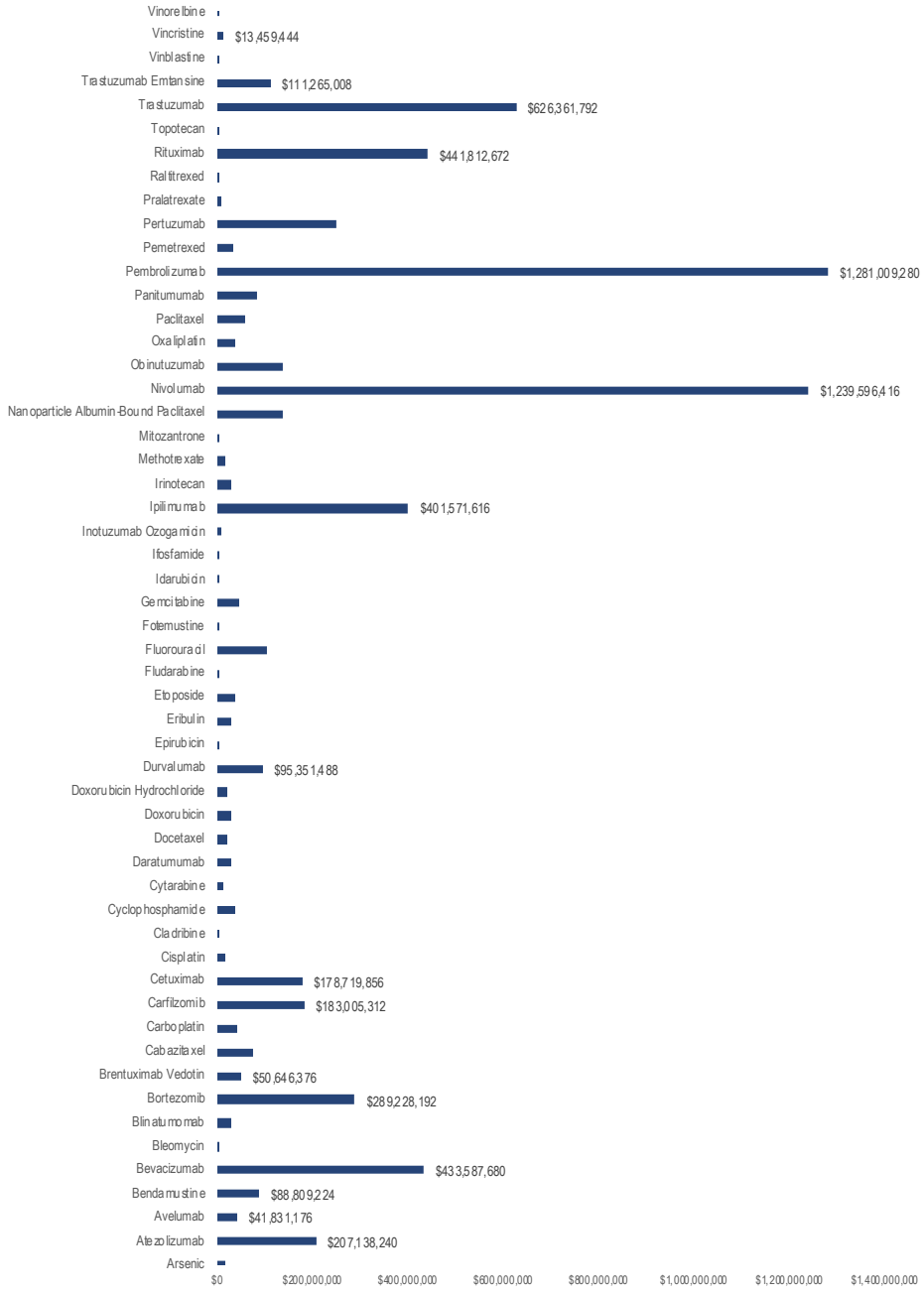
A summary of total government spending on Schedule 1 and Schedule 2 medicines (i.e., related benefit items) is presented in Figure 13. Overall, total Government expenditure for the period July 2016 to June 2021 was $7,100,970,748 ($7,073,197,870 for Schedule 1 medicines and $27,772,878 on Schedule 2 medicines). A detailed breakdown of expenditure by cancer medicine on the EFC per year for which data were available is provided in Appendix 6.

Of particular relevance to this Review is the change in the composition of spending that has occurred in EFC spending since its inception. As noted in the Introduction, previously cytotoxic therapies were

the main stay of treatment in cancer care and formed the majority of the drugs supplied and basis for expenditure on the EFC. The emergence of newer biological therapies, including proteasome inhibitors, MAbs and other immunotherapies has led to a shift in practice and a greater reliance on those newer therapies. Coupled with the high unit prices associated with those medicines (see Section 3.2.4), this has resulted in an increase in the proportion of EFC spending which is attributable to those newer therapies. In the period of PBS data observed, this increased from 76.9% of expenditure on Schedule 1 medicines in the second half of 2016 to 86.5% in the first half of 2021.

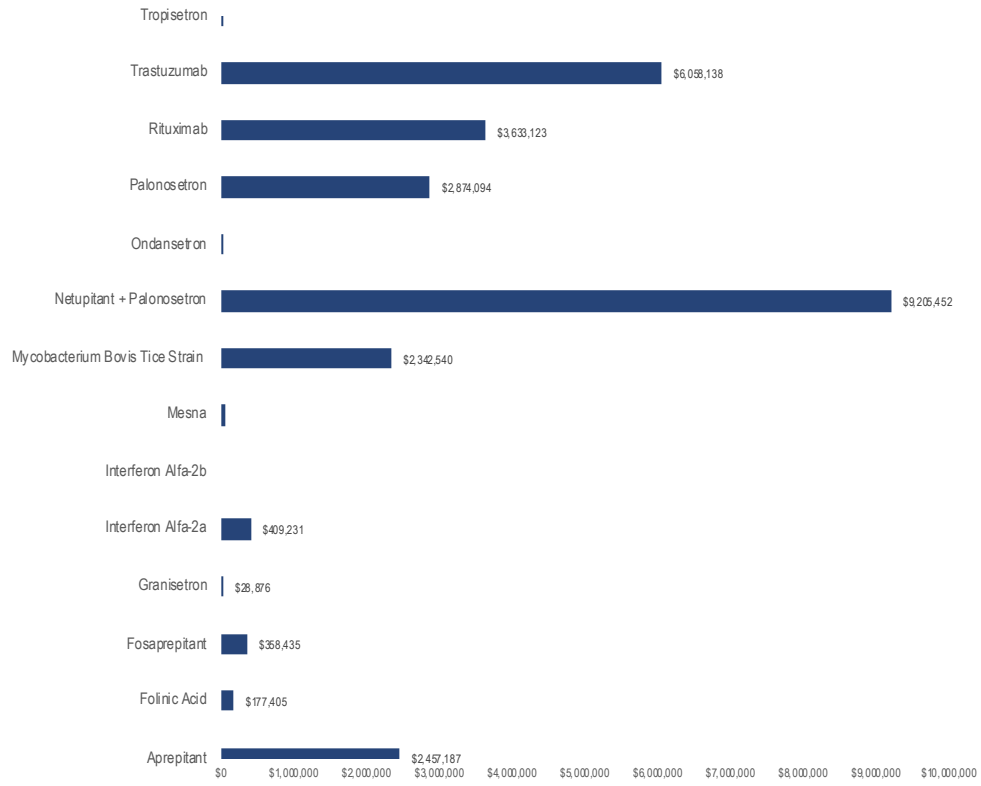
Of the total $7.1 billion in benefits paid for Schedule 1 medicines over the period 2016 to 2021, approximately two thirds ($4.7 billion) were accounted for by seven cancer medicines: bortezomib ($0.29 billion, 4.1%); ipilimumab ($0.40 billion, 5.7%); bevacizumab ($0.43 billion, 6.1%); rituximab ($0.44 billion, 6.2%); trastuzumab ($0.63 billion, 8.9%); nivolumab ($1.24 billion, 17.5%); and pembrolizumab ($1.28 billion, 18.1%).

Figure 13. PBS expenditure by EFC-listed drug, Schedule 1 (July 2016 - June 2021)



Source: Prepared for the Review using PBS line-level data (see Appendix 6).

Figure 14. PBS expenditure by EFC-listed drug, Schedule 2 (July 2016 - June 2021)

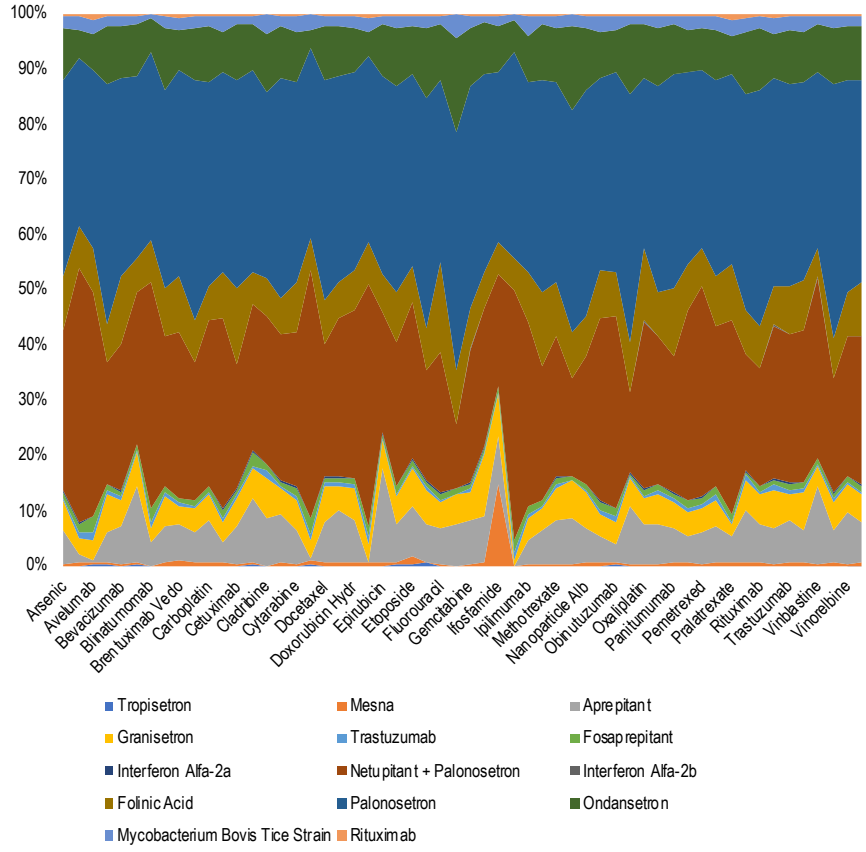


Source: Prepared for the Review using PBS Line Level Data, see Appendix 6

Utilisation of EFC-related items

EFC Schedule 2 medicines (Related Benefit items) are provided as part of the EFC largely because they are co-prescribed to cancer patients as supportive care. Accordingly, the nature of co-prescribing – demonstrating the Schedule 1 medicines with which Schedule 2 medicines were co-prescribed (for those patients where this occurred) is summarised in Figure 15. Overall, netupitant + palonosetron and palonosetron (both anti-emetics) were the most commonly prescribed EFC-related items.

Figure 15. Utilisation of related benefits by EFC Schedule 1 drug (July 2016 - June 2021)



Source: Prepared for this Review using PBS Line Level Data, see Appendix 6

Further analysis is to be undertaken looking at the use of drugs on a per patient basis to assess: the average number of scripts per patient per cancer medicine, and the extent of co-prescribing of Schedule 1 medicines in the period of data observation

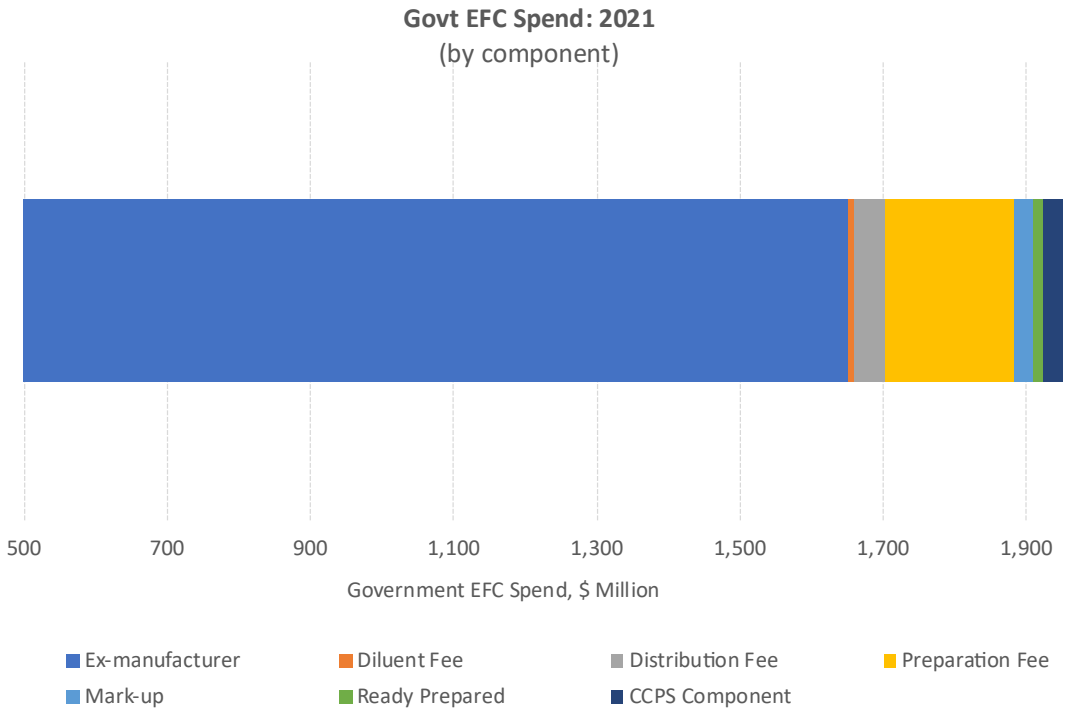
EFC distribution by section

As noted previously, the relative proportions of the reimbursed price accounted for by the various components of the EFC fee, including the AEMP, varies across the cancer medicines and settings (s90 and s94). To account for that variation, and to estimate the total quantum of the PBS spend on the EFC that is allocated to each of the respective fee components, the following process was undertaken:

- For each molecule, each cost component was weighted by the volume of claims per molecule in a given setting to derive a weighted average cost component per-setting;
- the weighted average cost component per setting was combined using the proportion of total claims on the PBS per setting in 2020-21 (38.5% via (s90) community pharmacies; 35.8% via (s94) public hospital pharmacies and 25.7% via (s94) private hospital pharmacies).

The resulting proportions were applied to the total net-benefit claims plus CCPS fees for 2020-21, as shown in Figure 16. From this figure it can be observed that of the total spend in 2021 (net benefits plus CCPS fee) of $1,951 million, $1,760 million (90.2%) was accounted for by the base manufacturer pricing component. The next largest single component was $116 million (5.9%) claimed in preparation fees to prescribers/providers of EFC products, $23.4 million (1.2%) in distribution fees, $22.7 million (1.2%) in pharmacy mark-ups, $18.2 million (0.9%) in CCPS fees, with $6.8 million (0.3%) and $4.8 million (2.5%) in ready prepared and diluent fees, respectively. From these figures, it can be discerned that the bulk of funding in the EFC supply chain flows to manufacturers as suppliers of the active medicines.

Figure 16. Distribution of EFC spend by component (2021)



Abbreviations: EFC, Efficient Funding of Chemotherapy; TGA, Therapeutic Goods Administration.
Source: Developed for this Review based on PBS line level data.

Reconciling these flows directly with participants in the supply chain is not straightforward for the following reasons:

- The Government does not directly purchase medicines from manufacturers, rather it reimburses pharmacies/hospitals for medicines supplied as PBS items. Thus, while it is reasonable that the bulk of payments for medicines (as paid via the ex-manufacturer pricing component) would be receipted by manufacturers, in instances of vial-sharing (where the

quantum of vials purchased by a pharmacy/hospital is less than that for which reimbursements are claimed), the payment for the ex-manufacturer component for those additional vials will vest with the hospital/pharmacist. Similarly, where a hospital/pharmacist has negotiated a discount in purchase terms from manufacturers a portion of the payment for the ex-manufacturer component will vest with the hospital/pharmacist. Neither of these amounts can be estimated given the information currently available to this Review.

- Multiple vertical transactions occur within the supply chain for which the value added by each additional actor cannot be discerned. This includes:
    - Hospitals/pharmacies who claim PBS reimbursement for infused cancer therapies may have purchased compounded products from third party compounders. Analysis of the CCPS data suggests that approximately 2/3 of EFC items claimed have been routed via a TGA-licensed compounder. It is understood from consultations to the Review that those compounders have contracting arrangements with hospitals/pharmacists by which medicines are supplied at an agreed price per mg. Those prices include elements of chemotherapy compounding intended to be covered by the components of the EFC fees (preparation fees, diluent fees). Thus, while third-party compounders do not directly claim payments from the PBS, those EFC components related to product compounding are passed through to them indirectly via existing pricing arrangements.
    - The use of wholesale distributors varies between actors – with some hospitals/pharmacies/compounders choosing to purchase directly from manufacturers. The utilisation of wholesale distributors across the supply chain is varied and not sufficiently described to ascertain whether payment of the existing distribution fee flows to wholesalers or is retained by those who lodge the PBS claim.

As described in the next section, a lack of visibility from stakeholders within the supply chain as to the specific resource inputs and associated costs for medicine compounding, wholesaling and dispensing as it relates to the EFC precluded an assessment by this Review of the flow of EFC component funds within the system.

4.3.2 Tracking EFC medicines supply

Sales of EFC medicines

Data on in-market sales of cancer medicines funded via the EFC were purchased from IQVIA for the

period January 2016 to December 2020. The IQVIA sales data provided information on the amount of the drug purchased in a single transaction on a unit per-molecule basis, the manufacturer's name, the molecule name, product name, the number of packs purchased, the price paid in a single transaction, the channel purchasing the drug (i.e. hospital or retail pharmacy), the compounding status of the drug (non-compounded vs. compounded), the state the pharmacy or hospital was from, and the month and date of sale. These data show sales of drugs from manufacturers or third-party providers (wholesalers/compounders) to hospitals/pharmacies. Within this dataset the use of a compounding flag indicated whether sales were from third-party providers.

Data were extracted by IQVIA in June 2021, providing information on 86,108 unique sales transactions on 51 cancer medicines (see Appendix 7). The IQVIA data reflect all in-market transactions – including supply for private prescriptions, clinical trials, and compassionate use programs. Information related to such transactions (either reporting 'sales' at no cost or a dollar transaction without a corresponding number for the units of the molecule exchanged) were excluded from the analysis. These transactions accounted for less than 0.01% of all movements within the dataset.

Total sales

The value of sales reported by molecule is provided in Table 7, with the growth per year visible from the data in Figure 17. Total sales recorded over the period were $5.86 billion, of which the two highest value drugs were pembrolizumab at $1.02 billion (17.3%) and nivolumab at $0.98 billion (16.8%). The predominance of these two immunotherapies in total sales reflects the broader balance of cytotoxic versus biological (and non-cytotoxic) therapies in sales. For the overall period, cytotoxic drugs accounted for $0.53 billion (9.1%) in sales, compared with biological therapies which accounted for $5.3 billion (90.9%) in sales.

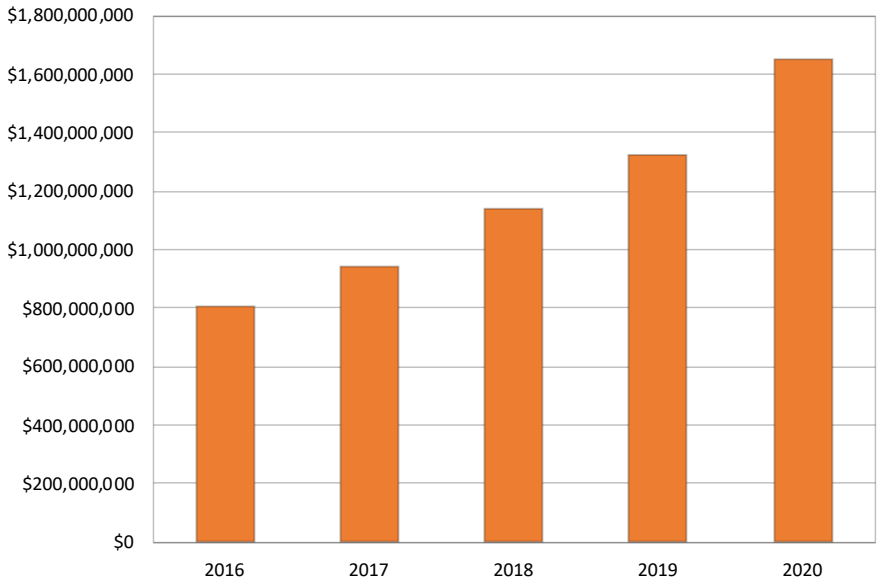
Table 7. Total sales value, Schedule 1 medicines (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic	$1,237,287	$1,318,501	$1,858,799	$2,614,061	$2,267,871	$9,296,519
Atezolizumab	-	-	$15,114,512	$40,873,841	$88,545,208	$144,533,561
Avelumab	-	-	-	$12,136,455	$18,892,073	$31,028,528
Bendamustine	$8,554,247	$16,576,607	$17,044,333	$17,779,098	$17,408,016	$77,362,300
Bevacizumab	$80,227,647	$80,128,772	$77,317,898	$71,180,468	$81,696,147	$390,550,931
Bleomycin	$962,555	$590,121	$336,725	$457,469	$478,898	$2,825,770
Blinatumomab	-	$3,312,224	$7,515,605	$5,194,457	$9,379,962	$25,402,247
Bortezomib	$57,147,883	$53,924,091	$46,914,214	$47,900,090	$51,907,339	$257,793,618
Brentuximab Vedotin	$4,340,389	$9,169,678	$11,790,640	$11,563,846	$12,463,495	$49,328,049
Cabazitaxel	$21,380,561	$11,605,227	$10,692,981	$13,076,497	$14,026,715	$70,781,980
Carboplatin	$2,312,936	$2,434,150	$2,427,736	$2,552,028	$2,698,320	$12,425,171
Carfilzomib	-	$143,392	$39,077,365	$45,157,344	$48,231,783	$132,609,883
Cetuximab	$39,257,621	$34,206,950	$31,424,565	$29,904,684	$30,165,430	$164,959,249
Cisplatin	$921,050	$889,251	$899,665	$963,616	$985,547	$4,659,130
Cladribine	$710,113	$584,395	$444,524	$665,576	$497,450	$2,902,058
Cyclophosph…	$3,553,851	$3,283,975	$3,331,477	$3,337,551	$3,113,627	$16,620,483
Cytarabine	$1,513,004	$2,050,952	$2,097,607	$3,207,250	$4,706,370	$13,575,183
Docetaxel	$1,558,281	$1,378,879	$1,215,594	$1,273,221	$1,170,784	$6,596,758
Doxorubicin	$6,282,812	$5,355,152	$5,006,517	$5,056,486	$5,307,594	$27,008,561
Durvalumab	-	-	-	$31,445	$53,473,997	$53,505,442
Epirubicin	$1,115,133	$741,536	$425,002	$279,015	$206,440	$2,767,126
Eribulin	$5,089,293	$6,135,473	$6,948,202	$3,995,269	$3,648,993	$25,817,229
Etoposide	$516,854	$1,303,111	$411,555	$304,097	$277,353	$2,812,970
Etoposide Phosphate	$2,842,965	$725,422	$3,280,041	$3,434,370	$3,498,021	$13,780,820
Fludarabine	$435,785	$364,526	$334,127	$346,448	$275,942	$1,756,829
Fluorouracil	$15,220,499	$14,663,309	$14,942,492	$15,806,628	$18,164,488	$78,797,415
Fotemustine	$108,979	$193,560	$32,379	$35,578	$67,683	$438,178
Gemcitabine	$2,739,678	$3,046,381	$3,061,008	$2,855,336	$2,735,837	$14,438,239
Idarubicin	$871,091	$619,401	$557,379	$333,599	$246,942	$2,628,412
Ifosfamide	$1,933,119	$1,770,328	$1,557,796	$1,453,326	$1,333,214	$8,047,783
Inotuzumab Ozogamicin	-	-	-	$3,080,682	$4,116,302	$7,196,983

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Ipilimumab	$27,209,751	$61,018,229	$69,424,710	$87,404,353	$95,331,444	$340,388,486
Irinotecan	$2,388,723	$2,366,503	$1,744,290	$1,647,462	$1,900,582	$10,047,559
Methotrexate	$2,213,579	$2,196,197	$3,322,572	$5,316,480	$6,835,505	$19,884,333
Nivolumab	$4,631,883	$90,776,566	$231,609,339	$277,123,820	$378,027,250	$982,168,857
Obinutuzumab	$5,529,755	$9,022,841	$11,144,532	$29,298,410	$46,898,273	$101,893,811
Oxaliplatin	$1,587,325	$1,999,401	$1,856,901	$1,894,228	$2,123,487	$9,461,342
Paclitaxel	$18,250,573	$19,180,220	$18,439,639	$18,565,635	$19,783,200	$94,219,267
Panitumumab	$12,192,213	$17,247,900	$16,727,621	$13,102,995	$12,560,580	$71,831,310
Pembrolizumab	$108,004,022	$125,711,142	$145,708,479	$254,677,967	$381,435,498	$1,015,537,108
Pemetrexed	$13,935,819	$4,889,411	$1,354,454	$1,023,627	$1,594,777	$22,798,087
Pertuzumab	$31,118,244	$39,491,831	$45,033,408	$50,370,985	$58,227,403	$224,241,869
Pralatrexate	-	-	$1,434,936	$2,471,220	$2,888,409	$6,794,565
Raltitrexed	$422,521	$417,612	$303,945	$330,495	$287,306	$1,761,879
Rituximab	$151,018,715	$143,725,732	$122,709,551	$99,221,277	$57,992,656	$574,667,930
Topotecan	$232,959	$184,455	$131,757	$120,881	$125,891	$795,943
Trastuzumab	$153,515,539	$157,735,426	$151,336,346	$124,805,592	$77,801,025	$665,193,928
Trastuzumab Emtansine	$17,983,780	$17,986,049	$16,527,548	$15,573,718	$27,418,690	$95,489,785
Vinblastine	$352,961	$313,513	$324,293	$345,144	$369,240	$1,705,150
Vincristine	$676,188	$756,682	$911,146	$981,898	$1,058,086	$4,384,000
Vinorelbine	$464,652	$429,396	$432,760	$386,336	$332,631	$2,045,774
Total	*$812,562,832*	*$951,964,468*	*$1,146,538,964*	*$1,331,512,351*	*$1,654,979,771*	*$5,897,558,386*

Source: Prepared for this Review using in-market sales data (IQVIA); see Appendix 7

Figure 17. Total indusry sales (2016 - 2020)

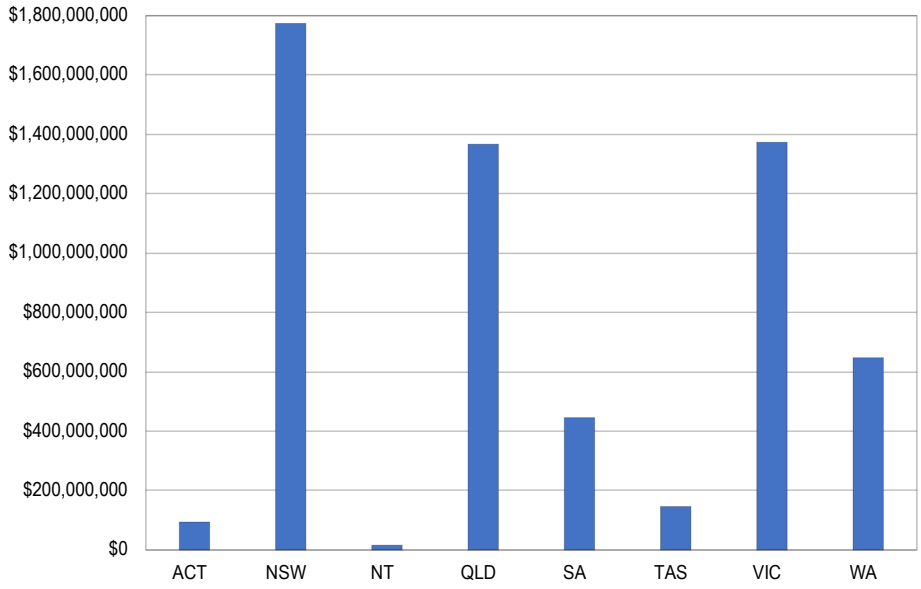


Source: Prepared for this Review using in-market sales data (IQVIA), see Appendix 7

National distribution

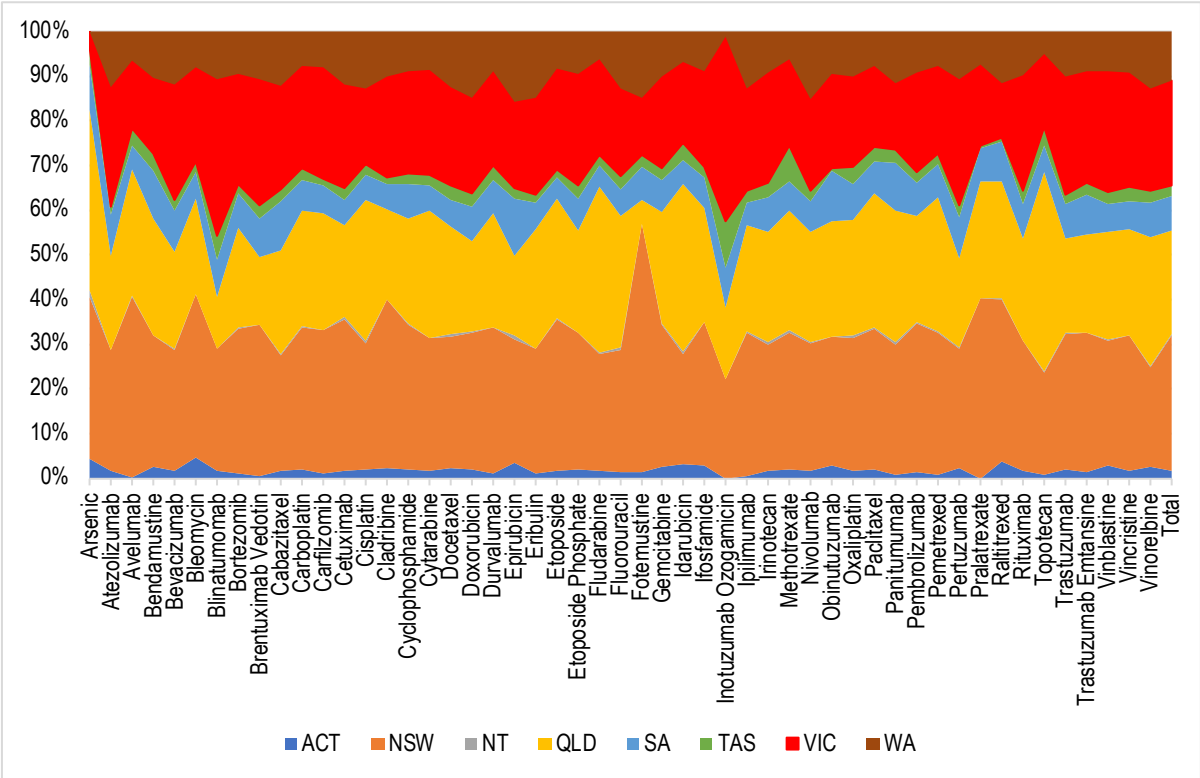
A summary of total purchases made by each state is provided in Figure 18. While sales of cancer medicines were highest in the most populous state, NSW, they were largely the same in Queensland and Victoria despite the latter having a larger population than the former. There was some variation noted across States/Territories with respect to the types of drugs being sold, e.g. NSW appears to account for a higher proportion of fotemustine use (relative to other states), QLD accounts for a high proportion of sales of arsenic while WA recorded none, and Victoria accounted for a high proportion of inotuzumab sales (see Figure 19).

Figure 18. Total in-market sales by State and Territory (2016 - 2020)



Abbreviations: ACT, Australian Capital Territory; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia.
Source: Prepared for this Review using in-market sales data (IQVIA), see Appendix 7

Figure 19. Distribution of sales by EFC-listed drug and State and Territory (2016 - 2020)



Abbreviations: ACT, Australian Capital Territory; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia.

Source: Prepared for this Review using in-market sales data (IQVIA), see Appendix 7

Distribution by sector

Within total sales for the period 2016-2020, the majority (94%) were accounted for by sales to hospital pharmacies as opposed to retail pharmacies (6% of all purchases). Over half of all sales (58.4%) were flagged as being sold as a 'compounded pack', with the remainder being not compounded (see Table 8 and Appendix 7 for a complete discussion by drug).

Table 8. In-market sales by compounding status ($ million) (2016 - 2020)

Status	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Compounded	$420.8m	$491.2m	$639.5m	$812.2m	$1,061.3m	$3,424.9m
Not compounded	$382.4m	$453.5m	$500.2m	$512.7m	$586.4m	$2,435.2m
Total	*$803.2m*	*$944.6m*	*$1,139.7m*	*$1,324.9m*	*$1,647.6m*	*$5,860.1m*

Source: Prepared for this Review using in-market sales data (IQVIA), see Appendix 7

Factors affecting sales prices

Results from the mixed linear regression models are reported in Appendix 7 and indicate the following with respect to the factors affecting drug prices:

- The number of manufacturers per molecule; each additional manufacturer (beyond the innovator brand) resulted in a statistically significant ($p<0.05$) drop in the per mg price.
- The number of presentations per molecule; each additional presentation (pack formulational) resulted in a statistically significant ($p<0.05$) drop in the per mg price.
- The location of sales; there was no statistically significant effect ($p>0.05$) of the location of sales (State/Territory) on the price per mg.
- Time; there was a statistically significant ($p<0.05$) decline in the price per mg with each successive year of sales.
- Third-party provider; purchasing products from third-party compounders was associated with a statistically significant ($p<0.05$) lower price per mg.
- Large purchaser status; hospital purchasing was associated with a statistically significantly lower price per mg ($p<0.05$) than retail pharmacy purchasing.

Lower prices associated with a higher number of providers or presentations per molecule and over time are to be anticipated as this reflects statutory price reductions associated with the introduction of second brands of any molecule and for market longevity. Differences in prices associated with

hospital and retail pharmacy status are likely to reflect the purchasing power attached to larger organisations. Similarly, lower prices provided to hospitals/pharmacies through third-party providers may also reflect the power of the latter to negotiate lower prices from manufacturers.

Prices across the EFC supply chain

As noted above, there are various actors within the EFC supply chain who at various times may function either as sellers or purchasers of cancer medicines depending on the nature of the transaction. For example, a hospital pharmacy may act as a purchaser when procuring ipilimumab from its manufacturer, BMS, but as a seller when seeking reimbursement from Government for dispensing ipilimumab as a PBS-related item. Numerous stakeholders illustrated that there are multiple factors at play, which result in differences between the prices paid by purchasers of cancer medicines within the supply chain and those paid upon reimbursement via the PBS. Thus, it was prudent to compare those prices. In order to account for potential differences in the basis upon which prices are expressed (e.g. per pack versus on a maximum quantity), all comparisons have been made on the price per-mg basis within molecule and for the calendar year of 2020 (the latest year for which information on both sale prices and PBS reimbursed prices are known). Sales data prices were sourced from the IQVIA dataset, while PBS prices were as listed on the PBS in December 2020. An itemised comparison of prices is presented in Table 9.

Table 9. Prices per-mg by EFC-listed drug, PBS and industry sales data (2020)

Molecule	*Compounded sales: PBS DPMA*	*Manufacturer sales: PBS DPMA*
Fludarabine	0.51	0.20
Vincristine	0.35	0.20
Etoposide	0.42	0.26
Cisplatin	0.75	0.28
Oxaliplatin	0.54	0.32
Vinorelbine	0.59	0.38
Gemcitabine	0.65	0.38
Fluorouracil	1.91	0.38
Carboplatin	0.57	0.39
Docetaxel	0.47	0.39
Vinblastine	0.69	0.41
Cyclophosphamide	0.79	0.41
Pemetrexed	0.61	0.41
Bleomycin	1.32	0.47
Fotemustine	0.75	0.52
Idarubicin	0.92	0.57
Ifosfamide	0.86	0.66
Blinatumomab	0.92	0.69
Cytarabine	1.56	0.70
Rituximab	0.89	0.72
Trastuzumab	0.80	0.74
Raltitrexed	0.97	0.75
Cladribine	1.05	0.78

Inotuzumab ozogamic	n.a.	0.83
Ipilimumab	0.93	0.83
Panitumumab	0.96	0.87
Eribulin	1.14	0.88
Cabazitaxel	1.39	0.89
Cetuximab	0.92	0.91
Nivolumab	0.98	0.93
Bortezomib	1.05	0.93
Bendamustine	1.02	0.94
Carfilzomib	0.98	0.96
Brentuximab vedotin	1.16	0.96
Trastuzumab emtansi	1.04	0.97
Topotecan	0.50	0.97
Pertuzumab	0.99	0.97
Arsenic	1.31	0.97
Pralatrexate	1.10	0.97
Obinutuzumab	0.98	0.98
Durvalumab	1.02	0.98
Avelumab	1.05	0.98
Atezolizumab	1.00	0.99
Bevacizumab	1.57	1.00
Pembrolizumab	1.04	1.02
Paclitaxel	4.97	1.89
Epirubicin	0.81	2.05
Methotrexate	2.09	3.39
Doxorubicin	3.87	5.13
Irinotecan	0.83	5.52

Notes: Data shown are the ratio of the average sales per mg (or unit as applicable) to the corresponding PBS DPMA for December 2020. PBS prices are average of public and private list prices. Molecules ordered from the lowest to highest ratio for Manufacturer Sales to the PBS DPMA.

A comparison was undertaken of the PBS reimbursed price per mg, the price per mg charged by TGA compounders, and the price per mg charged by manufacturers to hospitals/pharmacists using the following data:

- The price per mg as reimbursed by the PBS. These were determined based on the reported DPMA divided by the maximum quantity (expressed in milligrams) for each molecule listed on the PBS. The average of prices across the private and public hospital items for each molecule was utilised.
- The price per mg for items supplied by TGA-licensed compounders to hospitals/pharmacists. This was estimated based on the total sales (in mg and dollars) from TGA-licensed compounders as reported in the IQVIA data.
- The price per mg for items supplied by drug manufacturers to hospitals/pharmacists. This was estimated based on the total sales (in mg and dollars) from manufacturers to hospitals/pharmacies as reported in the IQVIA data.

For 49 EFC molecules PBS listed in 2020, the data indicate that the price per mg based on sales from TGA-licensed compounders was higher than the PBS dispensed price for 20 molecules (40.8%) and lower for the remainder. In contrast, the price per mg based on sales from manufactures to hospitals/pharmacies was higher than the PBS dispensed price for 7 molecules (14.3%) and lower for the remainder.

From these comparisons, it can be observed that in the majority of cases, the prices paid by hospitals/pharmacies to either TGA-licensed compounders or manufacturers were lower than the corresponding PBS listed price per mg. As hospitals/pharmacists are reimbursed at the dispensed price per mg (without regard to the application of further discounts which might arise due to special pricing arrangements between the Commonwealth and pharmaceutical manufacturers), these differences in the price paid per mg and price reimbursed per mg represent the capacity of hospitals/pharmacies to benefit from the existing separation of drug purchasing from subsequent PBS reimbursement.

The magnitude of those benefits and the extent to which they are realised depends on the extent to which hospitals/pharmacies purchase molecules that are associated with the largest gap directly from manufacturers or via TGA-licensed compounders. A comparison was undertaken of the prices per mg as derived from the TGA-licensed compounder sales and those from the manufacturer sales (to hospitals/pharmacies). For 43 (87.8%) of molecules, the price charged per mg by TGA-licensed compounders exceeded what was being charged by manufacturers. This may reflect the extent to which TGA-licensed compounders incorporate the costs of compounding into fees charged for service provision. The extent to which this differential reflects potential underlying cost structures for compounding of cancer medicines is obscured by the following:

- Whether price differentials across the molecules reflect differences in the complexity of compounding.
- Whether the differential varies with volume. This cannot be discerned for TGA-licensed compounders since only total mg sales are available from the IQVIA data (and this is influenced by dose per infusion) for products supplied via compounders. With respect to those molecules purchased directly from manufacturers, the two most commonly purchased molecules were not associated with pricing differentials. The two molecules that accounted for the greatest share of sales in value terms were both associated with small pricing differentials (having higher TGA-licensed compounder prices).
- The extent to which these differentials reflect the potential for TGA-licensed compounders to incorporate PBS fee equivalents (for drug preparation, etc.) into prices charged to

hospitals/pharmacists (noting that PBS reimbursements are paid to hospitals/pharmacists and not TGA-licensed compounders).

The potential for vial-sharing

The potential for vial-sharing is directly related to the quantity of a pharmaceutical (in mg or iu) as supplied per PBS dispensed item, relative to the vial sizes supplied. There are 25 PBS items (in each of the public and private settings) listed for subsidy with a maximum quantity (amount) less than the mg amount supplied in the corresponding vial size, 25 are available with an amount equal to the vial size and the remainder have a maximum amount that exceeds the vial size for that item (see Table 10).

For those with a maximum amount less than the vial size, the implication is that even if prescribing up to the maximum amount for these items, there will still be surplus in the vials supplied. As cited in the input from multiple stakeholders, one approach to minimise the inefficiency associated with surplus drug is to accumulate such "excess" pharmaceutical product across multiple prescriptions (patients) thereby facilitating the efficient use of all available pharmaceutical product within vials prepared for supply to patients. The existence of specific items in which surplus may result from the amount supplied exceeding the maximum amount permitted for supply under the PBS restriction may potentiate the need to accumulate surplus for these specific items.

Table 10. Maximum amount and vial size (mg) supplied, public presentations

Molecule	*Max Amount < Vial Size*	*Max Amount = Vial Size*
Atezolizumab		8
Bortezomib	6	8
Cabazitaxel	3	
Doxorubicin	2	
Etoposide	1	
Fluorouracil	4	2
Methotrexate	6	
Obinotuzumab		6
Pertuzumab		1
Topotecan	2	
Trastuzumab	1	
Total	*25*	*25*

Note: Public presentations indicative of both public and private settings.

One of the molecules for which this difference occurs is cabazitaxel. The sponsor of cabazitaxel has indicated that the accumulation of surplus across vials has at times resulted in that product being supplied at a loss. This is due to the impact of rebates to Government associated with the administration of Special Pricing Arrangements (SPA; see forthcoming section on SPA rebates and EFC

practices) resulting in the company calculating its rebates to the Government on a higher number of reimbursed vials than it recorded selling (due to surplus in vials sold being used to compound additional vials that were subsequently reimbursed).

While aligning vial sizes with maximum amounts might reduce the potential for vial-sharing, it does so only to the extent that doses prescribed can be matched to the vial sizes available. Information from pharmaceutical industry stakeholders is that the Australian market is essentially a product taker with respect to vial sizes, reliant on sizes which are available in other markets. To that end, it is not possible to tailor vial sizes for the Australian market as a means of minimising the potential for vial-sharing.

Comparison of PBS claims and in-market sales

As noted above, one of the questions of interest for this Review was the extent to which it is possible to reconcile PBS claims for the reimbursement of cancer medicines with sales of those medicines. Information available from the PBS line level data and IQVIA in-market sales data were investigated to explore the extent to which such a reconciliation of data was possible. This comparison was conducted for Schedule 1 medicines of the EFC only (see Appendix 7).

Sales of cancer medicines funded via the EFC were purchased from IQVIA for the period January 2016 to December 2021. The IQVIA sales data provided information on the amount of the drug purchased in a single transaction on a unit per-molecule basis, the manufacturer's name, the molecule, product name, the number of packs purchased, the price paid in a single transaction, the channel purchasing the drug (i.e. hospital or pharmacy), the compounding status of the drug (non-compounded vs. compounded), the state the pharmacy or hospital was from, and the month and date of sale. These data show sales of drugs from manufacturers or third-party providers (wholesalers/compounders) to hospitals/pharmacies. Within this dataset the use of a compounding flag indicated whether sales were from third-party providers.

Data were extracted in June 2021, providing information on 86,108 unique sales transactions on 51 cancer medicines available in Schedule 1 of the EFC (see Table 11). The IQVIA data reflect all in-market transactions—including supply for private prescriptions, clinical trials and compassionate use programs. To afford as consistent a basis as possible for the comparison of these data with PBS claims information, transactions reporting 'sales' at no cost for clinical trials or compassionate use programs were removed from the analysis. These transactions accounted for approximately less than 0.01% of all movements within the dataset.

However, it was not possible to remove medicines that were purchased for self-funded patients from the IQVIA sales data, or for uses beyond the PBS indication (see Appendix 7). Hence, in principle the IQVIA sales data are likely to be broader than the corresponding PBS line level data in scope. It is recognised that not all stakeholders contribute information on sales to IQVIA; sales of medicines provided via HPS to non-HPS facilities are not captured within the IQVIA dataset and will thus result in the under-reporting of total sales (it is unknown if this disproportionality affects some cancer medicines that may be preferentially supplied via HPS).

Table 11. PBS vs IQVIA data comparison, inclusions and exclusions

Criteria
Include as data was available in both the PBS and IQVIA datasets: arsenic; atezolizumab; avelumab; bendamustine; bevacizumab; bleomycin; blinatumomab; bortezomib; brentuximab vedotin; cabazitaxel; carboplatin; carfilzomib; cetuximab; cisplatin; cladribine; cyclophosphamide; cytarabine; docetaxel; doxorubicin; durvalumab; epirubicin; eribulin; etoposide; fludarabine; fotemustine; gemcitabine; idarubicin; ifosfamide; inotuzumab ozogamicin; ipilimumab; irinotecan; methotrexate; nivolumab; obinutuzumab; oxaliplatin; paclitaxel; panitumumab; pembrolizumab; pemetrexed; pertuzumab; pralatrexate; raltitrexed; rituximab; topotecan; trastuzumab; trastuzumab emtansine; vinblastine; vincristine; vinorelbine
Exclude as data was only available in the PBS dataset: doxorubicin hydrochloride; fluorouracil; mitozantrone; nanoparticle albumin-bound paclitaxel; ofatumumab
Exclude as data was only available in the IQVIA dataset: etoposide phosphate

As the IQVIA data contained sales information from January 2016 to December 2020 and the PBS line-level data contained information from July 2016 to June 2021, the comparison of the two was restricted to the overlapping period of January 2017 to December 2020.

Ideally, the intent of comparing the sales and PBS claims data was to investigate the extent to which it is possible to use these data sources to reconcile in-market sales with PBS claims (as might be required for compliance with RSA). This was not possible for all cancer medicines for which data were available due to the nature of the line level data available from the PBS dataset. For many of the cancer medicines subsidised via the PBS, there are multiple strengths available on the PBS under each PBS item code (see Appendix 6). However, within the PBS data provided, for any given PBS item only the first strength available is listed per claim in the database. This means the strength as shown in the PBS dataset may not reflect the basis upon which the most efficient combination of vials was estimated. Therefore, it was only possible to estimate the number of vials dispensed to patients when only one vial size (i.e. strength) was available.

Comparison of Sales

The total volume of cancer medicines for which a PBS claim was lodged compared to that purchased

from manufacturers/third-party providers is presented in Table 12.

Table 12. Volume of medicines purchased (IQVIA) vs claimed (PBS) (2017-2020)

Drug	*IQVIA Total Sales (mg/iu)*	*PBS Total Claims (mg/iu)*	*Difference (IQVIA - PBS)*
Idarubicin	373,290,848	401,585,824	-28,294,976
Methotrexate	42,759,464	45,479,696	-2,720,232
Paclitaxel	31,287,560	33,027,460	-1,739,900
Cetuximab	40,008,796	41,675,760	-1,666,964
Carboplatin	105,664,504	106,710,376	-1,045,872
Oxaliplatin	18,091,208	18,917,804	-826,596
Pemetrexed	20,530,638	21,285,580	-754,942
Durvalumab	6,582,718	7,208,687	-625,969
Pembrolizumab	9,232,200	9,839,980	-607,780
Obinutuzumab	47,350,228	47,954,448	-604,220
Carfilzomib	6,139,928	6,668,463	-528,535
Docetaxel	13,745,911	14,251,845	-505,934
Pralatrexate	26,159,056	26,450,350	-291,294
Arsenic	192,934	264,555	-71,621
Eribulin	53,109	68,826	-15,717
Ipilimumab	618	317	301
Trastuzumab	23,100	21,533	1,567
Rituximab	8,484	6,743	1,741
Cladribine	33,069	24,382	8,687
Raltitrexed	119,457	106,787	12,670
Epirubicin	1,974,820	1,961,220	13,600
Gemcitabine	58,895	40,585	18,310
Bortezomib	423,743	404,671	19,071
Vincristine	256,331	231,333	24,998
Vinblastine	4,519,444	4,489,221	30,223
Cabazitaxel	771,857	733,087	38,770
Vinorelbine	216,431	171,319	45,112
Irinotecan	2,636,977	2,585,226	51,751
Blinatumomab	316,043	244,600	71,443
Brentuximab Vedotin	447,139	366,735	80,404
Avelumab	4,224,718	4,091,699	133,019
Ifosfamide	212,533	33,457	179,076
Bevacizumab	81,539,032	81,359,240	179,792
Atezolizumab	23,706,800	23,458,374	248,426
Bendamustine	8,113,800	7,666,530	447,270
Pertuzumab	44,597,936	44,054,368	543,568
Cisplatin	11,033,151	10,489,346	543,805
Fludarabine	1,247,097	618,731	628,366
Doxorubicin	16,881,216	14,524,568	2,356,648
Etoposide / Etoposide Phosphate	37,203,332	28,534,224	8,669,108
Panitumumab	65,617,936	55,519,052	10,098,884
Trastuzumab Emtansine	104,398,152	91,880,272	12,517,880
Topotecan	147,753,632	104,793,104	42,960,528
Inotuzumab Ozogamicin	97,552,552	48,526,740	49,025,812
Cyclophosphamide	296,297,504	244,243,680	52,053,824
Nivolumab	122,988,792	21,689,176	101,299,616
Cytarabine	194,803,360	52,068,456	142,734,904
Fotemustine	2,452,928,256	1,656,057,856	796,870,400
Bleomycin	3,631,288,064	548,508,096	3,082,779,968

Source: Developed for this Review, see Appendix 6.

As it was not possible to uniformly compare the number of packs sold by manufacturers with those claimed via the PBS (due to the latter not reporting quantities supplied according to all available formulations) a proof of concept analysis was undertaken for those Schedule 1 medicines for which there is only one formulation per medicine available on the PBS: avelumab, brentuximab vedotin, cabazitaxel, cytarabine, fotemustine, idarubicin, ifosfamide, inotuzumab ozogamicin, pralatrexate, raltitrexed, vinblastine and vincristine. For each, the available sales data were compared with PBS claims data on the assumption that all mgs claimed were utilised (no wastage, implying that there was some element of vial-sharing), or that each claim reflects one distinct patient only (essentially, vials are patient specific such that whether or not actual vial-sharing has occurred, each claim implicitly incorporates wastage). The results in Appendix 7 show that under the assumption that each claim reflects one distinct patient (all of the claimed vial is used for that individual – there is no vial-sharing), PBS units claimed would have exceeded the IQVIA sales for cabazitaxel, pralatrexate and vinblastine. For the other drugs in this analysis, IQVIA sales exceeded PBS claims, even under the assumption that each claim reflects one distinct patient only.

4.3.3 The cost of activities for the supply of EFC medicines

EFC activities and fee components

One of the key activities of the Review was to assess whether the existing fee structure and levels are consistent with what is required to supply infused cancer medicines via the EFC. The information available for this purpose is assessed herein, as sourced from the following:

- Consultations with stakeholders to the Review. Stakeholders from TGA-licensed compounders and non-licensed facilities consulted for the Review were invited to submit information on the resource inputs and associated costs associated with key activities undertaken during the supply of infused cancer medicines. A reporting table was developed in consultation with stakeholders that drew upon: stakeholder input concerning the processes involved in the preparation of infused cancer medicines, as well as a detailed compounder contract template accessed online (HealthShare Victoria. (2021). Award matrix. HPVC2018-161 Grampians Compounded Chemotherapy and MAB Preparations). The resulting template is provided in Table 13.

  This template was provided to all TGA-licensed compounders who participated in round-table consultations, as well as one non-licensed compounder (a large public hospital facility). All recipients of the template were asked to: “Please indicate average costs for each component on a per line-item basis. Add item rows as required and provide any additional explanatory

notes on the composition of each activity as required. Please also provide an estimate of the average annual throughput of chemotherapy items compounded by your organisation." Participants were advised that the confidentiality provisions of the Review would apply to any information provided.

Table 13. Components of the compounding process

Process Component	*Category*	*Subcategory*
Drug acquisition	Labour	Drug receipt and stock management
Drug preparation	Labour	Order management, processing and QA
	Labour	Picking
	Consumables	PPE
Compounding process	Labour	compounding technician
	Consumables	PPE
Product container	Containers	Bag—non-PVC
		Bag—PVC
		FOLFusor - Small Volume
		Infusor
		Infusor—Large Volume
		Infusor—Small Volume
		Medication Cassette (CADD)
		Medication Cassette (CADD)—Other
		Surefusor
		Syringes
Infusion kit	Consumables	Adaptors
		Bag Spikes and Accessories
		Connectors
		Secondary Lines and Sets
Quality assurance	Labour	QA (all stages of preparation)
Logistics	Labour	Stock handling (internal, extermal)
	Consumables	Packaging

Abbreviations: QA, Quality assurance; PPE, Personal protective equipment; PVC, Polyvinyl chloride.
Notes: Adapted from tender template for third-party provision of compounded medicines, HealthShare Victoria. (2021). Award matrix. HPVC2018-161 Grampians Compounded Chemotherapy and MAB Preparations

To date, stakeholders have submitted no data according to the template circulated. Thus, a direct comparison of current EFC fees against compounders' empirical costs was not possible. Information on the costs associated with compounding services as they relate to the provision of stability, sterility and quality assurance procedures conducted by TGA-licensed compounders was made available. That information has been used as a means of substantiating the existing CCPS fee as paid to TGA-licensed compounders (and is discussed elsewhere in this Report).

In the absence of disaggregated cost information on the compounding and supply of infusion cancer medicines, two alternative approaches were considered:

- Development of a desktop-based time-and-activity costing model to estimate, on a protocol

basis, the time and activity requirements for the compounding and provision of infusion cancer medicines.

- Comparison of the existing EFC fee components with information available from:
    - Data extracted from consultations to the Review.
    - Per-unit costs underpinning the determination of the EFC fees as published in the 2013 Review.
    - A report prepared for a state-based Department of Health on the requirements and costs for compounding activities at three sites.

During the course of the consultations, it was noted that a number of suppliers of infused cancer medicines hold proprietary databases that log each step of the production process, including the use of physical and labour inputs, and time involved. Access to that information would provide a valuable basis upon which to construct a desktop-based time-and-activity costing model. However, due to the proprietary and commercial-in-confidence nature of that information, it was not possible access those data. Furthermore, it was not feasible to derive an agreed time-and-activity based approach (in order to develop a protocol to which costs could be applied) within the existing consultations. Developing such a model could be undertaken via a future workshop with contributors to this Review.

Accordingly, the approach to the consideration of fees utilised historical cost information contained in the 2013 Review. Historical costs were adjusted to 2021 prices by applying the AIHW health price index to upscale all prices to 2019 values (the last year for which the base index has been specified), and assuming growth in the index thereafter at an annual rate of 1.9% (the average annual growth observed between 2013 and 2019).

The current fees paid under the EFC are presented in Table 14, along with the information obtained from the 2013 Review (used to substantiate the establishment of the EFC fees). The information available to the current Review to assess whether those fees continue to be appropriate is reported by component below. Note, the payment of the CCPS fee for TGA-licensed compounders is separate from that of the overall EFC payments. Discussion of the cost information available to substantiate the CCPS fee is presented separately in this report.

Table 14. EFC fee schedule and stakeholder-informed costs

Component of PBS reimbursement	Existing EFC Fees	Supporting Costs (2013 Review)[4]
Drug ex-manufacturer price[1]	Efficient combination	
Mark-ups		
(s94) Private Hospitals	1.4% of AEMP	
(s90) Community (AHI) (3-tiered)	$4.28 - $99.28	

Wholesale/distribution	$27.75[2,3]	$14.72
Diluent	$5.50[2]	
Preparation fee	$86.28	$91.04
Dispensing fee, ready-prepared	$7.78[2]	$13.95
Clinical services		$13.48
Total (ex. mark-ups)	$127.31	$143.18

Notes:
1. Based on PBAC-recommended price, subject to periodic price review(s) and statutory price reductions.
2. Community pharmacy and (s94) private hospital authority only; fee not payable to public hospitals.
3. Distribution fee payable to (s94)-approved private hospital authority excludes trastuzumab.
4. Inflated to 2020/21 prices.

Advice received during the Review, and as noted in the 2013 Review (p. 36), was that hospitals/pharmacies engaging third-party compounders will negotiate fees that reflect the drug cost (paid on a per-mg basis), a compounding fee, general freight costs, container fees and a marginal business return. Thus, while EFC fees are paid to the hospitals and pharmacies who lodge the claims for payment with the EFC, it is reasonable to expect that third-party compounder visibility of these fees influences the negotiation of supply arrangements with hospitals/pharmacies.

Mark-ups

Mark-ups are included in fees paid to (s90) community pharmacies and (s94) private hospital facilities as a means of recognising the costs associated with the supply of EFC medicines not captured by the other fee components. In particular this allows for costs associated with stock management as it pertains to the purchase and holding of stock prior to deliver as an infused product.

Within the 2013 Review, the payment of the mark-up was justified on the basis of supporting other business costs (e.g. rent, overheads, delivery etc), with a cost per infusion of $24.72 (2021 prices). It was not possible to substantiate as part of the current Review whether the cost per infusion to support other business costs has changed since 2013. However, within the existing EFC arrangements, such costs are recognised as a 'claimable' item for (s90) community pharmacies and (s94) private hospitals only.

Advice received during the consultation process is that (s94) public hospitals face similar other business costs. Thus, excluding public hospitals from the receipt of that fee component adversely impacts that sector relative to the others. There does not appear to be a rationale to support the ongoing exclusion of public hospitals from the receipt of these mark-ups (given the nature of operating costs they are intended to cover). While it could be argued that such costs are the purview of public hospital funding arrangements, as supported by the NHRA 2020, applying this rationale to one element of the EFC structure and not others is not internally consistent. Accordingly, if the intent of the EFC is to reimburse actors in the supply chain for relevant activities, equivalent fees should be

applied across the sector.

On the basis of the available evidence, there is a case to extend the payment of mark-ups to (s94) public hospitals, but there does not appear to be a case for a change in the current mark-up levels across settings. The impact of extending the payment of mark-ups to public hospitals is examined in Section 6.

Preparation and diluent fee

A consistent preparation and diluent fee is paid across all sectors claiming from the EFC - $86.28 and $5.50 respectively (total $91.78). Information presented in the 2013 Review reported a cost for preparation of medicines (including diluent) of $91.04 (2021 prices).

On the basis of the available evidence, there does not appear to be a case for a change in the current level of funding allocated to drug preparation. This recommendation may change once further information on the activities and costs associated with the preparation of infused cancer medicines is provided by stakeholders to the Review (see forthcoming data, Section 7).

Wholesale/distribution fee

Feedback from multiple stakeholders during the Review identified that the existing EFC fee structure does not include a wholesaler mark-up as applies to medicines subsidised via other sections on the PBS (such as Section 85 medicines). However, the EFC fees do include a payment for distribution ($27.75) which was intended to cover the costs associated with logistics and distribution.

Evidence from a large logistics provider submitted during the consultation process identified that the cost for storage and freight for the average unit supplied via the EFC is approximately $5-6. This assumes that those units are able to be supplied as part of regular logistics shipments to hospitals/pharmacies. Furthermore, costs were unlikely to differ greatly between metropolitan and rural areas, particularly where those shipments to non-metropolitan areas are part of larger existing shipments. Costs per unit increase to approximately $20 per unit where a medicine is required via a specialised shipment (e.g. a one off order) and increase further if cold-chain storage is required for transport during such a specialised supply. Specific costs for specialised cold-chain transport were not provided.

Additional information received from the perspective of a medicines compounder indicated that on a national basis, there was a difference noted in the cost per delivery between metropolitan and non-metropolitan areas (with non-metropolitan areas incurring a cost approximately $100 higher per

delivery than metropolitan), and delivery costs being highest in Western Australia (noting the geographical spread of customers). The average delivery costs provided were assumed to cover multiple items per delivery; when total freight costs are apportioned over the number of items provided, the average cost per item was approximately $9.50.

A number of submissions to the Review suggested that the existing fees applied to the EFC for freight and distribution could be increased where services relate to non-metropolitan supply and to bring the EFC fees into line with other sections of the PBS with respect to inclusion of a specific wholesaler mark-up. Given the available information, there does not appear to be a basis on which to substantiate a change in the fee paid for distribution, or to include a specific wholesaler mark-up, on the basis that:

- Inclusion of a wholesaler mark-up would require that the EFC be incorporated into the existing CSO under the 6CPA as it applies to other sections of the PBS and for which wholesaler participation guarantees medicine availability. However, information provided to the Review from wholesalers is that they do not routinely carry all items (cancer medicines) on the EFC, either due to the unit costs of those items being too high or because manufacturers have a preference to supply those medicines directly to compounders/hospitals. Inclusion of EFC items in the CSO would therefore require a broader system change (the need for such a change has not been substantiated in the evidence presented to the Review).

- It is not clear that freight and logistics costs will routinely be higher for supply to non-metropolitan areas relative to metropolitan. Advice received during the Review was that logistics issues in metropolitan areas can be as complicated and costly to address (particularly for specialised, time-sensitive orders) as those in non-metropolitan areas. Including a specific loading on the distribution fee for non-metropolitan areas fails to recognise that metropolitan deliveries can be as costly. Furthermore, as noted in the 2013 Review (p. 66), existing IHPA recommendations include a loading for freight for regional (non-metropolitan) hospitals.

- Overall, the average freight/logistic cost per item (as above) falls within the amount allocated to that purpose within the existing EFC fee structure.

Dispensing fee

A number of contributors to the Review noted that the existing dispensing fee component within the EFC remuneration was insufficient to account for the specialised nature of medicine dispensing

associated with cancer care. To date, information has not been provided on the additional time taken for dispensing associated with an EFC medicine, relative to other medicines, that could be used to substantiate a fee increase above the existing $7.78 for ready-prepared items.

Additional proposed fees

Consultations to the Review proposed several additional fees be considered with respect to the reimbursement for EFC medicines, including for drug re-labelling/repurposing, drug and waste disposal, and container costs. Consideration of those fees is reserved for Section 6 under discussion of System improvements.

Overall fee

Under the existing EFC arrangement, the overall fee paid (excluding mark-ups and the CCPS fee) is $127.31. Discussion of the extent to which the Review was able to substantiate the individual components comprising that fee is provided above. Evidence from the audit of hospital-based compounding practices conducted for an Australian state-based Department of Health reported a total salary cost of just under $600,000 and non-salaried costs of approximately $60,000 per annum on a facility basis. This is understood to capture all elements of infusion cancer medicine preparation costs including consumables, freight/logistics, and requirements for quality assurance and sterile production (including training, staff health checks and product validation). When adjusted for facility throughput, this results in a total cost per service of $124.15 (2021 prices).

Submissions to the Review by a hospital pharmacy and pharmacy member organisation estimated the following per annum facility fees:

- $8,000 per m^2 for capital outlay for a cytotoxic cleanroom—based on a 'typical,' 20 m^2 hospital-based facility in a metropolitan setting.
- $110,000 for cleanroom equipment—based on a single cytotoxic drug safety cabinet ($45,000) and two-hatch negative pressure isolator unit ($65,000). Separately estimated cleanroom costs included $61,770 (excl GST) for an isolator, plus HEPA and carbon filters ($6,320, excl. GST, replaced annually) and sleeves ($1,150, excl. GST, replaced 'frequently').
- $500,000 per annum for labour associated with compounding (operation of a cleanroom), including the cost of recruitment, employment, training and validation of two compounding pharmacists and four pharmacy technicians.
- $10,000 for non-salary costs for cleanroom operations; including cleaning consumables and disinfectants, microbiological media plates and validation kits, personal protective equipment

and regular cleaning.

These costs were provided on a per-facility basis without accompanying information on facility throughput. Nonetheless, the quantums are consistent with those contained in the report provided by the state-based Department of Health. The concordance of the per-service costs in that report with the overall EFC fee ($127) suggests that EFC fee levels may be reasonable (noting that the available cost information is from a single centre in one jurisdiction) and that there is little new evidence to substantiate an increase in the quantum of fees paid for the components that currently comprise the EFC remuneration structure.

Fees specific to compounding

The Department of Health supplied AHA data on the value of administrative and CCPS fees paid to TGA-licensed compounders over the two most recent financial years. These are shown (on a monthly basis) in Table 15. From these data it can be observed that in 2019-20 a total of $16.6 million was paid to TGA-licensed compounders via the CCPS, increasing to $18.8 million in 2020-21. In comparison, total Government expenditure (PBS benefits) on EFC medicines and related benefits in 2019-20 was $1,653 million (see Section 5).

Table 15. CCPS Fees and Service Volume for TGA-licensed Compounders

Transaction Date	*Admin Fees ($)*	*Compound Fees ($)*	*TOTAL ($)*	*(inferred) Claims*
Jul-19	26,198	1,305,252	1,331,450	65,263
Aug-19	26,198	1,529,932	1,556,131	76,497
Sep-19	26,198	1,326,352	1,352,550	66,318
Oct-19	26,198	1,540,073	1,566,271	77,004
Nov-19	26,198	1,346,871	1,373,069	67,344
Dec-19	26,198	999,535	1,025,733	49,977
Jan-20	26,198	1,860,811	1,887,010	93,041
Feb-20	26,198	896,279	922,477	44,814
Mar-20	26,198	1,643,655	1,669,853	82,183
Apr-20	26,198	1,772,774	1,798,972	88,639
May-20	26,198	1,323,535	1,349,734	66,177
Jun-20	26,198	1,062,172	1,088,370	53,109
Total 2019-2020	*314,380*	*16,607,241*	*16,921,621*	*830,362*
Jul-20	26,198	2,088,110	2,114,308	104,406
Aug-20	26,198	1,329,533	1,355,731	66,477
Sep-20	26,198	1,308,290	1,334,488	65,415
Oct-20	26,198	1,764,628	1,790,826	88,231
Nov-20	26,198	1,352,058	1,378,256	67,603
Dec-20	26,198	1,470,113	1,496,311	73,506
Jan-21	26,198	1,640,870	1,667,068	82,043
Feb-21	26,198	1,435,353	1,461,551	71,768
Mar-21	26,198	1,448,680	1,474,878	72,434
Apr-21	26,198	1,359,414	1,385,612	67,971
May-21	26,198	1,823,810	1,850,008	91,191

Transaction Date	*Admin Fees ($)*	*Compound Fees ($)*	*TOTAL ($)*	*(inferred) Claims*
Jun-21	26,198	1,803,680	1,829,878	90,184
Total 2020-2021	*314,376*	*18,824,539*	*19,138,915*	*941,227*

Source: CCPS fees supplied by Department of Health.
Note: Inferred number of claims is estimated by dividing the payment for compound fees by $20.

TGA-licensed compounders who have contributed to this Review (as with the King Review) stressed that the payment of the $20 fee is essential in recognising the significant costs associated with maintaining and operating a TGA-licensed facility. Thus, is it relevant to consider whether information has been provided to this Review which can substantiate the need for a separate fee payment to TGA-licensed compounders; the extent to which the payment of a $20 per fee is consistent with the costs of maintaining a TGA-licensed facility that are attributable to the regulatory requirements of participating in the EFC program; and the mechanisms by which any appropriate fee payments might be enacted.

Relevant to these considerations are the findings of the 2017 King Review (p116) that the quantum of the fee ($20) could not be substantiated and that there was no evidence to support payment of a specific compounding fee to one element of the supply chain and not the others (i.e. non-TGA licensed compounders); see Text Box 3.

Text Box 3. TGA-licensed Compounder Fees: The King Review

The rationale for differential payments for compounding of chemotherapy preparations is not substantiated on the basis of patient risks or health outcomes medicines that must meet an appropriate level of quality, whether prepared at a facility that is Therapeutic Goods Administration licensed or not licensed.

Chemotherapy compounding is the preparation and supply of chemotherapy medicines. It is a highly specialised area within pharmacy practice. Less than fifty pharmacies supply 70 per cent of all chemotherapy compounding in Australia. To assist with the costs of these medicines, prices are subsidised under the PBS.

The government recognises that chemotherapy compounding requires specialised preparation methods. Fees are therefore paid to participating pharmacists in accordance with the Efficient Funding of Chemotherapy (EFC) measure. For community pharmacies these fees include:

- ready-prepared dispensing fee ($7.02);
- preparation fee ($83.22);
- distribution fee ($25.92); and
- diluent fee ($5.14).

Public hospital pharmacies authorised to supply PBS-subsided medicines are paid on a similar basis however, they are not currently eligible for the distribution or diluent fees.

As part of the PBS Access and Sustainability Package, the Chemotherapy Compounding Payment Scheme (CCPS) was introduced by the government as a revised payment arrangement for compounding fees that related to eligible EFC PBS claims. The scheme established a two-tier fee structure consisting of $40 per eligible PBS claim for compounding and an additional $20 for facilities that hold a TGA licence.

From the submissions received, there was a strong view that no therapeutic difference exists between products that are produced by a TGA-licensed facility and those produced by a non-TGA-licensed facility.

Facilities that hold a TGA licence contended that they had gone through greater effort and costs to acquire and maintain the license, and they should be remunerated an additional $20 to acknowledge the extra cost. The Panel is not satisfied of there being sufficient evidence to demonstrate the value of those additional costs or whether they should be valued at $20 per claim.

Furthermore, the Panel does not consider that medicines compounded in a TGA-licensed facility are any safer than those compounded in a non-licensed facility. There was no evidence provided to the Panel to refute this, including from the TGA. If TGA-licensed facilities were remunerated, it would imply that there is a difference in quality or safety, which is not the case. The Panel instead considers that appropriate standards should be in place for chemotherapy preparations produced in any relevant facility, to ensure that these preparations meet a required level of quality, with minimum risks to patient harm."

Excerpt from the Review of Pharmacy Remuneration and Regulation (2017, p. 116) [39]

Sourcing the information

All TGA-licensed compounders consulted in the Review were invited to provide data to substantiate the costs of complying with TGA regulatory requirements (including accreditation and ongoing licensing) as a means of supporting the payment of a $20 fee. Two stakeholders provided aggregated (overview) information on various aspects of their compounding operations. To ensure anonymity of the stakeholders and preserve the commercial-in-confidence nature of the information provided, the information reported here-in has been combined (based on information provided on compounder throughput of EFC services) at two levels:

- Costs associated with undertaking stability testing for EFC products.
- Costs of complying with other regulatory guidelines associated with being a TGA-licensed compounder. This included (variously by stakeholder): the cost per centre of undertaking

TGA compliance audits, the cost of upgrades per centre as required to continue to comply with TGA accreditation standards, and compliance with PICS standards.

It is possible that compliance with PICS standards may include some costs associated with good manufacturing practices (such as: maintenance of sterile rooms; appropriate training, gowning and equipping of staff for compounding practices; quality assurance processes etc) for the compounding process itself which, for the purposes of the EFC program, would be intended to be captured under the preparation component of the fee. The extent to which such costs were included in the data provided cannot be discerned but would represent an aspect of costs that might otherwise be captured by compounders' fees for services.

The cost information provided was weighted across stakeholders to estimate a cost per unit of production attributable to TGA processes. This afforded a comparison of that cost against the CCPS fee ($20) as currently paid to TGA-licensed compounders. Scenario analyses were subsequently constructed to show the operational requirements that would need to be in place to support a $20 CCPS fee.

In general, compounders have not provided substantiated costs to support the existing $20 CCPS fee, the claim that this fee should be increased along with inflation, or that the fee should be paid per item (i.e. that costs increase with scale). The breakdown of TGA Compounder costs associated with compliance with TGA regulation are presented in Table 16. From these costs the following was observed:

- There is a weighted cost per unit of production (infusion) for stability testing of $4.71
- There is a weighted cost per unit of production (infusion) of complying with TGA regulatory requirements of $8.71 ($6.95 to $10.47 using the bounds of the reported range).
- Combined these produce a total cost per unit of production associated with TGA licensing status of $13.46 ($11.70 to $15.22).

Table 16: CCPS Fees and Service Volume - TGA Compounders

Element	*Cost*
Stability Testing	
(A) Stability testing per unit	$4.71
Regulatory Requirements	
(B) Regulatory compliance	$8.71
(C) Total cost per unit produced for Reg Requirements (A+B)	$13.46

Notes: The range noted in costs for the cost of regulatory compliance is due to varying the cost for the upgrade of compounding centres. The base case used a mid-range of $550,000 per annum, with limits of $200,000 and $990,000.

During the consultation, stakeholders from the TGA-licensed compounders were asked whether compliance with TGA licensing requirements was dependent on their participation in the EFC program (was it possible to attribute the costs of compliance with TGA regulation to participation in the EFC program?). While some stakeholders obfuscated in answering this question, others were clear that the costs of TGA regulatory compliance were not directly attributable to the participation in the EFC Program but were as a result of good manufacturing practice.

Comparing the CCPS fee with the derived per-item costs (see Table 16) results in a difference of $6.54 (32.7%) per item in favour of TGA-licensed compounders, assuming all regulatory costs are the result of EFC participation. Based on infusions claimed in 2020-21, this represents a total of $6.3 million in payments specifically to TGA-licensed compounders (in addition to payments via the supply chain) for which a cost basis for the fee could not be substantiated.

Scenario analyses to substantiate a $20 fee

Given the available information on costs and supply settings, scenario analyses were undertaken to illustrate the conditions under which TGA-licensed compounders would have to operate to support the payment of a $20 fee. These scenarios were restricted to those which reflected consistent cost information across the contributing stakeholders with respect to the total number of units produced and the cost of stability testing. Based on these scenario analyses, to substantiate the $20 fee paid to TGA-licensed compounders the following conditions would be required (noting that these scenarios have been evaluated as occurring independently):

1. An approximate halving of the number of total EFC units produced and supplied (to increase the weighted cost of stability testing to $11.29 per item);
2. An increase in the annual cost of stability testing by a factor of 2.4 to achieve a cost per item for stability testing of $11.29 (implying that more molecules are subject to stability testing, more complex testing is conducted, or a combination of the two); or
3. An increase in the cost of regulatory compliance (non-stability testing) of $6.64 per item.

Scenarios one and two indicate the importance of production scale in substantiating the payment of the existing CCPS fee. Producing fewer units (lower volume throughput) increases the cost per unit largely due to stability testing costs being defrayed over fewer units. This rests on the assumption that the same number of EFC supplied molecules would be subject to stability testing, even with lower throughput (which assumes that all those molecules would continue to meet the minimum threshold level of throughput as set by individual compounders to qualify for stability testing). Similarly, increasing the number of centres increases facility infrastructure upgrade costs but would

also likely increase total throughput (for a given level of demand).

5 Access and safety

5.1 Stakeholder views

5.1.1 Service viability, flexibility and specialisation

To maintain and improve patient access to cancer medicines, hospital and community pharmacies, pharmacy member and consumer representative organisations, strongly advocated local, in-house availability of cancer medicine compounding services, particularly in rural areas, in contrast to increased reliance on third-party compounders.

In regional areas, in-house compounding facilitates urgent access to emergency cancer treatment closer to patients' homes and reduces the need to travel to urban centres to undertake treatment. There was a view that third-party compounders are unable to provide 'just-in-time' regional services due to their reliance on third-party logistics providers who often only do one run a day to some areas and may lack the capacity for coldchain distribution on weekends. Cancer medicines provided by third-party compounders must therefore be ordered in advance, compared to in-house compounders, who can prepare infusions on the day of treatment.

Stakeholders regarded in-house compounding as a means of streamlining treatment administration, reducing the burden on patients and reducing some forms of wastage. Patients receiving IV cancer medicines often have pathology tests ordered in the days immediately prior to treatment, with results checked on the day of drug administration. If pathology tests are abnormal or the patient is otherwise deemed ineligible (e.g., experiencing acute side effects), treatment may be postponed, or doses adjusted prior to administration. Where infusions must be ordered and delivered from a third-party compounder, treatment may be delayed. Such delays may impose significant burdens on patients, who often face additional travel and accommodation costs. Further, dose adjustments undertaken at the point of infusion may increase the risk of administration error. Access to in-house compounding allows cancer medicines to be compounded directly following receipt of pathology results and clinical review. A lack of in-house compounding was also cited as an impediment to regional patients' participation in clinical trials, as trials often require just-in-time supply and specialised orders.

Some stakeholders, including clinicians, hospital pharmacists and TGA-licensed compounders, noted that the main drivers of access to cancer care—particularly with respect to the rural/urban divide—were specialist staff, health infrastructure and logistics, rather than the availability of medicines. One example offers was that patients are often unable to receive treatment in rural settings lacking

oncology specialists. In addition, as most regional/rural cancer treatment centres are run on an outpatient basis, long-term and complex treatments are generally not accessible in these localities.

> *In the Queensland scenario, we have the concentration of really skilled clinicians, pharmacists, doctors and nurses on the southeast corner, and then sprinkled around as you go up the coast. Anywhere away from that, it's probably more a [matter of] capability to deliver the care, as opposed to any specific impact of the PBS. Likewise, the capability to manage complicated compounding, it's not so much a PBS thing, it's more about your skills.*
>
> *-Clinician*

A number of stakeholders suggested that patients in rural settings may be prescribed more 'convenient' treatments (e.g., oral medicines), due to the challenging logistics of access to IV cancer medicines (though this suggestion was uniformly rejected by clinicians and several other informants consulted in the Review, who maintained that patients requiring complex care not available in rural settings were simply referred to metropolitan centres).

> *Regional South Australia was a very good example that did often affect what sort of therapeutic regimen an oncologist might select, knowing the availability of that drug or combination may not be practical. That was why we tried to regionalise compounding facilities as much as we could in that state. And really the same situation we found in Tasmania, where patients on the northwest coast are less likely to be prescribed some of these monoclonals.*
>
> *-TGA-licensed compounder*
>
> *The restrictions are mainly in terms of longer or more complex treatments. So, if there is a really complex, multi-drug, multi-day treatment—that can potentially often not be given. And they may have to get referred to a larger centre for that.*
>
> *-Hospital pharmacy*

While local compounding was proposed by a number of rurally based stakeholders as one means to mitigate patient access issues, a majority of stakeholders acknowledged that there are numerous challenges to providing in-house compounding in rural settings, as these services are expensive to set up and maintain, and involve complex infrastructure, staffing, training and stock management. For smaller, regional compounders, sufficient stock needs to be kept on hand to facilitate just-in-time compounding, and such providers are keenly impacted by logistics issues.

> *If you're running a small hospital and you're gonna have someone who can go in and make some chemo every now and again, they might be on leave, you might not have many trained. You've got to run a facility; it becomes too hard. So just get it externally made. In most situations, you can do that. But with that comes a cost. And you still got to get the cabinet serviced and do all those things to keep it running. […] You got to get the place cleaned.*
>
> *You know, it's like opening a restaurant for dinner and having one person vs 15 people arrive. There are some fixed costs that make it impractical, and you don't want your choux-chef sitting there and no one's ordering pastries […].*
>
> *-Hospital pharmacy*

Attracting suitably qualified staff is challenging in rural/regional areas and may require flying staff to metropolitan centres for specialised training, thereby increasing costs. Additionally, limited availability of medical oncologists and oncology nurses to undertake the safe administration of cancer medicines may preclude the feasibility of rural compounding services. Hospital pharmacists underscored the difficulty of maintaining oncology services in rural settings, whose financial sustainability requires a minimum daily throughput (estimated by stakeholders to be between six and eight full-time chairs).

> *We really need to be running a site every day to make it viable. Turning it off and not having someone in it for two or three days—and then just starting it up on a Monday—probably isn't going to be viable.*
>
> *-Hospital pharmacy*

> *If none of that was an issue in terms of set up and workforce, to be profitable […] you'd need at least six chairs, at a minimum. It wouldn't go anywhere without that.*
>
> *-Hospital pharmacy*

Despite these challenges, widespread and growing dependence upon third-party compounders may erode these specialised skills in non-metropolitan areas, and in the public sector more broadly. Stakeholders from a hospital pharmacy noted that there is an increased need for rural capacity for in-house compounding, due to the rising cancer burden and emergence of enhanced cancer treatments requiring regular, long-duration treatment. There were instances noted of small compounding facilities in rural settings unable to accommodate local demand. Expanding local compounding was seen by some rurally based stakeholders to promote patient access by expanding the availability of proximate and home-based cancer treatment options.

> *It's increasing rates of cancer in the community. It's also the addition of the immunotherapies—you've got a treatment that is every three weeks or every two or four weeks, or every three or six weeks, depending on your drug. And that's got no end date at the moment. Patients are not inclined to stop treatment because there's no data to say that, you know, a year's worth of treatment will do you for another 10 years. So those rolling treatments continue on. Our treatments are better—people are living longer. Once upon a time, you had patients, it's hard to say, drop off after, six to 12 months of therapy. Now those patients aren't dropping off—they're living and we're treating longer.*
>
> *-Hospital pharmacy*
>
> *Our facility's not big enough to service the whole load of the public work. It's an add-on and that's one barrier.*
>
> *-Hospital pharmacy*

A public hospital pharmacist and a public health service administrator commented that third-party outsourcing of script-processing and compounding has reduced public hospitals' revenue from the

PBS over time, though the long-term implication of hospitals' evolving balance of accounts was not immediately clear. On the other hand, some stakeholders argued that the use of third-party compounders is value-added, as it promotes patient access to cancer medicines in situations where in-house compounding is not feasible. Medicines procured through third-party compounders often have extended stability and longer expiry dates relative to infusions compounded in-house, and hence can be stored longer, reducing spoilage and enabling the reassignment of prepared doses.

> *They might have an expiry on something [of] 100 days, where we've only got it for seven—so there are examples where it might be cost-effective for you to do more in-house if you were able to put that longer [expiry] on things. But you need to have that data.*
>
> *- Hospital pharmacy*

Notwithstanding some hospital pharmacists' view that access to stability studies conducted by third-party compounders would enable them to extend the expiry of drugs compounded in-house, TGA-licensed compounders maintained that stability studies are specific to the site and conditions under which they are performed, precluding the application of extended stability data by external parties (see Section 4.1.2).

Finally, it was noted that with respect to state-level regulations, discrepancies between states posed challenges, particularly for TGA-licensed compounders operating in multiple jurisdictions/providing services across state lines.

Auditing of facilities

As a means of promoting the safety and stability of cancer medicines, one TGA-licensed compounder recommended that pharmacies delivering EFC-listed products be audited to ensure compounded products were stored in accordance with compounders' guidelines. Currently, only TGA-licensed compounders are audited for compliance by the TGA. While pharmacies are not subject to any centralised auditing requirements, they may be variously subject to other state-based requirements. The recommendation to audit was based on anecdotal observations that at times, pharmacies failed to store chemotherapy products correctly (e.g., without light exposure), potentially affecting product quality and efficacy. Several community pharmacies and medical representative organisations considered that receipt of PBS funding by non-TGA licensed providers should be conditional on

meeting minimum standards. It was noted, however, that significantly increasing compliance requirements could threaten the financial viability of smaller compounding facilities.

5.1.2 Differential costs/clinical treatment based on location

In addition to issues of access, stakeholders (including hospital and community pharmacies, and pharmacy member organisations and patient representatives) reported differential patient costs according to treatment regimen, location and setting. Stakeholders noted differences in the coverage of ancillary treatments (e.g., anti-emetics), as well as disparate patient co-payment arrangements. For example, while larger urban hospitals are likely to cover script co-payments in full, rurally based centres often pass these costs onto patients—potentially impacting equity of access.

Stakeholders noted ostensible differences in costs between the public and private hospital systems, and that rural patients may not have a choice as to where treatment is delivered.

> *Consumers who elect to have IV etoposide d1-d3 do not incur a co-payment in the dispensing. Consumers who elect to have the oral etoposide at home will incur a co-payment in the dispensing. The decision to continue oral therapy at home should not come at a financial burden.*
>
> *-Hospital pharmacy*
>
> *Sites may absorb or pass on the co-payments to patients for infusion/oral chemotherapies/antiemetics. Depending where you are treated, patients may or may not incur a cost.*
>
> *-Hospital pharmacy*
>
> *The patient co-payment can be confusing for patients unfamiliar with the PBS and is a considerable charge for patients before the PBS safety net is reached. Consideration should be given to using the concessional co-payment amount for all EFC items or removing the requirement for patients to provide a contribution altogether.*
>
> *In NSW, for example, public hospital outpatients do not pay a co-payment, with a co-payment equivalent paid by NSW Health. Other outpatients, including in the NSW private hospital system, pay a co-payment for their original EFC script but not*

for their repeats. If there is a dose variation of more than 10% between individual scripts, then a new prescription is required, necessitating an additional co-payment.

-Commercial pharmacy

In addition, in public hospitals not operating under the PBS reform agreements (i.e., in NSW and ACT), the inability to claim for medicines provided to inpatients incentivises perverse discharging practices. For example, an inpatient may be discharged to the chemotherapy day-suite so that an infusion can be provided as an 'outpatient' script—and therefore claimed via the PBS—and then immediately readmitted to hospital to continue inpatient care. While local health systems and their comprising hospitals should theoretically receive state-level budgetary compensation/adjustment depending on PBS usage, at the local level, a hospital pharmacy may be treated more simply as a business unit needing to generate revenue and contain costs. Such 'gaming' of the system was seen by stakeholders as an inevitable outcome of financial pressures within the system (see Sections 3 and 6 for elaboration on financial flows and potential system improvements, respectively).

The one thing on my mind […] is the issue around infusional drugs for public hospital inpatients. Inpatients becoming outpatients and outpatients becoming inpatients. […] This is an issue in the clinical haematology space for a couple of drugs, but the big the big one at the moment is blinatumumab. The problem is this issue about reduced access for patients if the hospital feels it's paying for drugs that if the person is an outpatient, the Commonwealth would be paying for and if they're an inpatient, the Commonwealth view is that the hospital is paying for it.

-Clinician

It makes no sense at the patient or physician-level. And it leads to game playing and to use of drugs not strictly per protocol. So I think there's a lot of adverse consequences from that. I would wonder, particularly for a patient who might start as an inpatient but continue the infusional drug as an outpatient, which is the PBS bit and which isn't? Blinatumomab would be the example there. They might be ambulatory at the time of prescription writing. They might be inpatients at the time delivery is initiated. They might be ambulatory again as the infusion goes on,

> *because it's multi-day.*
>
> *[…] And the games that are playable—let me move away from acute leukemia and talk about what happens with the most commonly prescribed chemotherapy regimen in the haematology space, RCHOP for diffuse large B cell lymphoma. You know the regimen—day one is rituximab. When is it typically given if someone's an inpatient? The day of discharge, which is often day three, four, five, or even six. Is it as effective, who would know?*
>
> *There are hospitals in the country where they won't give these drugs—people decide they won't play games […]. They abide by the rules, so there are issues for patient access.'*
>
> *- Clinician*

Consumers added that there was disparity in access and the type of care received depending on patients' place of residence. Patients who live in urban areas were more likely to have access to the care needed in terms of hospitals and staff relative to those in rural/regional areas. Depending on the type of cancer, rurally based patients were generally observed to be more likely to travel to city centres for treatment.

There were also disparities of concern within large metropolitan areas. Patients living closer to teaching hospitals were seen to have access to all the care needed at a single facility. Patients required to travel farther were more likely to receive care in multiple facilities. Increased travel requirements typically entail additional out-of-pocket expenses for parking and tolls, which added to patient burden. Patients reported that having access to all the care needed in a single location made a significant difference and helped to promote continuity of care.

> *I am aware that people who go to hospitals that are not the major teaching hospitals do not have the level of care that was available where I went to. When I was in waiting rooms, which I spent a lot of time in, I came across people who had been at some of the hospitals in the southwestern part of Sydney […]. These patients were not only confused by their treatment, but they felt that they'd been discarded in a way—they couldn't get the proper attention they needed in terms of*

direction as to what their diagnosis was, what their options were, and how to organise their treatment.

These patients that I came across from those areas in Sydney were people who'd come to the conclusion they just had to go elsewhere than from their local areas and come to the major teaching hospitals.

-Consumer

Chemotherapy comes with some pretty serious side effects. I ended up in hospital with febrile neutropenia. And [I'm in] the same hospital, so my doctor just comes and sees me on these rounds. My friend had all sorts of issues—he had a feeding tube because it was throat cancer. He had chemo and radiation at the same time. Dealing with all of the side effects, if you're in one place, means that you can just have it all done, you go back to the same place. [Public hospital] provides subsidised—not free—but subsidised parking for people on chemotherapy. […] All those things make it pretty straightforward. I can just imagine that if you're in a more remote location, traipsing around to deal with different specialists with different problems would be problematic.

- Consumer

Consumers added that the decision on where and when to seek treatment is strongly informed by the information a patient is presented with at the time of diagnosis, underscoring that access to information is a critical component of quality care.

A lot of quality care comes down to quality explanations. I think that in the absence of crystal-clear explanations as to what the steps are to diagnosis and treatment and the recommended order of treatment—because some people have the neo-adjuvant therapy before they have surgery and other people like me have the surgery first. I think the fear of the unknown becomes overwhelming. And, also, people may not be able to speak to the various specialists and have the various scans in a geographically proximate area. People [may be] unwell even before they've started treatment or, even more so, after they've started treatment.

Traipsing around location to location, not being able to find parking and being fined for overstaying, etc., is incredibly stressful.

- Consumer

Particularly in the city, people have got options. The equity would be more about, I think, if you're in the country, do you have access to a public hospital that provides the services? I'm always amazed at people who say, "Oh, no, I ended up paying for radiation." I mean, surgery is different because most of the surgeons are private, but radiation and chemotherapy? Why did you pay for this? When they do it [for free] down the road at the public hospital? […] I think a lot of it comes down to people not knowing what their options are, because the information is not made available simply and clearly. There is obviously, in some circumstances, a vested interest for medical professionals to direct traffic to areas such as pathology, where there'll be higher rebates and things for shareholders or directors of those companies, etc. But it really it also comes down to people just not being confident of their options.

-Consumer

5.1.3 Clinical appropriateness of PBS quantities and restrictions

Representatives from pharmacy member organisations raised the issue that the maximum quantities currently permitted via the PBS for several EFC-listed drugs are insufficient for some standard courses of treatment (i.e., the current maximum quantities do not reflect monthly use in clinical practice). It was also noted that there are no incentives (and some financial disincentives in the form of application fees and potentially lower prices) for pharmaceutical manufacturers to submit PBAC applications for expanded indications, longer lengths of treatment or simplified restrictions, particularly for off-patent medications. Several stakeholders suggested that this leads to some PBS listings being out of date relative to current clinical guidelines and practice. Similarly, the TGA-registered product information for a given drug may not be up to date with current best practice. Yet, as with PBS listings, pharmaceutical companies lack incentives to update information for products without a new indication.

> *The product information absolutely is intended to guide how the drug is given, but given how outdated and inflexible product information is, it's standard practice for the product information not to be strictly followed. And that's recognised as appropriate. You know the term 'off-label,' right? So, there's off-label and then there's things between off-label and on-label. For example, a drug like bortezomib—the product information doesn't include the most commonly given regimens around the world. There's no incentive for the originator to update the PI unless they get a new indication.*
>
> *[…] I don't think there's a situation where the subsidies drive where the care is, except in terms of affordability, where it would be a consideration. It kind of goes back to blinatumomab and things like that. There's all sorts of interwoven threads. If the product information didn't say, "Thou shalt be an inpatient," then perhaps this would not have been in the rules, you know?*
>
> *-Clinician*

PBS listings reflect evidence presented to the PBAC as the basis for which a drug can be recommended to the Minister for Health as cost-effective (see Section 3). Sponsors (i.e., manufacturers) of products listed on the PBS may submit applications to change those listings at any point in the life-cycle of a medicine, noting the PBAC's guidelines for the evidentiary requirements underpinning such a request (see PBAC Guidelines, 2016) [9]. Despite manufacturers' ability to amend listings, some clinicians noted that PBS restrictions inadvertently hampered patient access to medicines. Mandatory approval processes for some prescriptions were seen by these stakeholders to waste time and cause unnecessary delays in treatment.

> *And pharmacists, we really like rules—we don't want to break them. […] What is even more challenging is people who are on a clinical trial for their first-line treatment, for example, and then they progress in their second-line treatment. But if something is only listed for first-line—or third-line or whatever—then it gets very murky, and that would not be captured from the PBS perspective at all. In our institution, it would be captured on the software because our trial protocols are built into our software. But again, if you're pro-trial, which you sort of have to be if you*

want new drugs to come to market, it does make it more tricky.

-Hospital pharmacy

I guess one quick win is increasing the maximum dose to account for people with larger body surface areas. So, when a person's BSA […] is large, it requires the prescriber to obtain authority approval, which is just a waste of time in my mind.

-Clinician

5.2 Evidence from the literature on access and safety

A review of peer-reviewed and grey literature was undertaken to further explore issues of access and safety associated with cancer medicine funding mechanisms and associated practices (see Appendix 3). In general, few identified studies specifically address the relationship between funding and access to cancer medicines. Identified studies in the Australian context, of greatest relevance to the Review, relate to trastuzumab (noting that prior to inclusion on the PBS, this medication was funded through the Herceptin Program). Evidence on the potential safety implications of cancer medicine funding arrangements is more diverse in nature.

5.2.1 Treatment protocol heterogeneity—the case of trastuzumab

Harris et al. conducted a retrospective comparison of prescriptions and PBS claims data for HER2-positive patients receiving chemotherapy and trastuzumab [40]. The study sought to determine the accuracy of dispensing data to identify treatment protocols, the number of treatment cycles and duration of therapy. Results demonstrate that treatment protocols and duration were consistent with protocols derived from prescription records; 76 patients (69.1%) were assigned the same protocols based on prescribing and claims data. However, dispensing claims did not reflect the number of treatment cycles accurately. As dispensed drug could be used for more than one cycle—and some therapies therefore administered more frequently than they were dispensed—the median number of treatments was underestimated in dispensing data [40].

Similar results were reported by Daniels et al. in a study investigating adherence to prescribing restrictions using dispensing records (2001-2016) for publicly-subsidised trastuzumab among a cohort of HER2-positive metastatic breast cancer patients in Australia [41]. The study used group-based trajectory models to cluster patients, first on their patterns of trastuzumab exposure, and then on

their patterns of lapatinib and chemotherapy exposure. Results highlighted the heterogeneity in real-world treatment of HER2 positive disease; for a substantial proportion (36%) of women who received trastuzumab in the period, treatment did not adhere to prescribing recommendations [41].

5.2.2 Drug preparation and safety

Five publications addressed potential safety aspects arising from the manner in which cancer medicines are prepared, including how this might be influenced by underlying funding mechanisms. Across these publications (four international studies and one Guideline reflecting Australian practice) it was noted that in general, the incidence of medication errors attributable to drug preparation and dosing is low. Moreover, given the tendency for those processes to rely on human involvement, the extent to which errors can be eliminated through the use of robotics and other forms of automation is limited. With the emergence of less toxic immunotherapies and MAbs, the risks associated with errors, both to patients and staff handling cancer medicines, are declining.

International publications: Gilbert et al. presented a review of eleven potential human failures in chemotherapy preparation [42]. The authors conducted field observations in four cancer-centre pharmacies in four Canadian provinces. Errors identified during the study involved the potential for patients to receive the wrong drug or dose, risking death or loss of function. The authors concluded that human errors were related to manual chemotherapy mixing practices and may be mitigated through greater use of automated compounding processes—from robotics to bar-coding and gravimetric weighing—with built-in error prevention functions.

Based on field observations in six Canadian cancer centres, White et al. examined the process for ordering, preparation, labelling, verification, administration and documentation of ambulatory IV chemotherapy [43]. Across the various centres, the authors reported a range of potential chemotherapy preparation and dispensing errors, including incorrect volume or type of diluent, selection of incorrect medication and incorrect drug labelling.

Weingart et al. conducted a review of studies investigating chemotherapy medication errors [44]. The authors presented the extent and nature of chemotherapy errors, estimated the incidence of prescribing errors reported in the literature and discussed safety measures to prevent errors before they occur. The authors referred to chart review studies reporting chemotherapy error rates with the potential for harm of one to four per 1,000 orders, affecting 1-2% of inpatients. However, the authors noted the validity of this estimate was subject to limitations of the chart review studies. Strategies aimed at chemotherapy error prevention included compliance with best practice and guidelines (e.g., use of checklists, prohibition of verbal orders, avoidance of ambiguous

abbreviations), prospective risk assessments and use of information technology (bar-coding medication administration, and smart-pump technology).

Reinhardt et al. performed an analysis of detected and avoided consecutive chemotherapy prescribing errors over a 24-month period (January 2013-December 2014) [45]. Analysed errors had the potential for immediate patient-safety consequences, including the prescribing of an incorrect anti-neoplastic drug, as well as chemotherapy dosing or timing errors (e.g., insufficient gap between cycles). The authors reported 2% of total chemotherapy orders contained prescribing errors, with an error rate of 1.9% for outpatient orders and 2.2% for inpatient orders. Error prevention by conventional measures resulted in error-free prescribing in 38% of cases with thorough knowledge of the chemotherapy protocol and in 35% of cases with examination of the patient's medical records. Error prevention using upgraded software with increased safety features resulted in the prevention of 61% of prescribing errors, with an additional 5% considered less likely to occur. However, the authors concluded that an estimated 39% of errors would remain unidentified and uncorrected by changes to software systems.

Jenkins and Wallis conducted a retrospective audit of side effects of acute chemotherapy in patients receiving 5-FU, epirubicin and cyclophosphamide for the treatment of breast cancer [46]. The authors applied a dose-rounding treatment algorithm, allowing drug doses within 5% of the standard dose based on BSA, to assess the impact on acute haematological and non-haematological toxicity. The study found that patients receiving a rounded dose of chemotherapy higher than would be calculated from their BSA were not at increased risk of acute haematological or non-haematological toxicity. The study concluded that dose-rounding of a standard chemotherapy regimen is not associated with a greater risk of acute side effects.

Australian publication: Alexander et al. presented an abridged version of the Australian consensus guidelines for the safe handling of parenteral MAbs for cancer treatment by healthcare personnel [47]. The guidelines provide recommendations that cover appropriate determinants for evaluating occupational exposure risk; occupational risk level compared with other hazardous and non-hazardous drugs; stratification of risk based on healthcare personnel factors; waste products; interventions and safeguards; operational and clinical factors; and handling recommendations. The guidelines, informed by a survey of current practices and synthesis of published information, make seven key observations/recommendations:

- The occupational health and safety risk to healthcare personnel handling MAbs is dependent on internal exposure risk and toxicity.

- From an occupational health and safety perspective, it would be prudent to require greater handling precautions for MAbs than other non-hazardous injectable medications. MAbs do not, however, warrant full cytotoxic precautions, with exceptions only where sufficient evidence exists of safety concerns for specific molecules.
- Safe handling procedures should be stratified according to staff role and health consideration.
- Waste products generated during the preparation and administration of MAbs—including bodily fluids of patients—should be disposed as per standard operating procedures for parenterally administered agents, that is, not classified as cytotoxic waste.
- There are a range of interventions to minimise occupational exposure, such as the use of personal protective equipment (i.e., gloves, gown, respirator mask, protective eyewear), discipline-based aseptic technique, and isolator cabinet, cytotoxic drug safety cabinet and closed-system transfer devices (CSTD).
- The following factors (not related to occupational exposure risk) should be considered when determining preparation and handling recommendations: vial-sharing, complexity of preparation and medication error. Regarding vial-sharing, best practice recommendations and pharmaceutical product information maintain that opened vials should not be shared. Stated risks pertain both to the possibility of cross-contamination between shared vials prepared for immediate use and to the stability, sterility and expiry of vials stored for later use. Anecdotal evidence from individual institution procedures suggests that only when compounding occurs in a pharmacy under aseptic conditions is it appropriate to vial-share.

The authors noted the PBS funding model reimburses costs of chemotherapy drugs based on the most efficient combination of vials to produce a dose. In some circumstances, this may result in residual volume and may influence a preference towards vial-sharing. The authors stated that while not recommended by manufacturers and not endorsed by major health and safety bodies, vial-sharing is widely practiced. The study recommended that while increasing risks associated with microbial contamination, the practice of vial-sharing in the preparation of MAbs is essentially no different to vial-sharing of other parenteral medicines, hence institutions should follow extant local policy relating to this practice.

Finally, the authors recognised that MAb preparation involves numerous complex techniques and manipulations that may result in error when undertaken by inexperienced staff. They recommended that complex (i.e., gentle agitation) or multiple-vial (i.e., >3 vials) preparations should be reserved for well-trained, experienced staff. In some institutions, this may be achieved in the ward environment, while in others, a pharmacy cleanroom or similar controlled manufacturing environment may be

required.

5.3 Quantitative analysis of access and safety data

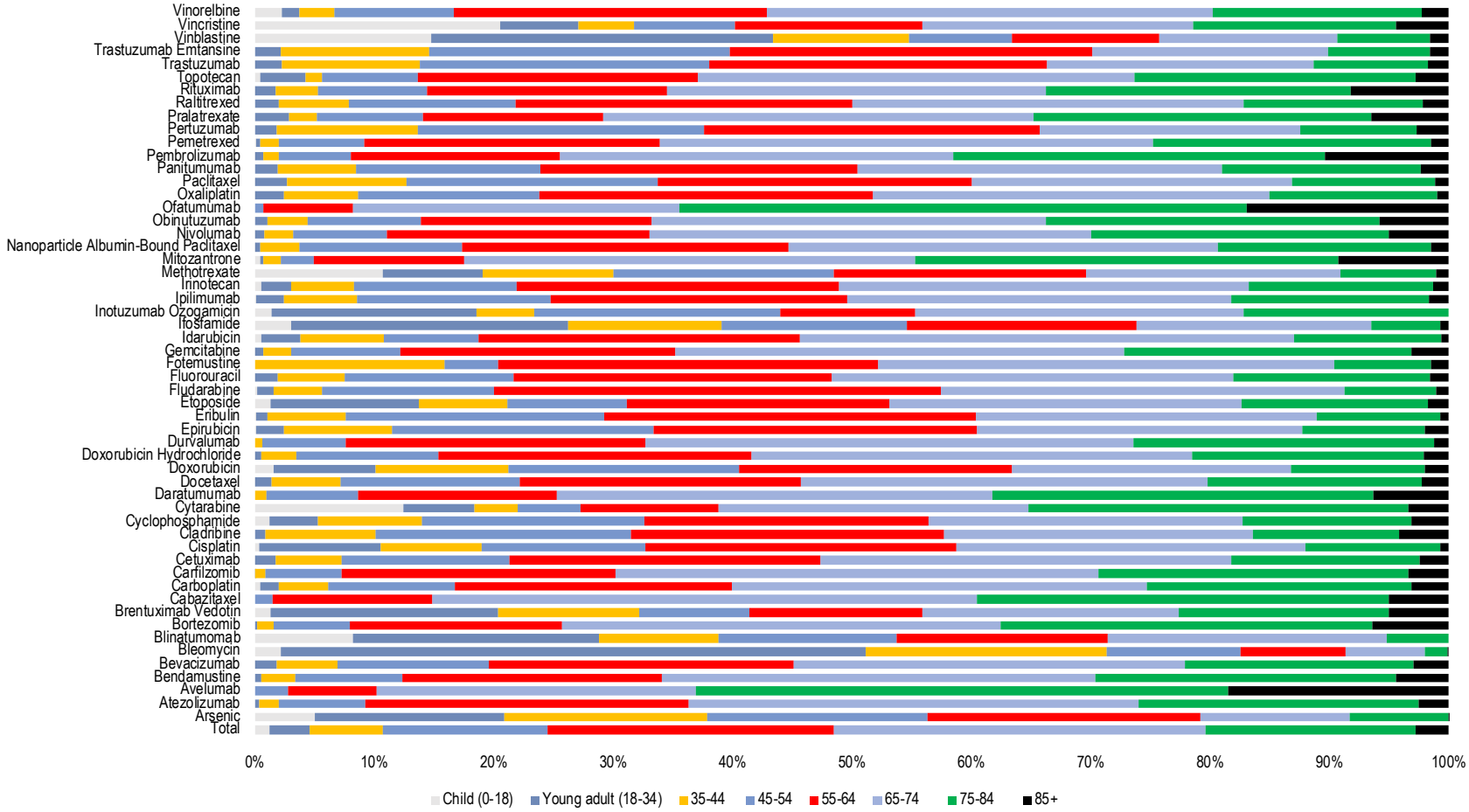
5.3.1 Who is using EFC medicines?

Line-level data on the PBS claims data for EFC medicines (Schedule 1 and 2) for the period 1st July 2016 to 30th June 2021 were obtained from the Department of Health. A total of 6,303,730 dispensing records were provided, which pertained to 270,676 unique patient records. Information from those data on patients' age, concessional status and access to care with respect to distance travelled is summarised in this section (details of the dataset and analyses are provided in Appendix 6).

The mean age of patients at the date of dispensing PBS items for the overall period (July 2016 to June 2021) was 62.7 years for Schedule 1 medicines and 61.5 years for Schedule 2 medicines. Use was described by age cohorts for each medicine (see Figure 20). In children, the most commonly used medicines were vincristine (35%), methotrexate (23%) and cytarabine (11.7%). These medicines are commonly used for leukemias and lymphomas. In young adults, the most commonly used medicines are etoposide (12%), doxorubicin (9%) and cisplatin (8%), which are used to treat a variety of cancers.

In the 35-44, 45-54, 55-64 and 65-74 age cohorts, the most commonly used medicines were fluorouracil, paclitaxel, gemcitabine and trastuzumab. These medicines are used in the treatment of a variety of cancers, including colorectal, pancreatic, and hormone-sensitive cancers such as breast, cancer. In patients aged 85 years and over, the most commonly used medicines were pembrolizumab (10%), rituximab (9%), bortezomib (9%). These medicines are most commonly used to treat blood cancers and solid tumours.

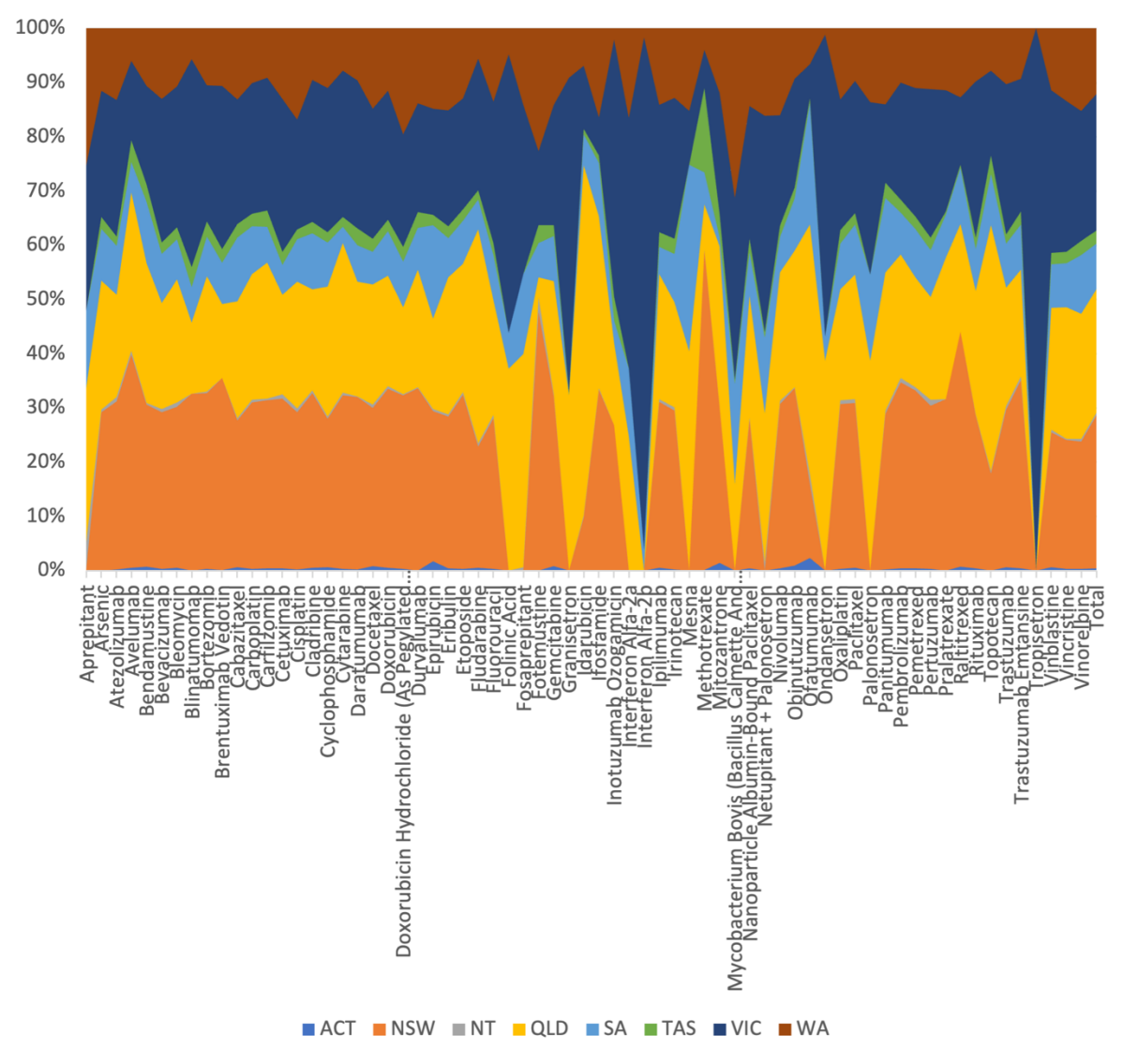
Figure 20. EFC consumers by age and molecule (July 2016 - June 2021)



Source: Prepared for this Review using PBS Line Level Data, see Appendix 6

Overall, states with the largest populations had the greatest consumption of EFC medicines; the consumption of EFC medicines by each state is proportional to the size of the population (see Figure 21). Use of cancer medicines was highest in New South Wales and Victoria and lowest in the Northern Territory and the Australian Capital Territory.

Figure 21. Distribution (by volume) of EFC items by State and Territory (July 2016 - June 2021)



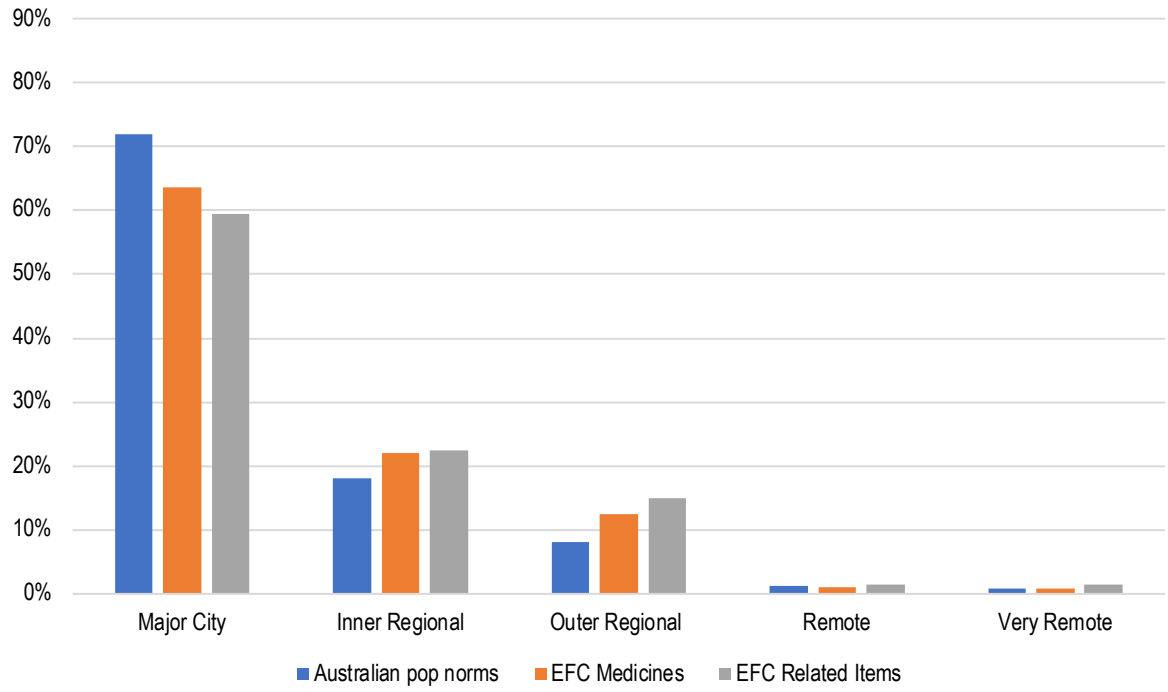
Source: Prepared for this Review using PBS Line Level Data, see Appendix 6

Regional distribution of drug use

A comparison of the proportion of patients accessing cancer medicines by ARIA score with Australian population norms (on place of residence by ARIA score; [48]) shows that a higher proportion of

recipients of EFC medicines lived in more rural and remote locations when compared with the general Australian population Figure 22. While over 70% of the Australian population live in major cities, approximately 63% of patients prescribed a Schedule 1 medicine on the EFC lived in major cities. In contrast, approximately 35% of patients prescribed a Schedule 1 medicine lived in an inner/outer regional area compared with just under 30% for the Australian general population.

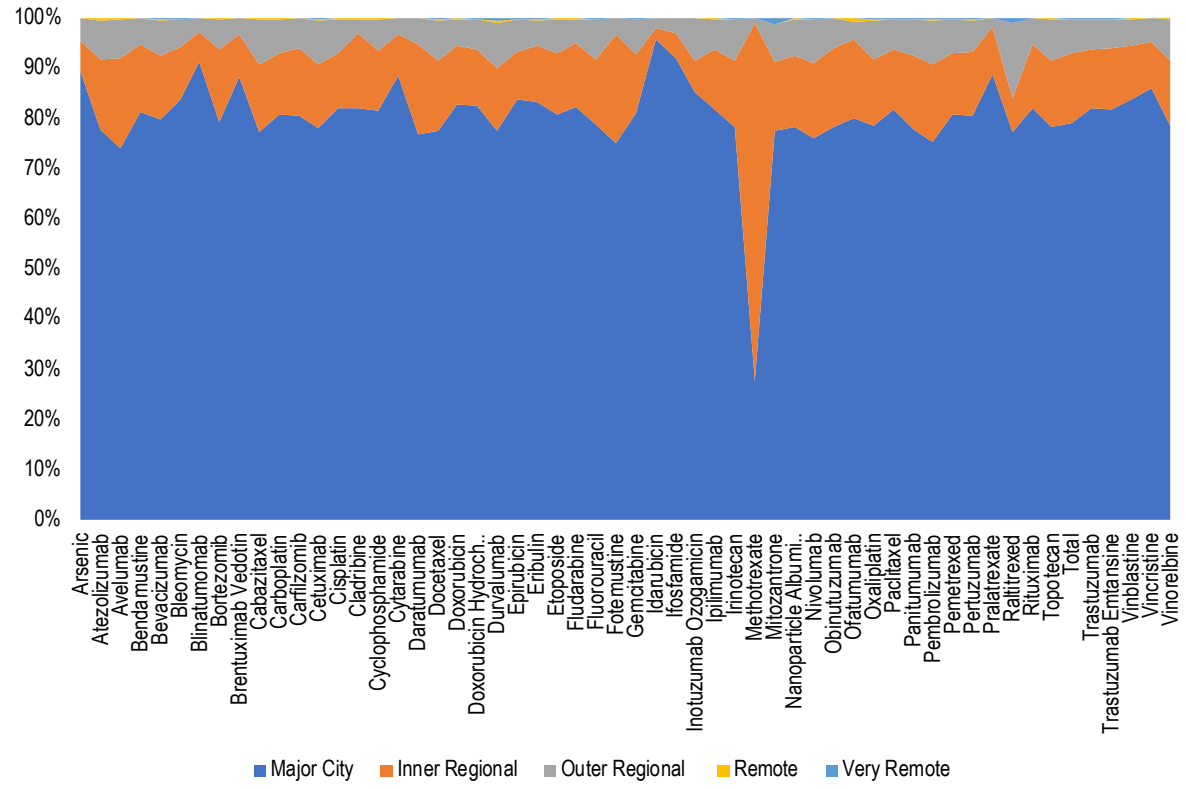
Figure 22. Consumers of EFC-listed drugs by remoteness of residence (July 2016 - June 2021)



Source: Prepared for this Review using PBS Line Level Data (see Appendix 6).
Note: EFC Medicines is specific to Schedule 1 medicines; EFC Related Items is specific to Schedule 2 medicines under the EFC legislation.

A summary of Schedule 1 medicine utilisation by ARIA score is provided in Figure 23. For all medicines, the overwhelming bulk of use was among patients living in cities, being highest for fotemustine and blinatumomab (70-71%). Inotuzumab ozogamicin and avelumab had the highest proportion of patients living in inner regional areas (32-30%). Raltitrexed and ofatumumab had the highest proportion of patients living in outer regional areas (23-18%) and remote and very remote areas (4-3%). The same pattern of use can be observed for Schedule 2 medicines (see Appendix 6).

Figure 23. EFC consumption by remoteness of residence, Schedule 1 (July 2016 - June 2021)



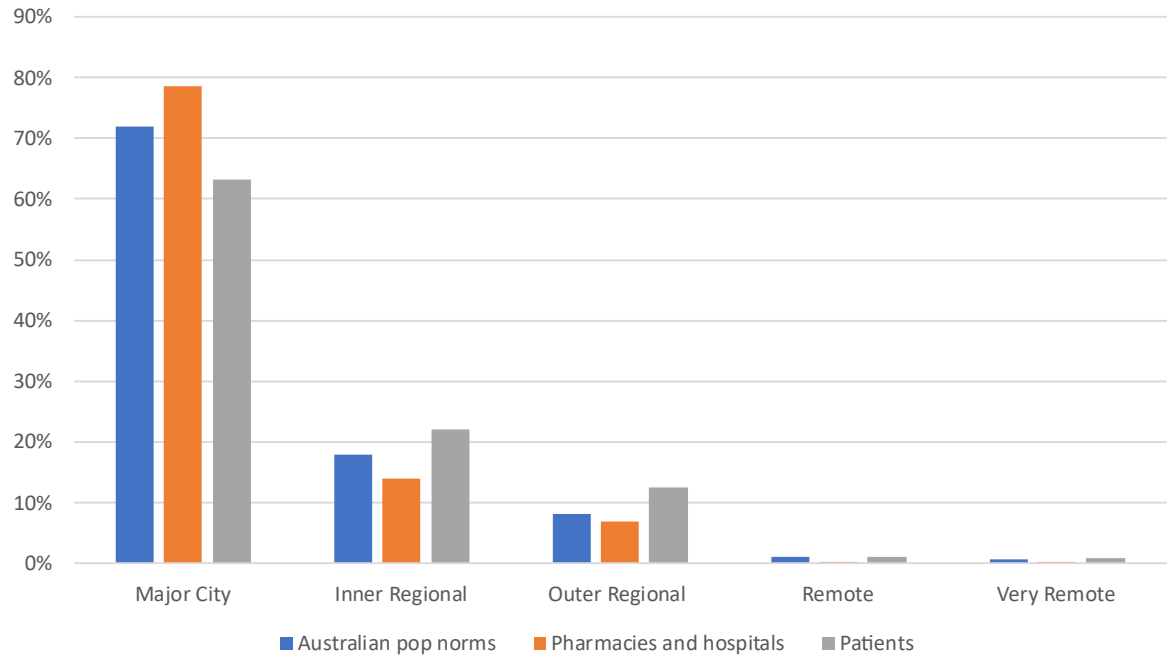
Source: Prepared for this Review using PBS Line Level Data (see Appendix 6).

Patient Access to Care

An assessment of the impact of geographical distance on patient access to care was conducted by comparing patient location (by postcode of residence) with dispensing hospital/pharmacy location (by postcode) and with Australian population norms [48]. From the comparison in Figure 24, it can be observed that whilst a higher proportion of patients accessing cancer medicines via the EFC are located in rural locations than the general Australian population, a higher proportion of hospitals and pharmacies dispensing these medicines are located in more urban areas than Australian population norms. This difference is tempered to the extent that regional differences in cancer incidence may affect comparisons between the Australian population and PBS utilisation with respect to location.

The existence of such a distinction as observed from these data reinforces the importance of addressing issues of access as might be faced by cancer patients in non-urban areas, particularly given the apparent disparity between where patients live and where they are treated. Further detail on the assessment of access by region, including the distribution of use by specific medicine across ARIA categories, is provided in Appendix 6.

Figure 24. Remoteness of service by stakeholder group (2016 - 2021)



Source: Prepared for this Review using PBS Line Level Data (see Appendix 6).

Access to co-payments

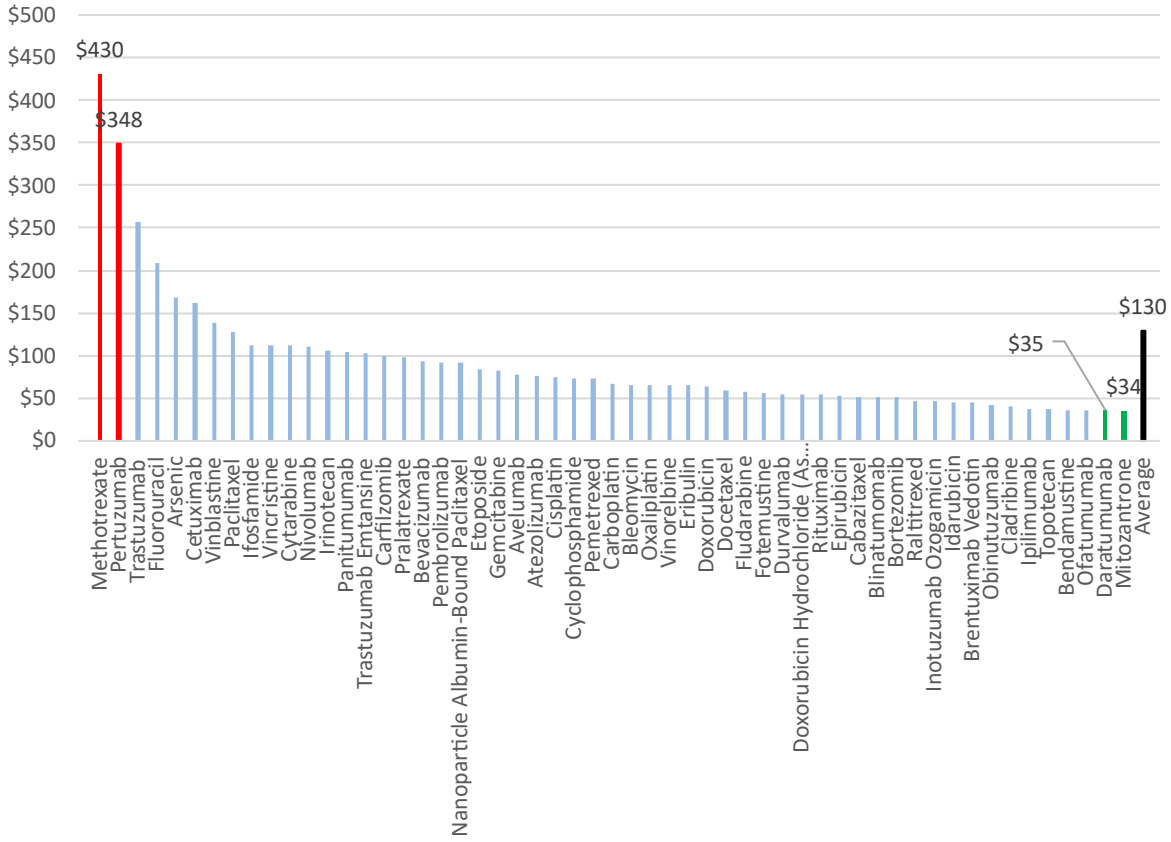
As with all items funded under the PBS, patients receiving medicines listed on the EFC are subject to specific co-payment arrangements. These fall broadly under the categories of general benefit patients ($41.30 per prescription) and concessional benefit patients ($6.60) per prescription; with both patient types eligible to qualify for safety net co-payments ($6.60 and free) once mandated thresholds are reached on out-of-pocket expenditure in a 12-month calendar year. Patients accessing EFC medicines via the Repatriation Pharmaceutical Benefits Scheme (RPBS) qualify as concessional patients. Under the EFC legislation, co-payments are only levied on the initial prescription (repeats do not incur a co-payment) and some jurisdictions have mandated that public patients pay no co-payment (including NSW and the ACT).

Overall, general benefit patients accounted for half of all patients accessing cancer medicines via the EFC, with the remainder being concessional (< 2% of patients were covered under the RPBS). A summary of the average total 'out-of-pocket' costs by Schedule 1 and Schedule 2 medicines is provided in Figure 25 and Figure 26, respectively. Methotrexate and pertuzumab had the highest average total out-of-pocket costs for Schedule 1 medicines. Interferon alfa-2a and trastuzumab had the highest average total out-of-pocket costs for Schedule 2 (related benefit) medicines.

From these data, the average out-of-pocket cost on a per drug basis was $130. However, taking into

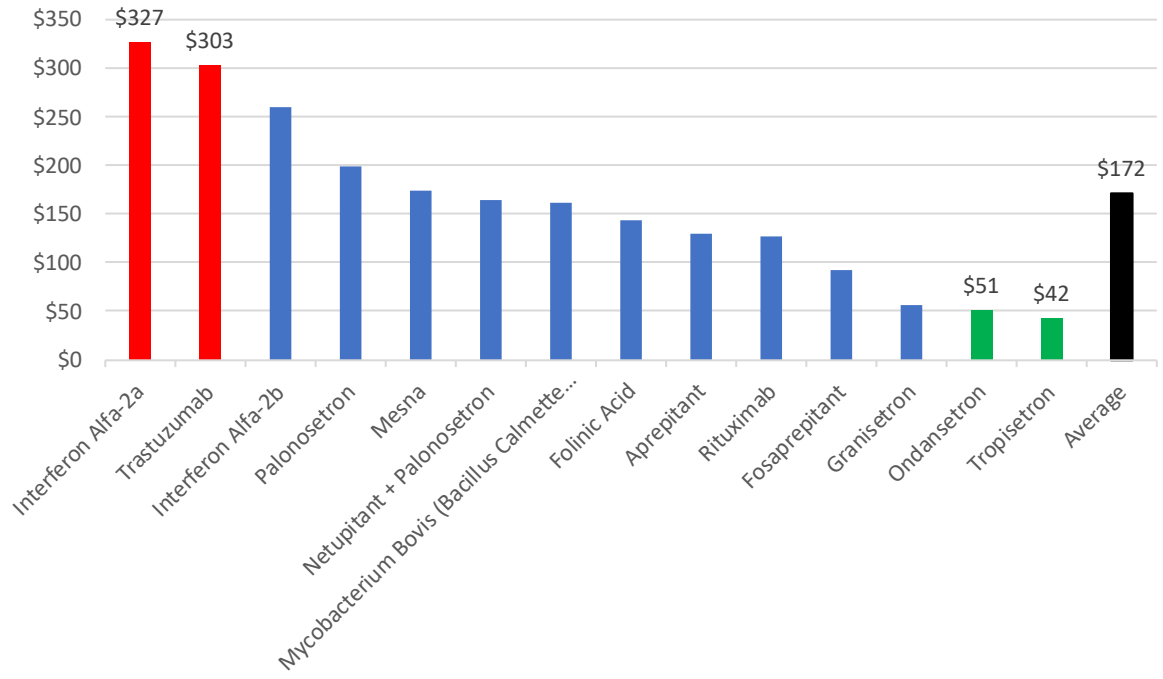
account the potential for patients to be on multiple drugs and to have drug exposure over multiple years during the period of data observed (July 2016-June 2021), the average out-of-pocket cost was $342 per patient.

Figure 25. Mean out-of-pocket costs, EFC-listed drugs, Schedule 1 (July 2016 - June 2021)



Source: Prepared for this Review using PBS Line Level Data, see Appendix 6

Figure 26. Mean out-of-pocket costs, EFC-listed drugs, Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS Line Level Data, see Appendix 6

Access to Closing the Gap subsidies

A summary of EFC-medicine utilisation by 'Closing the Gap' (CTG) eligibility is provided in Appendix 6. Under the EFC legislation, access to CTG is restricted to public patients in public hospitals. Overall, less than 0.3% of items within the PBS dataset were associated with a CTG benefit. ATSI people represent 3.3% of the total Australian population. The bulk of CTG claims (94%) were lodged via (s90) community pharmacies, with the majority of all claims being lodged within NSW (95%).

5.3.2 Analysis of TGA-reported adverse events

Overview

The potential impact on patient safety of the adoption of EFC funding was investigated by examining the incidence of spontaneous adverse events (AEs) related to the use of cancer medicines listed on the EFC as recorded on the TGA Database of Adverse Event Notifications (DAEN; [49]. Cancer medicines were selected for inclusion in the analysis if they were on Schedule 1 of the EFC, had a TGA indication that was consistent with the PBS indication and did not have a general (Section 85) benefit listing. This resulted in the inclusion of 40 EFC medicines for analysis, with analysis restricted to events reported over the most recent full five-year period; January 2016 and December 2020 (see Appendix 8 for a full exposition of the methods).

Data

AEs in the TGA's DAEN are coded using terms in the Medical Dictionary for Regulatory Activities (MeDRA) [49]. The extracted data comprised 6,268 unique case reports of AEs involving at least one EFC-listed cancer medicine. However, as cancer patients often receive combination-based regimens, some AE reports involved more than one EFC-medicine. This resulted in a total of 8,899 unique case reports of AEs and EFC-medicine combinations (hereby referred to as instances).

Of the 8,899 instances reported, 931 contained MeDRA terms that were suggestive of events that may have been associated with errors affected by the mode of reimbursement. This included the potential for off-label use (as might arise when additional infusions can be compounded as a result of vial-sharing, allowing more patients to be treated than might otherwise occur within a given volume of PBS prescriptions) and/or medication errors (see Table 17). The MedRA search terms were further defined into deliberate off-label use (96%, N = 891/931) and non-deliberate / unclear off-label use (4%, N = 50/931). The list of MeDRA search terms used in classifying AEs as potentially of interest in relation to the mode of cancer medicine funding was verified by a clinical expert. Disproportionality analysis – a method which looks for a signal of likely significant effects for AE among a given sample of interest relative to other drugs - was used to identify medicines with higher or lower than expected rates of 'off-label' use (see Appendix 8).

Table 17. Reported off-label use of EFC-listed drugs by adverse event type (2016 - 2020)

MedRA Search Term	*Deliberate*	*Non-deliberate/ unclear*	*Total*
Accidental overdose	-	2 (5%)	2 (<1%)
Drug effective for an unapproved indication	2 (<1%)	-	2 (<1%)
Drug ineffective for an unapproved indication	8 (1%)	-	8 (1%)
Drug monitoring procedure incorrectly performed	-	3 (8%)	3 (<1%)
Inappropriate schedule of product administration	12 (1%)	-	12 (1%)
Incorrect dose administered	-	3 (8%)	3 (<1%)
Incorrect drug administration rate	-	3 (8%)	3 (<1%)
Incorrect product administration duration	-	1 (3%)	1 (<1%)
Incorrect route of product administration	-	9 (23%)	9 (1%)
Intentional product misuse	1 (<1%)	-	1 (<1%)
Intentional product use issue	117 (13%)	-	117 (13%)
Intercepted drug administration error	-	1 (3%)	1 (<1%)
Off label use	441 (49%)	-	441 (47%)
Prescribed overdose	2 (<1%)	-	2 (<1%)
Prescribed underdose	5 (1%)	-	5 (1%)
Product administered to the patient of inappropriate age	3 (<1%)	-	3 (<1%)
Product administration error	-	1 (3%)	1 (<1%)
Product dose omission issue	-	7 (18%)	7 (1%)
Product storage error	-	6 (15%)	6 (1%)

MedRA Search Term	*Deliberate*	*Non-deliberate/ unclear*	*Total*
Product use in	1 (<1%)	-	1 (<1%)
Product use is unapproved in	1 (<1%)	-	1 (<1%)
Product use in an unapproved indication	241 (27%)	-	241 (26%)
Product use issue	56 (6%)	-	56 (6%)
Product used for unknown indication	1 (<1%)	-	1 (<1%)
Wrong product administered	-	2 (5%)	2 (<1%)
Wrong technique in the product usage process	-	2 (5%)	2 (<1%)
Total	*891 (100%)*	*40 (100%)*	*931 (100%)*

Abbreviations: EFC, Efficient Funding of Chemotherapies; MeDRA, Medical Dictionary for Regulatory Activities.

No apparent link to increased reporting of adverse events

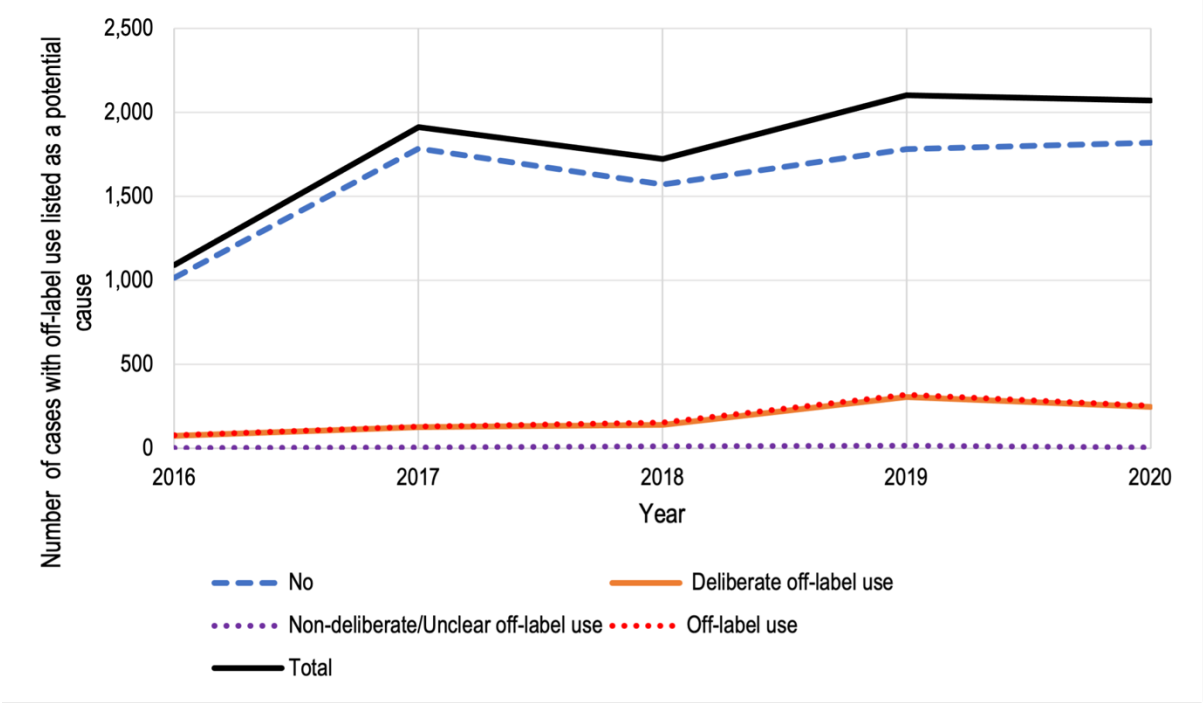
Of the 8,889 instances of AEs, 10% (N = 931/8,889) were potentially related to off-label use. Almost all of the reported instances of off-label use were characterised as 'deliberate' (99%, N = 891/931) (see Table 18). A breakdown of instances of off-label use by year reveals an apparent increase in the number of 'off-label' cases in 2019 (see Figure 27).

Table 18. Reported off-label use of EFC-listed drug by apparent intent (2016 - 2020)

Event	*n*
Uniquely case reports	6,268
Instances	8,899
Instances associated with off-label use	931 (10%)
Deliberate	891 (10%)
Non-deliberate/unclear	40 (<1%)
Other adverse event	7,968 (90%)

Abbreviations: EFC, Efficient Funding of Chemotherapy.
Note: Between January 2016 and December 2020, 6,268 uniquely identified cases of adverse events involving EFC-listed chemotherapy medicines were reported to the TGA. A number of these cases involved more than one EFC-listed medicine, comprising a total of 8,669 'instances.'

Figure 27: Reported off-label use (2016 - 2020)

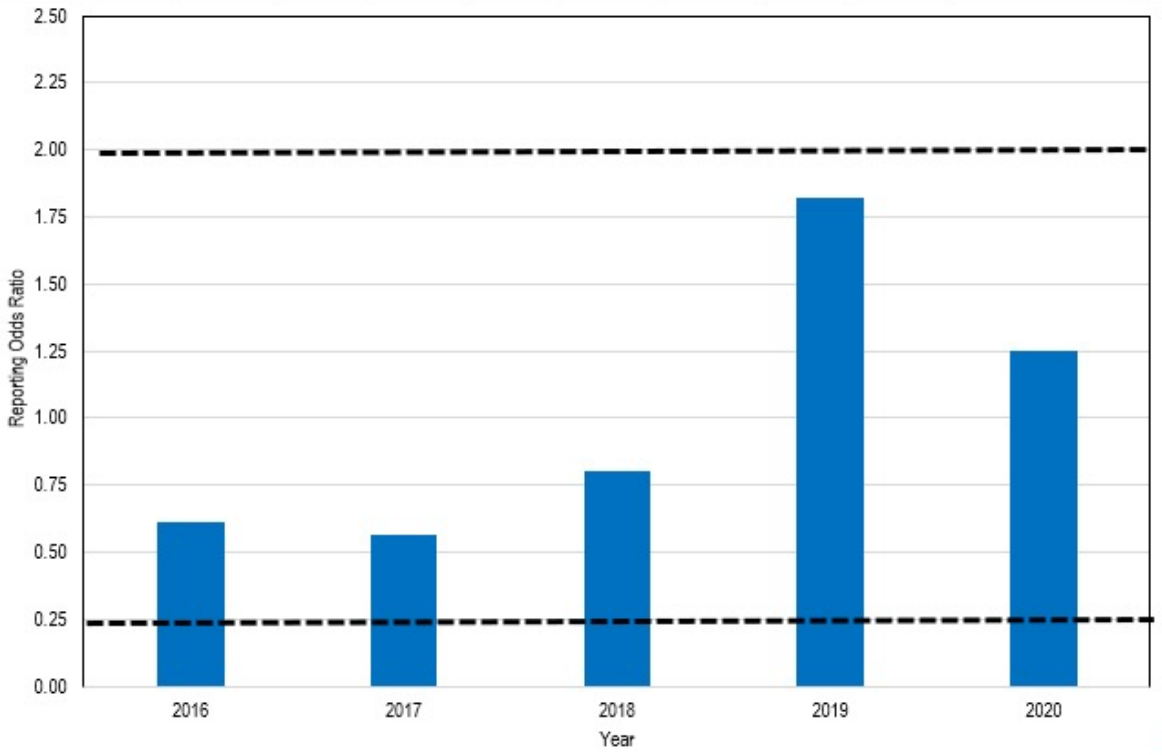


Source: Produced for this Review using DAEN data.

The results of the disproportionality analysis are presented in Figure 28. A reporting odds ratio (ROR) ≥ 2 indicates a clinically significant, higher-than-expected rate of off-label use in a given year; an ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use in a given year; and an 0.25 < ROR < 2 indicates a rate of reported off-label use that is proportionally consistent with all other years [50]. From these results, it can be observed that there was no single year in which the ROR reached a level of clinical significance (i.e., the number of reported events in any given year is statistically consistent with all other years).

This was not consistent across all EFC listed drugs in the analysis. As can be observed from Figure 29, the ROR was >2 for brentuximab vedotin, bevacizumab, doxorubicin hydrochloride, pembrolizumab, topotecan, and vinorelbine for the period 2016-2020, indicating that each of these drugs had potentially clinically significant, higher-than-expected rates of reported off-label use relative to other EFC-listed drugs. In contrast, arsenic trioxide, durvalumab, epirubicin hydrochloride, eribulin mesilate, fotemustine, inotuzumab ozogamicin, raltitrexed, idarubicin hydrochloride, oxaliplatin, carfilzomib, and fluorouracil all had an ROR < 0.25, indicating a potentially clinically significant, lower-than-expected rate of reported off-label use relative to other EFC-listed drugs.

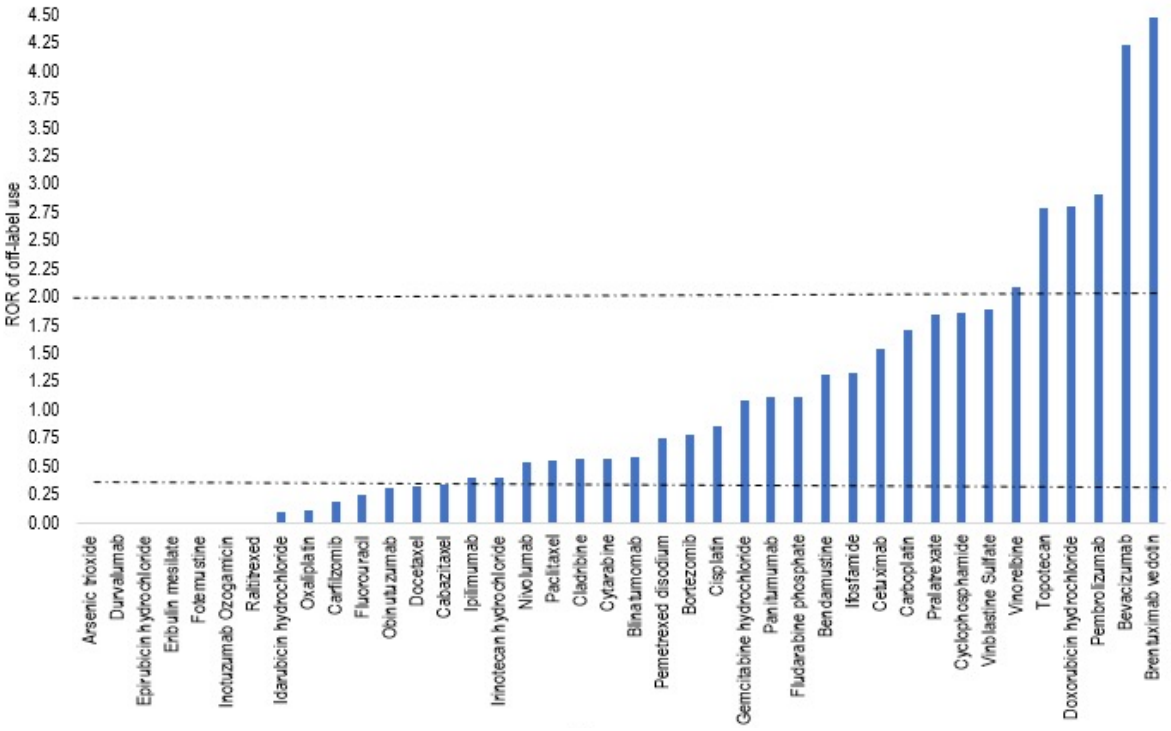
Figure 28. Disproportionality analysis, reported off-label use by year (2016 - 2020)



Source: Produced for this Review using DAEN data.

Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use in a given year. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use in a given year. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other years

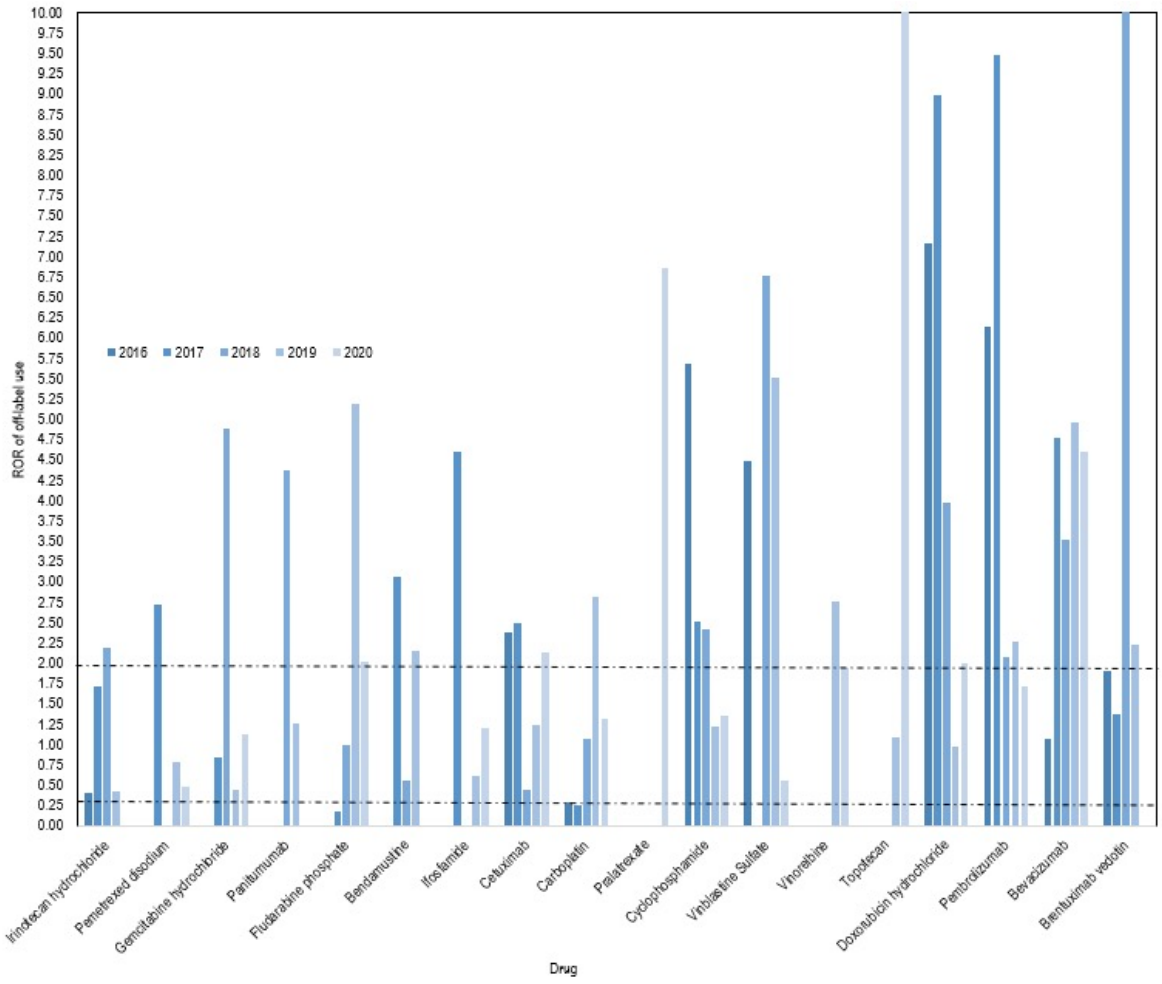
Figure 29. Disproportionality analysis, reported off-label use by EFC item (2016 - 2020)



Source: Produced for this Review using DAEN data.
Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use in a given year. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use in a given year. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other years

When the rate of off-label use for EFC-drugs was examined by the year of reporting, substantial variation was observed between years across drugs as can be observed in Figure 30 for those drugs with the highest ROR (see Appendix 8 for a tabulated listing for all drugs across all years).

Figure 30. EFC-listed drugs with disproportional rates of reported off-label use (2016 - 2020)



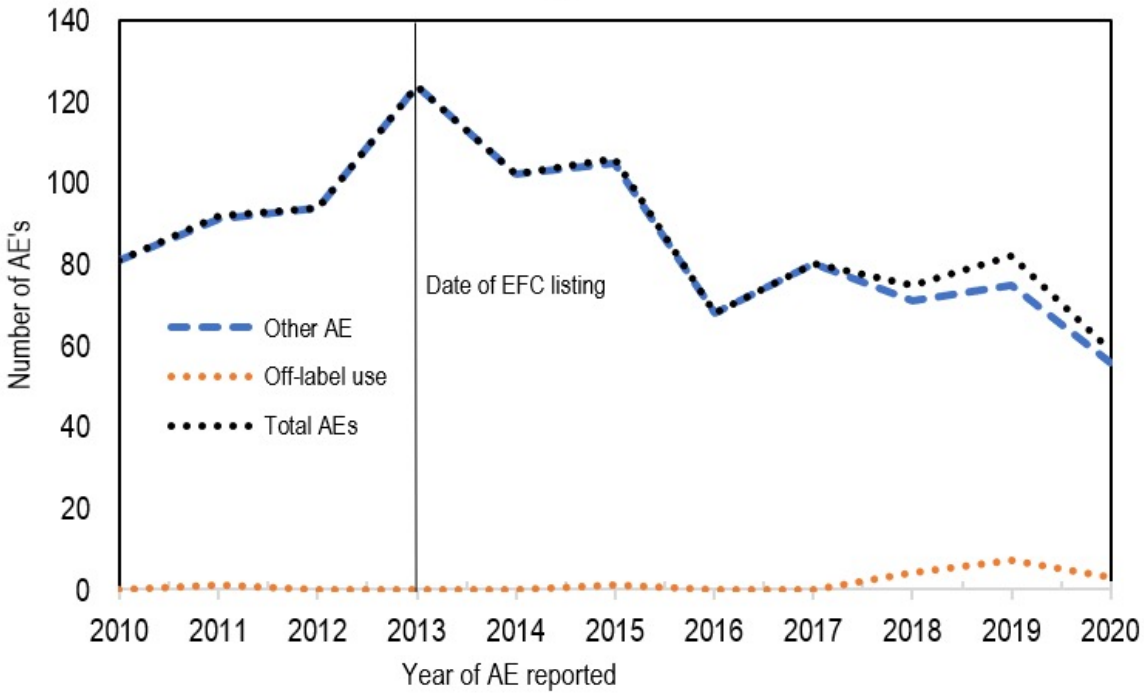
Source: Produced for this Review using DAEN data.
Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use in a given year. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use in a given year. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other years

However, these analyses are informing a comparison between EFC listed drugs. In order to consider the potential impact of EFC listing on the observed ROR it was necessary to restrict the analysis to medicines for which sales on the PBS were observed prior to 2012 (when the EFC came into effect) and for which a clinically significant ROR had been observed in the preceding analysis. Two exemplar cases were investigated: doxorubicin hydrochloride and vinorelbine sulfate (as both showed clinically significant ROR in the 2016-2020 analysis period, and both were PBS subsidised prior to the EFC) (see Figure 31 and Figure 32).

For both medicines, AE data were compared for the period 2010 to 2012, with two subsequent periods: 2013-2020 or 2013-2015 (both as indicators of the EFC period). Based on this data, the ROR for doxorubicin hydrochloride and vinblastine sulfate suggested EFC-listing increased the rates of off-

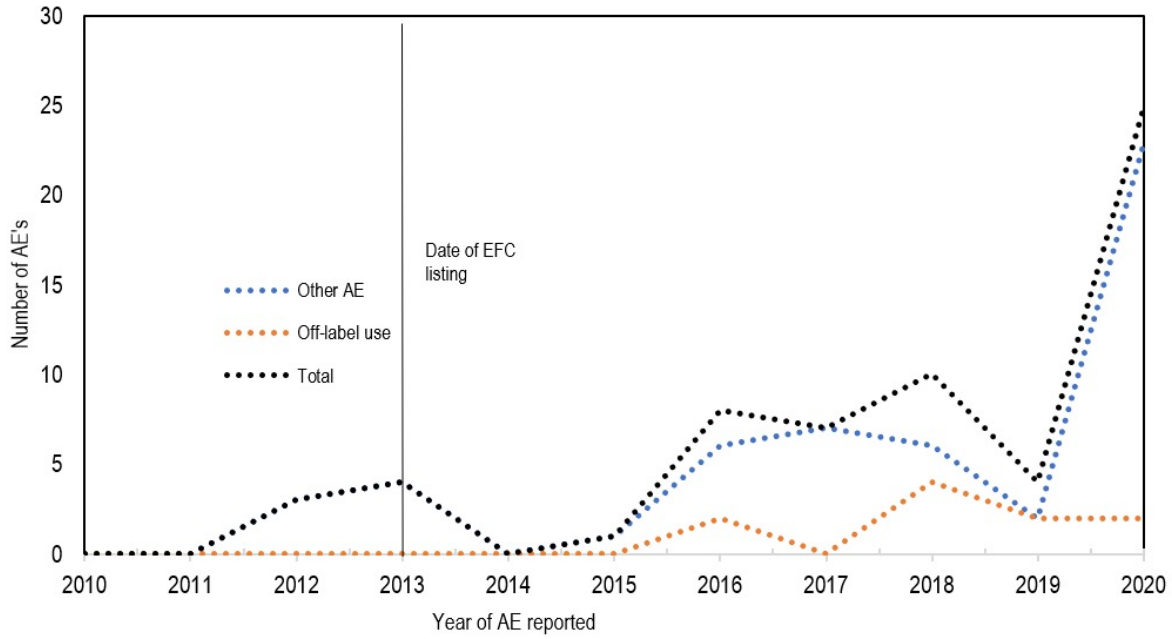
label based on the longer time period (the comparison with 2013-2020). However, when restricted to the immediate post-EFC listing period (2013-2015), EFC-listing had no apparent impact on the rates of off-label use.

Figure 31. Reported off-label use, doxorubicin (2016 - 2020)



Source: Produced for this Review using DAEN data.

Figure 32. Reported off-label use, vinblastine sulfate (2016 - 2020)



Source: Produced for this Review using DAEN data.

This analysis finds that while there are likely to apparent differences between the drugs listed on the EFC with respect to the incidence of AE, these are unlikely to be as a result of the remuneration method. Some of the medicines with the highest ROR, for example pembrolizumab, are prescribed on a flat dose basis and therefore unlikely to be influenced by incentives to vial-share as might arise from the EFC payment mechanisms (and the potential impacts this might have on medicine safety).

However, any conclusions drawn from this analysis are tempered by the nature of the data itself. First, there is no certainty that the reported event (AE or medication error) was due to the medicine to which it has been attributed; the TGA does not require that a causal relationship between medicine and event be proven, and reports do not always contain enough detail to properly evaluate an event [49]. Secondly, the TGA does not receive reports for every AE or medication error that occurs with a product [49]; it is likely that the number of events is underreported in the DAEN. Finally, there are also duplicate reports where the same report was submitted by a consumer and by the sponsor (albeit that the potential for duplicates is somewhat addressed via the use of ROR across medications).

5.4 Access to cancer medicines in the context of the EFC

Equitable and affordable access to quality cancer care, including cancer medicines, is a central goal of modern health care systems based upon a foundation of universal health coverage. Yet Australia's

health system is complex, featuring multiple payers, public and private care settings, and a mix of federal, state/territory and local jurisdictional responsibilities. In addition, Australia's expansive geography and diffuse rural population present challenges to the equitable and affordable provision of health care in general, and to specialist services in particular.

Access is likewise a complex concept. While often taken to refer to the availability of a health service or product (e.g., cancer medicines), it has been more holistically considered "the opportunity or ease with which consumers or communities are able to use appropriate services in proportion to their needs" (p. 1) [51]. In addition to the availability of health care, user characteristics influence service utilisation and further impact the quality of care and outcomes achieved.

Levesque et al. revisited the concept of access, defining it as the opportunity to have health care needs fulfilled, combining availability with the ability of users to actually access that care. The authors defined five key features of access—approachability, acceptability, availability and accommodation, affordability, and appropriateness), matched by five dimensions of users' ability to access the system—i.e., their ability to perceive, seek, reach, pay and engage [51].

Quality comprises a further dimension in consideration of access to equitable and affordable cancer care. It is important to recognise that not all services, providers and institutions are created equal. The delivery of chemotherapy in a major tertiary centre with specialist doctors, pharmacists and nurses is likely to differ from delivery in a small regional centre where care is predominantly provided by generalists. While these differences may not necessarily impact patient health outcomes, there are clear differences in what can be achieved in each setting. With respect to maximising quality of cancer care and treatment outcomes, then, the question is whether care should be taken to the patient—regardless of treatment setting—or the patient taken to receive care in a specialist centre.

5.4.1 The EFC and access to medicines

While Government seeks to ensure equitable access to cancer medicines across Australia, the EFC scheme itself only pertains to those aspects of supply that relate to the purchase, preparation and delivery of cancer medicines. Other aspects of quality cancer care relating to health infrastructure and administration of health services are beyond the purview of the EFC, falling largely to the States and Territories, and to individual health services. Thus, while the EFC is an important component of ensuring affordable access to cancer medicines for all Australians, the program is not designed to influence the myriad other aspects of access to quality health care, such as the availability of specialist doctors, nurses, pharmacists or infrastructure. These factors are the responsibility of the

State and Territories, together with the private sector, in the long-term planning and administration of health services.

5.4.2 Access to cancer medicines as part of quality cancer care

A significant proportion of stakeholder contributions to the Review identified issues of access to chemotherapy that are not directly related to the EFC (for a breakdown of supply chain activities considered within scope of the Review, see Table 3). While many of the issues raised fall beyond the purview of the EFC—predominantly relating to workforce and infrastructure—they are nonetheless important features of the safe delivery of high-quality cancer services.

Workforce

Cancer treatment is complex in terms of the drugs themselves, their preparation and administration, and the education of patients. Recognised best-practice approaches to the delivery of cancer medicines involve medical oncologists/haematologists, specialist cancer nurses and pharmacists, and adherence to safety and quality guidelines [52]. Often, the requirement of a highly specialist workforce is in tension with the desire to treat patients as close to home as possible in localities where specialist services are limited. While innovations in telehealth are addressing this challenge in some jurisdictions, collaborative telehealth enabled approaches between specialist and non-specialist centres are not yet the norm.

Infrastructure

Staff and patient safety are at the centre of the compounding of cancer medicines. All infused products must be sterile, while cytotoxic cancer medicines must also be prepared with consideration of small-molecule exposure risk. Additional sterility and stability requirements are required to extend product expiry. The specialised systems, infrastructure and human resources needed to meet these requirements are expensive and subject to strict quality standards. While TGA-licensed compounders are the most closely regulated, all compounding pharmacies are required to strict quality standards. Over time, the costs associated with the establishment and maintenance of such facilities has led to their concentration in specialist centres.

Submissions to the Review suggested it may be timely for jurisdictions to consider chemotherapy services as part of wider, role-delineation activities across their health services. Among other factors, capacity to adhere to the National Safety and Quality Health Service Standards for Medication Management in Cancer Care will inform whether it is possible for an individual health service to undertake in-house compounding or to sub-contract the services of a third-party compounder. There

will be important additional considerations, including affordability and workforce availability, when planning for the sustainable provision of high-quality cancer services into the future.

6 System improvements

6.1 Stakeholder views

6.1.1 Information technology and systems automation

Integrated digital information systems and electronic prescribing

Many stakeholders referred to the need for end-to-end solutions related to the ordering, compounding and claiming of cancer medicines. They recognised, however, significant challenges to the integration of the myriad disparate systems currently covering clinical notes, pharmacy ordering, third-party ordering, dispensing and PBS claiming. Additionally, the implementation of a fully integrated oncology information management system (OIMS, e.g., Citadel Health's Charm Evolution) is expensive and beyond the capacity of most small pharmacies. However, proprietary and third-party OIMS solutions were noted to add considerable value—facilitating multidisciplinary coordination across settings, reducing waste and enhancing operator safety—and are in use among a number of larger stakeholders.

One TGA-licensed compounder referred to its own bespoke software solution to manage the complexities of its just-in-time compounding processes, including tracking all component batch numbers, assignment of expiry dates and linking stock, prescription and compounded product records throughout the system. Representatives of pharmacy and medical member organisations cited the ability of OIMS to mitigate potential waste when orders for cancer medicines are compounded in good faith on the basis of a verbal order from the physician, but then cancelled. Use of OIMS facilitates the timely identification of appropriate alternative recipients for prepared infusions, avoiding the waste and lost revenue otherwise associated with having to discard the prepared infusion.

Stakeholders also noted the ability of electronic prescribing to reduce errors (such as with dosing, scheduling and communication) and other process inefficiencies.

> *Those are [all] manual processes for us at the moment. Lots of paper trail and lots of inefficiency. […] We're having all sorts of issues with paper charts at the moment. And an electronic system would take out all of those issues in a heartbeat.*
>
> *-Hospital pharmacy*
>
> *Even with clinical review, in those systems, they have some smart work-arounds. Is*

> *[the prescription] appropriate for the parameters inputted […]? At the moment, we're doing that manually ourselves. And same with adjustments to pathology and things like that—[OIMS] will pick that up—whereas we're having to recognise that manually, [OIMS] will pick up scheduling errors. We make sure we got the right dose for the person on the right day, rather than manually having to recognise, 'Oh, we actually gave that 10 days ago should have been 14.' Communication errors as well. Changes are often not communicated effectively. […] If there's a breakdown in communication, sometimes it can be hard to identify from a manufacturing position.*
>
> *-Hospital pharmacy*

Doctors added that work has begun on a proposal to introduce a unified electronic chart for the prescribing of cancer medicines.

Automation

As a rule, representatives of community and hospital pharmacies, as well as Government, indicated that automation technology—including the use of robotics in compounding—is by and large not appropriate or feasible in the preparation of infusible cancer medicines, as such systems remain too costly and unreliable for current service requirements and throughputs.

Telehealth

Several hospital pharmacists, members of medical representative organisations and a TGA-licensed compounder advocated for the use of telehealth to support the delivery of cancer medicines and follow-up services in rural and remote areas. It was also noted that telehealth solutions could potentially be utilised to deliver specialist training, facilitating the setup of other remote services.

6.1.2 Additional fees or incentives

Establishing a service obligation

At a higher level, TGA-licensed compounders, as well as representatives of a pharmacy member organisation, advocated the introduction of a Quality Service Guarantee (in addition to the CCPS, and similar to the CSO), to fund timely access to EFC-listed drugs, stability studies for extended molecule expiry, and compliance costs for TGA-licensed compounders.

Re-labelling/repurposing

Several hospital pharmacists, as well as representatives of pharmacy and clinical member organisations, raised the potential to incentivise recycling of 'orphaned' infusions. Currently, if a patient dies or has their treatment changed between compounding and dispensing, the infusion may either be thrown away or reassigned for subsequent administration (if still within its expiry date). If a discarded infusion was compounded 'in good faith' then the original preparation may still be claimed on the PBS. If the infusion is reassigned, the pharmacy may only claim for the new patient. Avoiding claims for discarded drug thus represents value to Government. Notwithstanding some mitigated costs of waste disposal, however, the labour and other costs involved in repurposing (including in some cases, transportation between hospitals to maximise potential for re-use) are not remunerated by the PBS.

As discussed in Section 4.1.2, there is currently no explicit external financial incentive for pharmacies to repurpose doses. Representatives of a hospital pharmacy and a group of clinicians proposed the introduction of a wastage code to reimburse pharmacies for the repurposing of drugs. Such a code would account for administration costs and all other costs associated with drug repurposing.

> *Sort of like a wastage incentive. Somehow you report your wastage, and the lower you are, you get bracketed. So if you have wastage between zero and 2%, they will give you x amount. […] There could be a wastage code that you could put through on your claiming. And then maybe that doesn't reduce the amount of repeats available—so you're incentivised to document that wastage.*
>
> *-Hospital pharmacy*

Additional fees/loadings

Stakeholder submissions and consultations proposed a number of additional fees/loadings:

- Rural/regional loading in consideration of the purported higher costs (on a per-service basis) in non-metropolitan settings.
- Pharmacy services loading for prescription checking, clinical review, quality assurance and consumer education associated with dispensing cancer medicines. It was noted by a representative from the PBAC that pharmacies are paid by state and territory governments for the work they do as staff and that Government is only responsible for the reimbursement

of medicines.

- Payment for the conduct of stability studies, which are of particular relevance to the delivery of cancer care in rural/regional settings. It was noted by one TGA-licensed compounder that the TGA is undertaking a review of guidelines concerning the assignment of extended expiry by TGA-licensed compounders. It was suggested that should the TGA revise its guidelines to further constrain medicine expiry dates, additional remuneration would be required to offset higher logistics expenses associated with service delivery in non-metropolitan settings.
- 'Exemption code' to allow claiming of an EFC medicine that was prepared for a patient but not administered due to logistical delays. It was proposed that provision of an exemption would also be reflected in the underlying script's status as initial/repeat (since this would have implications for the number of repeats available on a script for subsequent treatments and also co-payments).
- Device/container fees, including increased or additional fees for CSTD, which are expensive but are a good option for maintaining sterility and stability of compounded products.
- Waste management fee for the safe disposal of cytotoxic drugs.

Representatives of a public health service suggested reimbursement for personal protective equipment in the light of the current Covid-19 pandemic, though it was unclear how that was specifically relevant to the compounding of cancer medicines.

6.1.3 Addressing administrative burden

PBS system complexity

Hospital and community pharmacists, as well as representatives from pharmacy and clinical member organisations, outlined the significant administrative burden imposed by current EFC arrangements. Representatives of two hospitals reported outsourcing script management to a third-party provider, despite the associated costs of doing so. One also cited administrative delays in claiming for reimbursement for unadministered doses compounded 'in good faith.'

With respect to overall interactions with the system, stakeholders frequently noted that the PBS website is 'clunky' and that it is often challenging to identify the appropriate code for a given indication. Dual-processing of PBS scripts (i.e., requiring not only the medication ordering chart but also a specific PBS script) was considered time-consuming and wasteful, as was the requirement to store paper scripts. All contributors agreed that utilisation of the chemotherapy medication chart for claiming (fast-tracked in response to the Covid-19 pandemic) was sensible and effective, and should be continued beyond the pandemic.

The need for authority scripts (including written authority and phone authority) was often named as a key administrative burden due to the time required to obtain such authorities. Clinicians and pharmacists consistently requested a move to streamlined authorities, or at the very least, phone-based authorities. Additionally, the requirement to specify a patient's public/private status was seen as challenging and often arbitrary, as patients move frequently between systems and settings, particularly in rural areas. Harmonisation of PBS codes across the public and private systems was proposed.

> *The forms that you've got to upload for the new prescriptions—they can be quite time-consuming. I'm not sure how else they can get around it, but it seems like some of the prostate cancer drugs, like abiraterone—you've got to call up. And there's 10 questions and first, you have to now listen to the music. They give you a nice speech that due to Covid they're a bit slower than usual and then you wait, wait, wait, and […] it can often be 10 minutes before we can complete the script. And the next drug you do—a streamlined—takes you five seconds. So why is one streamlined and one's not?*
>
> *-Clinician*
>
> *When the pharmacy is dispensing Panadol and there's 10 item codes, they don't know [if the patient has had that prescribed] because you have a sore head, a sore shoulder, sore knee. So, item code one, two, three—they have to go through the list to pick and choose which one out of the 10 they've got. And potentially, then they're getting warnings going, 'Nup—that doesn't match the authority.' Especially if there's different costs. So, from a pharmacy perspective, this is leading to a lot of confusion.*
>
> *-Government program administrator*

While a number of stakeholders made reference to the substantial time required to obtain authorisations, no specific solutions were proffered in this regard (beyond the wholesale removal of authority requirements).

To simplify processes with respect to PBS item numbers writ-large, representatives of Government, industry, clinicians and hospital pharmacists recommended streamlined prescribing, with separate

coding for drugs based on indication, not place of dispensing. Representatives from Services Australia noted, however, that it is difficult to make changes in the current IT system without knock-on effects for other PBS items. The Department of Health's ongoing Data Distribution Project was cited as a key step in resolving cumbersome PBS-item structures. A follow-up interview with a representative from the Data Distribution Project confirmed the aim of the project in simplifying the underlying IT system, to facilitate changes to MBS and PBS listings and improve access by end-users. The Data Distribution Project is slated to streamline all data associated with MBS and PBS listings, especially from the perspective of Services Australia, and is expected to be fully operational in about four years' time.

> *The departments use codes to marry up different datasets behind the scenes. […] The primary focus of this sub-project inside the program is to get away from that clunky Excel, XML, dot-distribution method. We're trying to build a system that's super flexible.*
>
> *-Government IT administrator*

More flexible PBS restrictions

In response to the increasing number of overweight/obese patients—for whom a calculated dose may exceed the maximum quantity available on the PBS—a number of stakeholders proposed increasing the allowable maximum quantity for weight-based dosing. One hospital pharmacist additionally recommended uncapping dose reductions for the same patient. Currently, if the new dose varies by more than 10% from the original script, a new script and/or approval is needed, leading to increased administration, potentially increased patient co-payments, and delays to treatment whilst obtaining the new script.

Regarding co-payments, a range of suggestions were made by community and hospital pharmacies, and clinician member organisations. Some suggested removing co-payments for cancer medicines altogether; others suggested making any such co-payments concessional.

Hub-and-spoke model for regional health services

Representatives of a pharmacy member organisation, hospital pharmacy and Government recommended that consideration be given to developing 'hub and spoke' models of cancer care—including compounding—in which larger regional centres are partnered with smaller satellite services for cancer care delivery in non-metropolitan areas.

It might be setting up regional hubs around where there's enough volume to sustain an on-site provider.

-Hospital pharmacy

We've got two big hospitals within [our area]. We've got capacity to provide more specialist care at both those hospitals, to expand the service, just for this area, because the population is growing here. But then also that would recruit and attract a broader base of specialist and trained staff, to then provide that hub-and-spoke model of training, upscaling mentoring, education—all of that stuff—to the regional areas. Certainly, you know, [we are] expanding service from a cancer treatment perspective—they started off with a small unit in the main hospital, and now we've got a specific cancer centre built. […] So there could be another hub from which services could be rolled out and expanded for the northern and western part of our area. There is definite scope for expansion and utilisation of skills, but also being able to provide that level of sustainability, in terms of service.

-Public health service

I did some activity mapping over the last 10 years, and there were no dips in activity at all. If you're starting a new unit, you would look at what the projected activity would be for that area. We'll start with, you know, three chairs, three days a week, and then we'll allow for expansion once it's up and running.

-Public health service

Hospital pharmacists emphasised the importance of establishing 'hub-and-spoke' models of cancer care to partner larger cancer centres in the delivery of cancer care. These models of care adopt a clinical activity-based funding model, which could use PBS funds to enhance clinical services. It was suggested that to ensure the sustainability of 'hub-and-spoke' centres, activity mapping be conducted beforehand to ascertain the number of cases likely to be seen in the area. However, it was also acknowledged that there may be challenges in such a model, including the difficulty of recruiting and maintaining part-time staff, and lacking trained staff on-site to undertake dose adjustments when required.

One hospital pharmacist proposed the (re)classification of pharmacies based on service volume and/or remoteness, rather than (community/hospital) service setting.

> *Something like the [Modified Monash Model], which works on how regional/remote that location is […]—you have to be really regional/remote for that system to kick in with some of the funding. They changed it recently, and I know a lot of pharmacies were a bit hard done by that. Like […] Darwin—it's not really considered regional/remote anymore.*
>
> *-Hospital pharmacy*

6.1.4 Policy recommendations

There were a number of general policy recommendations on various elements of the EFC and the supply of cancer medicines forthcoming from the consultations:

- De-link IV and subcutaneous forms of a medication for pricing purposes (to reduce the risk of one form being de-listed should the other be subject to price disclosure. This was noted to be most likely to affect subcutaneous forms of brands like trastuzumab and daratumumab, which were introduced more recently, while their IV forms would be off-patent sooner and hence subject to earlier price disclosure).
- Introduce a grace period between announcement and enactment of price reductions due to disclosure in order to mitigate the financial risk of holding stock. It is noted that all stakeholders are currently advised of price disclosure recommendation outcomes four months prior to enactment of price reductions (see https://www.pbs.gov.au/info/industry/pricing/price-disclosure-spd).
- Incentivise manufacturers to conduct stability studies and develop products with longer expiry dates better suited to local Australian market conditions.
- Regulate biosimilar products to have the same vial sizes, strengths, storage conditions and expiry dates to reduce training needs.
- List cancer medicines in the freight category of 'life-saving medicine' to reduce errors in cold-chain transport and storage.
- Expand the scope of the EFC to include oral chemotherapy medications, supportive care and chemotherapy similarly administered in other disease areas.

- Review the underlying principle of the PBS as funding only outpatient services.
- Review existing pricing models on the PBS and adopt a model that would allow like-pricing of similar groups of drugs (no further elaboration of this suggestion was provided to the Review). Alternative payment models, including implication of a per-mg reimbursement model, are addressed in detail in Section 6.3.

6.1.5 Reconciling industry sales and PBS claims—the challenge of vial-sharing

One of the key issues raised during consultations to the Review was the practice of vial-optimisation (i.e., vial-sharing) (see Section 3.2.2). Stakeholders acknowledged a shared desire for cancer medicines to be used efficiently and that the process of 'vial-sharing' generally serves to reduce the volume of discarded drug. However, as discussed, there are a number of well-recognised challenges associated with vial-sharing, including the impact on subsequent reconciliations between Government and drug manufacturers with respect to Deeds of Agreement. Stakeholders proposed several options to address these issues.

Per-mg pricing

To address the challenges associated with vial-sharing and the consequent impact on SPAs and rebates, pharmaceutical manufacturers proposed moving remuneration of cancer medicines to a per-mg pricing basis. Hospital pharmacists and compounders, however, noted the following impediments to a per-mg pricing model for reimbursement:

- Per-mg pricing may affect patient access and quality of care. Many hospital pharmacies rely on PBS claims as a source of immediate cash flow. The current approach to reimbursement allows facilities to generate funds (i.e., through utilisation of overage) used to run facilities and provide a range of services. Moving to a per-mg funding model would reduce that cash flow, potentially forcing low-volume service providers to refer some services to larger facilities. Compounders would also be adversely impacted as they rely strongly on revenues generated through vial-sharing.
- Per-mg pricing would distinguish the EFC from other sections of the PBS, adding yet more administrative complexity to the program. Representatives from the PBAC added that a shift to per-mg pricing would influence the pricing of drugs as current pricing arrangements are on a per-treatment basis. Altering the basis upon which costs are determined would necessarily impact the cost-effectiveness ratio presented by the sponsor, influencing the criteria upon which funding recommendations are made and prices negotiated with pharmaceutical

companies.

Proponents of the per-mg pricing model recognised that low-volume compounders would be disadvantaged by not being able to vial share. A 'safety net' (whereby low-volume claimants would be exempt from per-mg pricing) was therefore proposed for such compounders, though it was unclear how the proposed carve out would be implemented in practice. Manufacturers suggested that a 'wastage table' could be employed to compensate compounders in hospital settings whose low service volumes do not enable them to fully utilise vial contents.

Flat-dosing

Flat-dosing was proposed by some hospital pharmacists and TGA-licensed compounders to allow pharmacies to stock prepared doses of commonly used cancer medicines with longer shelf lives. Not having to compound individualised doses on a named-patient basis would streamline management of some stock, especially in small pharmacy settings. Flat-dosing is reportedly practiced for a number of cancer medicines, including carboplatin, etoposide, rituximab, pembrolizumab and nivolumab.

Flat-dosing of pembrolizumab and nivolumab was also cited as a potential solution for reconciliation issues, as patients receive standard doses equivalent to available vial sizes (i.e., vial-sharing is not required). Better alignment of vial sizes with recommended dosing was seen as key to addressing reconciliation issues more broadly (see below).

Optimal vial sizes

One industry stakeholder proposed resizing vials to meet local market demand, such that vial sizes in Australia would more closely match drugs' respective PBS maximum quantities (see Section 4). However, manufacturers noted this was only possible if the required vial size already exists elsewhere in the global market. The Australian market was characterised as diminutive relative to other international markets, hence it is was deemed commercially unviable for pharmaceutical companies to customise vial sizes for local purposes.

> *... particularly for Drug X, the average dose required for most patients was about 2.4 milligrams. And our nearest vial size was three milligrams. And that's something that we actually introduced, from memory,…. I think the nuance is where the other markets also need that vial size. So I think if you was just Australia, then I think you would have a real challenge in getting that agreed to make a vial size for such a small country. Whereas if other countries also need it, which is probably what the case*

with the three milligram was. That's why we were able to leverage.

-Pharmaceutical manufacturer

Being such a small percentage of the market—to get a different vial size for Australia than the rest of the world is almost impossible. And that's just supply chain management. For example, different vial sizes have different sized tops, so the procurement of materials is more complicated. There's increased validation work, demand management. All of those things mean the global company will generally not allow one affiliate to have a different vial size. So you know, economies of scale manufacturing, all those sort of things.

-Pharmaceutical manufacturer

Vial serialisation

Vial serialisation was proposed by pharmaceutical manufacturers as further means to address reconciliation issues. Serialisation would enable every vial of cancer medicine transacted to be tracked throughout the supply chain, from manufacturer, to compounder and pharmacy, up to the point of administration to the patient. Stakeholders noted that introduction of vial serialisation would require:

- Barcodes attached to the product vial by the manufacturer (i.e., not to the batch packaging);
- Integrated track-and-trace infrastructure, which must not compromise the sterility of the compounding environment (e.g., scanning devices introduced into compounding suites would have to operate outside of laminar flow hoods to not breach the sterile environment);
- Requisite new IT infrastructure and software that would have to be compatible across stakeholders, to ensure seamless track-and-trace throughout the supply chain.

Other barriers to serialisation discussed with stakeholders included: an increase in labour requirements for all users; administrative and implementation difficulties across the supply chain; and the significant financial burden of integrating the multiple distinct information management systems already in use.

A number of clinicians suggested the introduction of a single, integrated OIMS solution across manufacturers, compounders, hospitals and pharmacies. This was posited to facilitate vial 'track-and-

trace' and resolve a number of 'administrative' complexities raised by stakeholders with respect to ordering, stock management and EFC claims administration. Consultation with a stakeholder involved in the Commonwealth Department of Health's Data Distribution Project revealed that implementing a track-and-trace system would be easier once the PBS data project is completed, since all existing PBS software will be linked.

6.2 Literature review—Innovations in the efficient funding of cancer medicines

A systematic literature review (see Appendix 3) was undertaken to identify alternative funding, technology and service delivery approaches driving innovation, collaboration and other improvements in the provision of cancer medicines. A range of reforms are summarised, including the introduction of technologies for the preparation and delivery of cancer medicines, new approaches to the funding and delivery of care, and system changes underpinning how care is organised.

6.2.1 Technological innovations

Four publications (three international, one Australian) reported on the use of technologly driven approaches to manage the efficient use of cancer medicines; all demonstrate it is possible to reduce costs associated with wastage through the adoption of such practices. Importantly, while these publications reported drug cost savings they did not include evidence of cost-effectiveness which would be required before adoption of these technologies could be recommended.

International publications: Two studies reported on solutions to improve cancer drug utilisation through automated dose-banding strategies [53]. Vandyke et al. showed that the use of computerised routine dose-rounding (within 10% dose range for biologic anticancer agents and within 5% dose range for cytotoxic products) achieved cost savings through the reduction of drug wastage [53b]. The authors showed that pharmacist-managed automatic dose-rounding saved approximately US$200,000 in product inventory costs, of which biologic products accounted for 78% of potential savings.

These findings were consistent with a more recent study by Fahey et al., which examined the integration of automated banding with patients' electronic health records [53a]. The authors conducted a post-implementation retrospective review of an automated dose-banding system (based on pre-defined dose-banding tables adhering to 5% or 10% maximum rounding parameters) comparing automatically rounded doses administered during the post-implementation phase against manually rounded doses administered during a pre-implementation phase. The authors concluded

that dose-banding within the electronic health record reduced variation in rounded chemotherapy doses, increased drug and monetary savings, and reduced patient safety risks associated with manual manipulation of the medicines.

Respaud et al. conducted a retrospective analysis of cost savings resulting from the use of a computerised system for the management of unconsumed drug [54]. The authors assessed the potential to utilise the unconsumed portion (compounded product) of 37 anticancer drugs based on their remaining stability over a one-year period. The use of a computerised system was shown to minimise wastage and yield cost savings of around 5% of annual cancer drug expenditure.

Australian publication: Gilbar, Chambers, et al. discussed the use of CSTD in conjunction with other strategies to facilitate vial-sharing and extension of product expiry dates to maximize drug savings [55]. CSTD systems such as PhaSeal were shown to extend effective expiry by maintaining the sterility of vial contents.

6.2.2 Tele-oncology

There is increasing interest in the application of tele-health to cancer care, which has gained importance as a means of maintaining continuity of care during the COVID-19 pandemic. Four publications—three international, one Australian—discussed the application of tele-health services to the delivery of cancer medicines. From these studies, it is observed that access to care may be improved through tele-health services as a means of expanding the reach of existing resources. This expansion is not without its own costs, however, with respect to both infrastructure and changing local practices to facilitate a tele-health model.

International publications: In a prospective study, Gordon et al. evaluated a tele-pharmacy program among community cancer centres in Alberta, Canada [56]. The tele-pharmacy services were developed and adopted to compensate for the absence of a pharmacist in rural areas. Pharmacy technicians at two remote community cancer centres were connected by tele-health with pharmacists at one of two coordinating centres to oversee the compounding of IV cancer medicines and provide clinical review of physician orders and included access to shared electronic records and laboratory data. The authors observed a reduction in the distance travelled by patients and positive satisfaction survey results from patients and pharmacy, medical and nursing staff. Medical and nursing staff preferred having a pharmacist on-site if possible. The pharmacy staff considered the visual checking of tele-pharmacy as good as (75%) or better than (25%) the unaided eye. When compared to treatment delay, tele-pharmacy was preferred by 100% of the patients (n=22), nurses

and physicians (n=28), and pharmacy staff (n=60). However, processing time was impacted for pharmacy staff (an additional 10 minutes on average to process and compound drugs) and nurses (an additional 27.5 minutes on average to coordinate information for each patient order). Nonetheless, the authors concluded that savings generated through use of the tele-pharmacy model at the remote site compensated for the additional time needed to coordinate activities.

Vo and Gufsafson, and Sirintrapun and Lopez conducted scoping reviews of the range, critical benefits, and barriers of using tele-pharmacy services in oncology care [57]. The authors reviewed a total of 21 articles across a wide range of applications for tele-pharmacy in oncology care including: as patient follow-up, monitoring and counselling, IV chemotherapy, sterile compounding, expanding availability of pharmacy services, and remote education. Reported efficiency gains of tele-pharmacy included improved staffing and workload, as well as cost savings achieved through expanded hours for pharmacy services at night, weekends and holidays.

Vo and Gufsafson reported a total annual saving of US$23,770 with the use of tele-pharmacy for IV chemotherapeutic compounding materials, and cost savings of US$25,000 in educational activities for healthcare professionals via the use of videoconferencing. The authors suggest that the use of tele-pharmacy in the IV chemotherapy/sterile compounding field may improve the accuracy of antineoplastic preparations by allowing pharmacy technicians to take digital photographs at each stage of the preparation process, allowing verification of the correct quantity of anticancer drugs throughout the process regardless of their physical location. In addition, the authors claim that tele-pharmacy contributed to improved accessibility of pharmaceutical services to underserved cancer populations. The authors identified a number of barriers to the implementation of tele-pharmacy in oncology care related to resource shortages, technical problems, prolonged turnaround time, safety concerns and patients' willingness to pay.

Sirintrapun and Lopez underscored the 'tremendous' potential of telehealth and other technological innovations, including blended services, in the delivery of cancer care [57b]. The authors state that "tele-oncology is generally found to be equivalent to in-person care and demonstrates cost savings and patient satisfaction" (p. 544). Sirintrapun and Lopez also noted a range of barriers to the adoption of tele-health approaches in oncology, including cost, incompatible billing and reimbursement regulations, data security risks and clinical licensure requirements.

Australian publication: Sabesan et al. described the development and implementation of a tele-chemotherapy model in rural North Queensland between 2014 and 2016 [58]. The model comprised rural generalist nurses administering chemotherapy and biological therapies under the direct

supervision of chemotherapy-proficient nurses at larger primary centres using a tele-nursing platform. The model was implemented in six rural areas, ranging in population between 500 to 3,000 individuals at a distance of 125 to 1,000 km from their primary sites.

A total of 62 patients received 327 cycles of chemotherapy and systemic therapy regimens through supervision by medical oncologists and chemotherapy proficient nurses at two large primary cancer centres utilising third-party compounders and the tele-nursing model. Factors enabling implementation of the model included development of (and adherence to) common governance and guidelines, allocation of adequate resources, and collaborative leadership among managers and clinicians. Barriers to implementation included high staff turnover and technical issues with internet connection.

6.2.3 Process enhancements

Three publications (two international, one Australian) focused on improving patient access and outcomes linked to the prescribing, preparation and delivery of cancer care. While these studies do not specifically address changes to the reimbursement of cancer medicines (they focused largely on workflow management and practices), they highlight that changing the underlying processes affects the quantum of care delivered and, by extension, patient access and costs of care. In particular, Ligaratnam et al. demonstrated the ways in which internal ordering and stock management processes can positively influence the timeliness of care delivery and potentially the extent of wastage within the system [59].

International publications: Bunnell et al. reported the effectiveness of a team-training initiative in breast cancer care to address chemotherapy treatment failures [60]. Based on clinic observations, interviews with key staff and analyses of incident reports, the study developed interventions (including pharmacy screening and an email reminder system for orders) to address high-risk areas for errors. The incidence of non-communicated order changes was low at baseline (1.9%) and during follow-up (1.5%). The incidence of missed chemotherapy orders for unlinked visits decreased from 30% at baseline to 2% within two weeks of implementing the pharmacy screening and email reminder system ($p<0.001$ Pearson χ^2). All providers (i.e., physicians, nurse practitioners, and physician assistants) included in the study reported it was easier to communicate change-orders following the intervention, and the vast majority had a better understanding of when and how to call for a change-order. Infusion nurses reported a decrease in the frequency of non-communicated change-orders and more than three-quarters reported a decrease in the necessity to page clinicians. The authors also reported an improvement in patients' perception of the degree to which their care was well-

coordinated among doctors and other caregivers (from 93.5% for the six months prior to team training to 97.4% for the six months following team training implementation).

Jeon et al. developed guidelines for the development of pre-printed, standardised chemotherapy orders to reduce communication failures [61]. The authors demonstrate the potential for 'human factors' professionals, clinicians and designers to leverage each other's expertise to reduce drug administration, dose and time errors.

Australian publication: Lingaratnam et al. investigated the application of a 'lean improvement methodology' to improve access and reduce waiting times at a chemotherapy day unit (CDU) and cytosuite chemotherapy production facility at a major tertiary hospital in Australia [59]. Using historical data to establish demand patterns among combined modality patients (chemotherapy plus radiotherapy), the project aimed to remove non-value adding steps, reduce variation and analyse inefficiencies at the CDU. Interventions to improve operations included:

- Development of drug-specific scheduling business rules (based on manufacturing constraints pertaining to product cost and shelf-life);
- Increasing advanced preparation of medical records and pathology requests (i.e., five vs one day in advance) by clerical, nursing and pharmacy staff;
- Individual physician audits, with feedback on performance around medical record availability and pathology requests;
- Adoption of just-in-time manufacturing (i.e., 24 to 48 hours in advance vs up to seven days in advance) to reduce drug waste and pharmacist time spent repurposing cancer medicines;
- Improved visual management of priority orders through the cytosuite by writing the appointment time and date on the outside of each tub in the production line;
- Use of daily team huddles between cytosuite, CDU pharmacist, and CDU nurse coordinator to improve daily workflow;
- Pre-release of cancer medicines to CDU within 10 minutes of appointment.

Results demonstrated a reduction in median patient waiting time of 38%. Improved efficiency allowed a two-fold increase in timely availability of fully authorised cancer medicines, and a 22% reduction in wastage associated with expired drug and pharmacist work to repurpose compounded cancer medicines [59].

6.2.4 Policy reform

Four publications (two international, two Australian) related to cancer medicine funding policy. The

information in these reports varies from presenting case study evidence on the impact of different payment mechanisms, to more general reviews of policy as it affects cancer medicine pricing and funding. Reports in the Australian context speak to the setting of prices for the reimbursement of medicines, including cancer medicines, though they generally do not address policy for the ongoing funding of those medicines (i.e., based on the most efficient combination of vials). A report included from the World Health Organisation (WHO), however, identifies the EFC as an Australian Government policy aimed directly at improving system efficiency. Importantly, the Review of Funding Arrangements for Chemotherapy Services (2013) and Review of Pharmacy Remuneration and Regulation (2017) are not summarised in this section, as findings of these reports are presented throughout the Final Report (with key findings and recommendations highlighted in Appendix 13*).*

International publications: The WHO's Technical Report on Pricing of Cancer Medicines and its Impacts provides a global comparison of policies affecting the initial price setting of cancer medicines, and subsequent efforts to manage cancer care expenditure in national settings [62]. The report highlights that initial price setting by the manufacturers of cancer medicines is opaque "with a focus on extracting the maximum amount that a buyer is willing to pay for a medicine" (p. ix). While many national governments (including the Australian Government via the PBAC) have implemented policies to maximise system efficiency (including, as they apply to Australia, a value-based approach to reimbursed prices, managed entry schemes and risk-sharing arrangements, authority restrictions on reimbursed products, and the EFC program), prices for cancer medicines, the report observes, continue to rise. The authors highlight several policies that may enhance system efficiency, affordability, access to medicines and pricing transparency, including:

- Strengthening pricing policies: encompassing the structure, implementation and enforcement of pricing policies as they apply to cancer medicines.
- Improving efficiency: prioritising high-value care and managed-entry schemes; do not separate cancer funding from other health care funding; and consider all costs in setting prices.
- Improving transparency: comprising the disclosure of net prices; price controls throughout the supply chain, knowledge of cost inputs (e.g., R&D), and public dissemination of reimbursement decision outcomes;
- Promoting cross-sector, cross-border collaboration: share pricing and HTA assessments; harmonising regulation of biosimilars to increase competition; harmonising regulation to allow ease of supply management; pooling regional/national resources for procurement; and promoting use of voluntary licensing agreements.

- Managing of demand side factors: removing financial incentives to prescribe low-value cancer medicines; restricting promotion of cancer medicines; promoting biosimilars; regulating substandard/falsified medicines.
- Realignment R&D incentives: promoting research in low - incidence cancers; focusing on health service research to improve efficiency and rational use of cancer medicines.

Ward et al. evaluated the impact on clinical revenue of including drug costs into bundled payments compared with fee-for-service (FFS) cancer care in the USA [63]. Using Monte Carlo simulations to assess hypothetical scenarios in advanced-stage III colon cancer and metastatic non-small cell lung cancer, the authors showed that a shift from FFS to bundled payments created substantial variation in revenue. They concluded that practices treating small numbers of patients would be at greater risk of experiencing a loss of >10%. Similarly, practices treating a substantial proportion of patents with molecularly or clinically complex disease, relative to the average patient in the bundle, were expected to see a decline in revenue associated with bundled payments below that expected with FFS. In contrast, practices treating patients with less complex disease were expected to earn revenue with bundled payments above that associated with FFS. The authors noted that one of the potential unintended consequences of shifting from FFS to bundled payment may be the use of less expensive, but less efficacious, drugs. Furthermore, the study found that adopting a bundled payments model that includes drug costs could, with respect to revenue, disadvantage practices that take on tertiary referrals and patients seeking aggressive care.

Australian publications: In its 2013 report, (A Collaborative Assessment of) Access to Cancer Medicines in Australia, Medicines Australia explored international policy developments to identify factors that influence policy change and potential opportunities for further reform [64]. Largely informed by local and international stakeholder interviews, the report identified opportunities for change related to investments in real-world evidence, revision of evidence requirements for the valuation of cancer medicines, the implementation of provisional listing, and further enhancements to consumer, clinician, and community involvement. Key findings included:

- Medicines registration and funding pathways—better utilisation of overseas evaluation reports; introduction of expedited approval pathways; enhanced post-marketing monitoring of approved medicines; and streamlined post-market requirements, with improved transparency and predictability of processes and decisions to ensure timely access to medicines.
- Valuing cancer medicines—the current use of the QALY, with its reliance on multi-attribute utility instruments, is inadequate to express the true value of innovations that matter to

patients and their caregivers. Although all stakeholders placed value on innovation in medicines, their definitions of innovation were not uniform. As genuine breakthroughs in medicine are rare, some stakeholders questioned R&D funding, while others suggested that overstating R&D costs may lead to inflated prices of new medicines. Some stakeholders referred to underestimated survival benefits of some cancer patients.

- Stakeholders' role in determining the value of innovation—consumers' views should centre in funding decisions by integrating consumer organisations within PBAC decision-making process. This includes expanding consumer and clinician representation on the PBAC, enhancing existing avenues for stakeholder input, including the use of consumer and patient hearings, incorporating public perspectives on overarching moral, ethical and opportunity-cost considerations into PBAC decision-making processes, and including consideration of models employed by comparable regulators overseas. While the report acknowledged clinician and consumer input to the PBAC, it alleged the PBAC under utilises the deep clinical expertise needed given the ever growing complexity of cancer medicines.
- Real-world evidence—The report identified potential for increased use of real-world evidence to improve regulatory and reimbursement decision-making, including monitoring of authorised products post listing, as well as providing additional support for new medicines approved under managed entry and conditional registration and reimbursement pathways. Data collected on medicine use, such as administrative claims data, linked health data and registry data, the report asserts, has the potential to inform ongoing decisions in health care. However, challenges remain, including data collection, ownership, governance and quality control. While examples of the use of real-world evidence exist, such as data linkage of the PBS and MBS, these have not been designed to address challenges specific to high-cost medicines.

The 2015 Review of Medicines and Medical Devices Regulation concurred with a number of Medicine Australia's recommendations, noting opportunities to improve transparency throughout the assessment process, engage with sponsors and other stakeholders to better tailor applications, match assessment resources to the complexity of applications, and facilitate cooperation between the various HTA agencies (PBAC, TGA and MSAC) [65]. Recommendations included enhanced formal mechanisms for consumers and clinicians to play a more central and substantive role in the evaluation of new medicines and technologies.

Most recently, the Parliamentary Inquiry into Approval Processes for New Drugs and Novel Medical Technologies in Australia (2021) similarly recommended further alignment of Australia's HTA

processes, particularly as they relate to the initial decision to reimburse a health technology [66].

6.3 Consideration of alternatives

The Review considered the potential impacts of alternative reimbursement approaches, including changes to the composition and distribution of EFC payments, according to the principles articulated in Text Box 4.

Text Box 4. Policy impact key

The potential impacts of altering EFC remuneration policies were considered according to the following principles:

- Efficiency—reflects the likely impact of the policy change on the costs to the system, either as assessed by the operating viability of those within the supply chain or the total cost to the PBS associated with the reimbursement of chemotherapy services.
- Access—reflects the likely impact of the policy change on patient access to infused cancer pharmacy services. This may include changes in access attributed to disparities in service provision between regional, remote and urban areas, or between public and private hospital settings.
- Simplicity—an assessment of the impact of a policy change on the administrative complexity of the PBS and its associated processes as required to access and be reimbursed for infused pharmacy services.
- Accountability—reflects how the proposed policy change is likely to impact transparency with respect to drug supply, the flow of funds and other system-wide aspects.

Categorisation of these impacts is presented using a 'traffic light system':


negative impact on that principle (e.g., a reduction in efficiency)


positive impact on that principle (e.g., an improvement in access)

no notable impact on that principle.

6.3.1 Addressing reconciliation issues

The following solutions have been considered with respect to the impact of vial-sharing on the reconciliation of sales and PBS claims:

- Per-mg pricing as the basis for reimbursement of drug supplied via the PBS;
- Serialisation of vials (i.e., 'track-and-trace') to allow product units to be tracked as they move through the supply chain.
- Third-party 'Escrow' model for drug reimbursement (i.e., use of a third-party payment clearing house for the independent reconciliation of unit supply and PBS reimbursement claims).

Per-mg pricing

Proponents of per-mg pricing suggest that a shift to reimbursement based on dispensed volume would ensure the most efficient use and subsidy of drug via the PBS. Indeed, reimbursement on a per-mg basis would reduce the extent to which there is double-payment for drug overage (see 3.2.2). It would also simplify the reconciliation of pharmaceutical sales (ex-manufacturer) against PBS claims, since it would not be possible to generate 'phantom' vials via the compounding process (i.e., total mgs claimed (ex-PBS) could not exceed total mgs sold (ex-manufacturer).

However, there are potentially perverse incentives associated with the introduction of a per-mg pricing system:

- Providers may seek to batch the preparation of drugs to certain days of the week;
- Providers may not offer infusion services for 'low-volume' agents, potentially influencing the prescription of therapies in affected settings and/or leading to further geographic concentration of cancer care in high-volume centres.

Such changes have the potential to negatively impact patient access if they lead to: patients having to travel further to access care; misalignment of treatment administration and other clinical appointments (e.g., due to the timing of batched treatment preparations); prescribing that is not clinical best-practice.

As noted above, pharmaceutical industry stakeholders suggested that the introduction of per-mg pricing for reimbursement include a 'carve-out' for low-volume compounders as a means of recognising the potentially deleterious effects of per-mg pricing on PBS receipts, particularly for hospitals/pharmacies that are unable to vial-share. Such a carve-out would enable low-volume providers to continue to claim PBS reimbursement based on the efficient combination of vials (in recognition that they do not have sufficient patient throughput to allow efficient vial-sharing).

Moving to per-mg pricing for EFC medicines would also add to the existing complexity between the

EFC and PBS more broadly. That is, other products made available via the PBS are reimbursed on the basis of the pack quantities dispensed (as with drugs subsequently listed on the EFC prior to its introduction in 2011). Stakeholder consultation made clear that the PBS reimbursement mechanism influences provider incentives to utilise particular (clinically appropriate) drugs. Thus, it cannot be discounted that disparities in reimbursement mechanisms between EFC-listed medicines and those in other sections of the PBS may influence prescriber choice.

Moreover, a per-mg reimbursement system with a 'carve-out' to exclude low volume providers would further complicate management of the system both for pharmacy providers and EFC program administrators, particularly Services Australia. For any given EFC-reimbursed drug, a threshold of throughput would need to be defined, below which it would not be considered 'viable' to operate on a per-mg basis. However, the determination of that threshold is not dependent on volume alone but also the time-period over which drug might be reasonably compounded (i.e., allowing for the impact of drug expiry and stability on the capacity of any given centre to vial-share within its patient pool) and potentially used to prepare infusions for multiple patients (vial-sharing). Furthermore, the viability of relying on per-mg pricing cannot be considered on a per-drug basis but must consider the overall suite of drugs supplied through a pharmacy/hospital service and its capacity to provide care to patients. That mix varies between centres and over time.

Thus, carve-outs would have to operate on a per-centre basis. This may incentivise centres operating near the threshold to shift patients to larger centres to ensure that they can continue to qualify for 'carve-out' status. The latter would have negative consequences with respect to the principle of equity of access, where a patient's access to care may be influenced by local funding arrangements, rather than capacity.

The caveat to this complexity is whether a 'carve-out' system is actually required. Feedback from consultations to the Review suggested that most low-throughput pharmacies/hospitals purchase EFC cancer medicines through a third-party TGA-licensed compounder; the application of carve outs in this instance would not be required. The substantial requirements underpinning the compounding of cytotoxic drugs mean that small facilities are often not equipped to do in-house compounding (with the potential exception of some immunotherapies, which can be compounded in a sterile cabinet). As many of these drugs are now prescribed on a flat-dose regimen, there is less potential for vial-sharing and per-mg reimbursement is less likely to be an impediment to service viability.

Stakeholders' principal objection to the introduction of per-mg based reimbursement is that it would erode the capacity of pharmacies/hospitals to use PBS reimbursement to cross-subsidise their other

operations. Feedback during the consultation process suggested that the ability to vial-share has allowed pharmacies/hospitals to maximise differences between what is paid for EFC drugs and subsequently claimed for PBS reimbursement, thereby allowing PBS reimbursement to be used for other purposes. However, the Independent Hospital Pricing Authority (IHPA) has clarified that in setting the Nationally Efficient Price used to negotiate funding to public hospitals as part of the National Health Reform Agreement (NHRA), all PBS claims are taken into account to ensure there is no double payment for those services [67]. Thus, for public hospitals and private hospitals contracted to provide public services that attract NHRA funding, PBS remuneration is 'netted-out' (i.e., accounted for in IHPA calculations of the efficient price used to allocate NHRA funds). At the State/Territory-level, then, any increase in PBS remuneration in a given period would result in a commensurate reduction in NHRA-allocated funds (and vice versa). The purported financial impact on hospital pharmacies' budgets of moving to per-mg based reimbursement would appear to be: (1) temporal, i.e., a reduction in short-term cash flows associated with diminished PBS receipts, to be offset by increased NHRA receipts; and (2) a matter for 'internal' negotiation between State/Territory departments of health, hospitals and their comprising business units. Further discussion between the Commonwealth and State/Territory Governments is required to better understand the extent to which adopting a per-mg reimbursement model for the EFC could be introduced without unduly affecting patient access to hospital services.

Compounders did not provide the Review sufficient detail on their operating costs to evaluate the potential impact of a per-mg basis for remuneration on these organisations' financial sustainability. Nonetheless, it is important to recognise that moving away from remuneration on the basis of the combination of vial sizes adopts a narrower, Government-payer perspective and may not be consistent with broader, system-wide notions of efficiency.

In its submission to the Review, Medicines Australia cites internal research estimating material differences between the quantity of medication sold by manufacturers and the amount reimbursed by Government: for five medicines, representing some $551 million in Commonwealth expenditure (FY 2018), MA estimated this difference at a value of $49.5 million (AEMP). An excerpt of the underlying report provided to the Review did not allow for this figure to be independently substantiated. The Review undertook a modelled comparison of the cost to Government over the period 1 July 2016 to 30 June 2021 under the existing per-vial basis and counterfactual per-mg basis for three EFC-listed items (i.e., cabazitaxel for prostate cancer, avelumab for merkel cell carcinoma and bortezomib for multiple myeloma). Results are provided in Appendix 9.

Per-mg reimbursement	Efficiency	↑	Access		Simplicity	↑	Accountability ↑
Per-mg reimbursement with carve-out	Efficiency	↑	Access	↓	Simplicity	↓	Accountability ↓

Vial serialisation

As noted in the consultations, previous reviews identified the serialisation of vials (i.e., 'track-and-trace') as a mechanism to reconcile product sold by manufacturers against subsequent PBS claims for reimbursement. It is understood that a proposal is under development at the Department of Health to introduce track-and-trace across the entirety of the PBS. In response to the 2018 review of pharmaceutical funding, TGA-licensed compounders and the Community Pharmacy Chemotherapy Services Group (CPCSG) commissioned Ernst and Young to investigate various models for the reimbursement of EFC products, including a track-and-trace based model dubbed 'Model A' [68]. Model A was estimated to cost $152-$158 million to establish (though the report did not explicitly state the operational cost of the track-and-trace system itself, p. 8).

Objections to a track-and-trace system were raised by stakeholders within the supply chain at that time (e.g., compounders, hospitals, pharmacists) on the following basis:

- It would reduce working capital for pharmacies and harm service viability for compounders, due to the change in the operating model and loss of PBS revenues. Contributors to the report suggested that a change in operating model may threaten the continued operation of compounding operations in Australia and by extension, patient access to care.
- An increase in the IT requirements, time and space required to carry out compounding activities. The report did not clarify why the introduction of serialised vials would require additional 'space' for compounding activities.
- An increase in administrative burden associated with the introduction and ongoing monitoring of the system.

Critical objections to track-and-trace appeared to arise from the linking of serialised vials with a change in the remuneration model. In particular, Model A incorporated a credit-based payment system in which payments to manufacturers essentially bypassed intermediary agents (pharmacists/hospitals) and were settled directly by Government. That is, pharmacists/hospitals would purchase stock 'on credit' from manufacturers and then submit claims for product used for PBS purposes. Enabled by serialisation, Government would release funds for identified stock directly to manufacturers. The report implied that Model A would operate under a per-mg basis, though this

link was unclear, hence the objections. While it is clear that the introduction of serialised vials would require enhanced IT infrastructure, further information is required on how it might impact other operational costs (e.g., space requirements).

The concept of track-and-trace rests on the notion that the 'barcoding' of vials it should enable drug claimed via the PBS to be traced back through the supply chain. Where multiple source vials are used in the preparation of an infusion, multiple barcodes may pertain to a single prepared dose and subsequent patient claim. Where partial source vials are used in the preparation of an infusion, the same barcode may pertain to multiple infusions and patient claims. To ensure efficient remuneration in such cases, it would be necessary to record into the system the proportion of drug in each source vial allocated to each specific preparation. This implies that the system not only be capable of tracking vials as they are used, but also the proportion of each vial used in the preparation of a given infusion. This could be enacted by requiring that each vial barcode also contain a numerical suffix to indicate the proportion of that container used in a given infusion; provision of that information for each vial would invariably rest with the compounding facility (given their role in allocating vials to the preparation of an infusion). A proportion-amended track-and-trace system would effectively operate in much the same way as per-mg pricing (since payments for partial vials would be equivalent to payments on a per-mg basis).

Serialised vials (payment on % vials) Efficiency  Access  Simplicity  Accountability 

Third-party payment model (ESCROW model)

The preferred model in the Ernst and Young report was the Simplified Electronic Payment Platform (or ESCROW model). The basis of this model was to maintain current operating procedures and structures for the EFC supply chain—ensuring profitability is maintained—by introducing a payment clearing house to facilitate secured payments between Government, manufacturers and other supply chain stakeholders. The third-party clearing house would facilitate payments to wholesalers/pharmacists, reducing their stock-holding requirements (and associated financial risk), and better aligning drug sales and subsequent PBS claims.

While the report suggests that such a model could be sufficiently flexible to allow the introduction of serialised vials, it does not detail how, in the absence of a track-and-trace system, the ESCROW model would facilitate matching of drug sales and PBS item claims. The estimated cost of implementing the system ($21-$28 million), was therefore likely to be understated, as the capacity to reconcile drug sales with PBS item claims would entail the additional costs associated with a track-and-trace system

(p. 8).

Further, the introduction of an additional stakeholder (i.e., a third-party payment clearing house) within an already complex system is likely to represent a significant impediment due to:

- the confidential nature of SPAs (and the underlying effective prices);
- the associated administrative burden of forming and maintaining a new remuneration body that oversees the EFC only; and
- widening disparitiies between the approach to funding of cancer medicines and other PBS-listed therapies.

ESCROW model Efficiency ↓ Access ↓ Simplicity ↓ Accountability ↓

6.3.2 *Cost-effectiveness considerations and PBS restrictions*

Serialised vials to inform price change

The current approach to the incorporation of wastage in pricing and volume calculations for assessments of cost-effectiveness relies on the interface between average doses, as observed in clinical trials, and product vial sizes available in Australian clinical practice. An alternative may be to adjust calculations of the efficient combination of vials to reflect the empirical amount of drug per vial used on a per-patient basis. In time, this could be achieved through the serialisation of vials and recording of the proportion of vials dispensed on a per-patient basis.

A product could thus be initially PBS listed and reimbursed on the basis of trial-identified dosage and estimated wastage, with a subsequent adjustment to the PBS list price after a suitable period of in-market use agreed to represent a steady state (e.g., after 12 months of in-market utilisation). Such a system, leveraging anticipated changes to the PBS system resulting from the PBS Data Distribution Project, could operate as follows:

- Product serialisation, which records the proportion of vial used, is introduced throughout the supply chain (from compounding to distribution) to allow the linking of barcoded vials to unique PBS claims.
- Subsequently, empirical utilisation data are used to estimate the proportion of vials consumed in the constitution of the within-market average dose, and to determine whether adjustment is required to the estimate of the efficient combination of vials and/or PBS list price.

Adopting proportion-weighted serialisation would be akin to the existing price disclosure system as it applies to estimating changes to PBS list prices to account for differences in within-market prices. Furthermore, it would allow compounders who are unable to share vials to reflect such use within their serialisation entries (i.e., to show 100% vial utilisation).

Proportion-weighted serialisation Efficiency  Access  Simplicity  Accountability 

Patient eligibility and maximum quantities

One of main themes raised by stakeholders focused on the administrative burden associated with PBS restrictions and authorities for EFC medicines. It was suggested that the existing system of maximum quantities as applies to PBS listings results in delays to access and increased administrative burden, particularly where requests for additional quantities are required to prescribe the correct dose based on patient weight or BSA.

Key suggestions included removal of indication-specific authorities—with preference for clinical autonomy in deciding on how drugs are prescribed—and higher maximum quantities to obviate the need for special requests when prescribing (particularly as might apply to weight and BSA-based dosing). Data on the extent to which such requests have been required at a national level were not available.

Suggestions on revising PBS maximum quantities and restrictions, however, belie an understanding of the basis on which restrictions and authorities are applied to EFC medicines and all drugs on the PBS, more broadly (see Section 3). While access to EFC drugs could be theoretically be simplified by removing the system of authority/streamlined requirements, this may come at a system-wide cost in that broadening PBS restrictions would likely yield a reduction of PBS reimbursed prices. For some products, this may have the unintended consequence of reducing product viability in Australia (witness the withdrawal of the innovator bevacizumab, Avastin, associated with the introduction of biosimilars of that molecule), negatively impacting patient access to medicines. Moreover, removing/broadening restrictions may serve to increase drug utilisation in indications that have not been assessed as cost-effective, or for which comparative effectiveness evidence has not been presented. Such increased utilisation may trigger caps in existing RSAs and result in further price reductions.

Remove authority requirements Efficiency  Access  Simplicity  Accountability 

6.3.3 Consolidating public and private items and fees

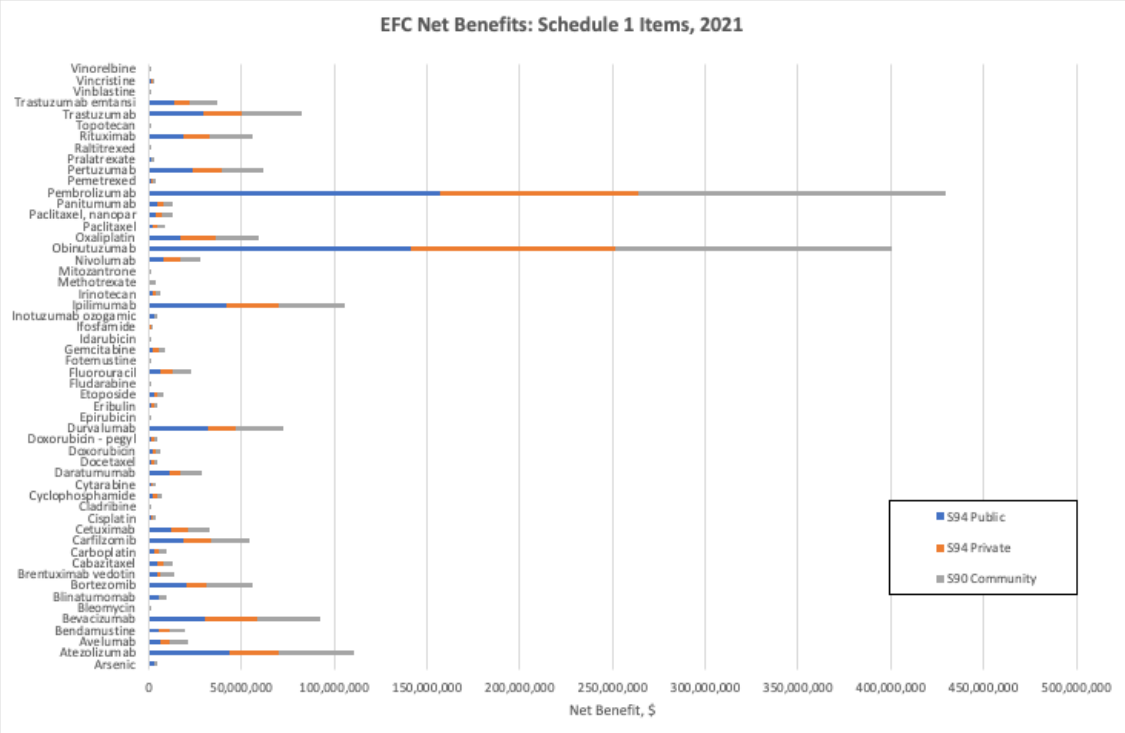
Several stakeholders suggested consolidating the fees paid in the private and public sectors. This may be interpreted in two ways: (1) setting fees in (s94) public and (s94) private settings at the same level; and/or (2) setting fees in all settings to the level paid to (s90) community pharmacies (see Section 4.3.3 for a comparison of mean fees across each setting).

The impact of removing the distinction in fees between the various sectors was estimated as follows:

- Mean DPMAs were estimated and compared for all three settings. This necessitated estimation of DPMAs for (s90) community pharmacies based on the application of the known fees and mark-ups for that setting to the AEMP as applicable to the maximum amount for each molecule. The difference between the sectors was expressed as a percentage on a per-molecule basis.
- The net-benefit paid for Schedule 1 EFC items in 2020-2021 per pharmacy type was extracted on a per-molecule basis from the PBS database (note, this included all items for rituximab and trastuzumab despite some being funded via Schedule 2 of the EFC; the impact is negligible with the inclusion of approximately $3 million of benefits that would otherwise have been excluded from a total of $1.9 billion dollars of benefits in that year).
- The proportional difference in DPMAs estimated between (1) (s94) private and (s94) public items and (2) (s94) private or public and (s90) community pharmacy items was applied to the net-benefits for items in 2021 for the sector for which the fee change was being estimated, i.e., (s94) public, and (s94) private and public in the two scenarios, respectively. This provided an estimate of the cost to Government of applying consistent EFC fees across sectors.

Analysis of the PBS net-benefit data for 2021 shows that 38.5% of items were claimed via (s90) community pharmacies; 35.8% via (s94) public hospital pharmacies and 25.7% via (s94) private hospital pharmacies (see Figure 33 for the distribution across molecules).

Figure 33. EFC net-benefits by pharmacy setting (2021)



Source: Developed for this Review from PBS line level data.

The comparison of DPMAs for private and public hospital items showed a difference of 17.6% in favour of private hospitals, with (s94) private hospital benefits per item being 2.6% higher than those in (s90) community pharmacies. The two scenarios for fee consolidation resulted in the following impact to estimated Government costs:

- Applying the per-molecule difference between the public and private hospital DPMAs to the net-benefits observed in 2021 resulted in an increase in the net-benefits for (s94) public hospital items of $28.2 million (from $690.6 million to $718.8 million); a change of 4.1%.
- Applying the (s90) community fees to (s94) private hospital items would have reduced private hospital expenditure by $1.1 million, but added $25.2 million to (s94) public hospital expenditure; an estimated increase in total Government spending of $24.1 million.

This illustrates that consolidation of fee items across settings produces similar per annum impacts on EFC expenditure. However, in implementing such a change, consideration must be given to how it would further differentiate the payment of fees to providers of EFC items relative to other PBS listed items, and whether this would create unwanted disparities within the medicines supply chain.

6.3.4 Recognising the importance of compounding

Changes to the CCPS

There are a number of considerations with respect to potential amendments to the payment of the CCPS fee to TGA-licensed compounders for EFC participation:

- Whether payment of the fee should be extended to all compounders who are accredited to participate in the supply of EFC medicines regardless of TGA licensing status.
- The quantum of fee to be paid.
- Whether fees should be paid on a per item basis or a lump sum, supplier basis.

Feedback from stakeholders to the Review differed with respect to whether there is a difference in the activity performed or costs incurred by TGA-licensed compounders versus non-TGA licensed compounders. In short, both groups adhere to strict local and international standards for the handling, compounding and supply of infusion products (see Sections 4 and 5 for discussion of PICS and USP787). Currently, only TGA-licensed compounders are audited for compliance.

The key differentiator is the capacity of TGA-licensed compounders to conduct their own inhouse stability testing, and thus to issue 'extended' expiry dates with their compounded products. This has been identified as a key benefit associated with TGA compounder services, particularly with respect to the supply of cancer medicines to facilities outside of the metropolitan area. Thus, of the cost components under the current EFC fee arrangements that could be substantiated, it may be reasonable that a specific, separate, payment continue to be made to TGA-licensed compounders in recognition of stability testing (estimated at $4.75 per service).

The restriction of stability testing to TGA-licensed compounders reflects two aspects: the infrastructure required for stability testing (including the availability of sterile facilities capable of hosting stability testing functions) and the proprietary nature of stability testing data generated by the TGA-licensed compounders. If requirements to undertake stability testing change in the future, making it feasible to undertake such testing more widely and for the results of testing at non-TGA-licensed centres who choose to undertake such testing to be recognised, it would be reasonable to consider the extension of stability testing specific fees to all eligible compounders within the supply chain.

Separate Stability Fee Efficiency – Access – Simplicity ↑ Accountability ↑

With respect to the remaining elements of the CCPS fee (those associated with compliance with TGA and good manufacturing practice requirements), there does not appear to be a reasonable rationale as to why payment of those fees should be restricted to TGA-licensed compounders given that: (1) other compounding facilities are also required to meet regulatory requirements, and; (2) compliance with TGA regulatory requirements by TGA-licensed facilities is not specific to their participation in supplying medicines to the EFC program. In line with the findings of the King Review (p 116), it would be reasonable that there be parity within the EFC supply chain for fees paid to compounders for compliance with regulatory arrangements where such compliance undergoes external audit.

Fee Available to All Compounders Efficiency ↑ Access ↑ Simplicity ↑ Accountability ↑

The available information appears to substantiate a cost of $8.71 per cancer medicine service for compliance with regulatory arrangements. However, this cost appears to be a fixed cost which is defrayed with increasing service volume, resulting in a lower cost per service as volumes increase. Thus, setting a fee on the basis of that cost per service would result in a gain per service when service volumes exceed that used in the estimate of the cost per service (and conversely a loss when volumes are below that level). This advantages high volume service providers while disadvantaging low volume service providers. Furthermore, no evidence was provided to the Review to substantiate that the cost of regulatory compliance (including audits, compliance with regulatory authorities and infrastructure upgrades) is variable or increases with service volume.

Consideration could thus be given to whether compensation to compounders for regulatory compliance could be removed from the CCPS and paid on an annual facility-fee basis. In addition, in recognition that compounders (of all types) engage in multiple service types (from preparation of parenteral nutrition, to compounding of IV antibiotics, non-EFC cancer therapies and biological therapies for use in a non-cancer setting) it would be reasonable that payment of the facility-fee be weighted to reflect the proportion of all activity related to EFC activities. This weighting would be estimated in terms of the volume in units of materials produced which require adherence to regulatory guidelines for production accounted for by the compounding of infusion therapies for cancer care. It is recognised that this cannot be linked directly to the compounding of materials for the EFC since third-party compounders do not have visibility as to whether compounded medicines are intended for use as an EFC reimbursed item (but would rely on what proportion of compounder activity is accounted for by the compounding of cancer medicines as opposed to other preparations).

Fee Available to All Compounders Efficiency ↑ Access ↑ Simplicity ↑ Accountability ↑

National Centre for Stability Testing

The importance of stability data in affecting access to medicines and the potential for drug to be discarded was highlighted throughout the consultations to the Review. The absence of medicine-specific stability data that might permit an extension to product shelf life was seen as a limiting factor in the provision of medicines outside of metropolitan areas and to the retention of compounded stock for longer periods of time. Moreover, the costs of conducting stability sites de-novo were recognised by stakeholders as prohibitive, vesting the conduct of those studies in a few, highly specialised units, who then treat this data as commercial-in-confidence.

Where a medicine can be compounded in accordance with the controlled conditions under which stability data have been generated, the extension of shelf-life offered by those stability data should apply. Two avenues by which this could be achieved are for stability data to be held centrally via a national repository once conducted, or to have all testing conducted centrally and shared with compounding services that meet national standards.

Within the UK, the National Health Service collates data on the stability of compounded medicines prepared under regulated conditions. Those data are collated according to guidelines released by the NHS on the conduct and reporting of stability testing. Use of those guidelines ensures consistency in the standards applied to testing and that aseptic units can apply stability provided they follow those standards (see https://www.sps.nhs.uk/articles/content-page-for-cytotoxic-drug-stability-monographs/). Such a centralised repository could be housed within the TGA alongside product regulation and the existing PICS standards. In addition, consideration could be given to linking payment of any stability specific fee elements of the CCPS (see above) to participation in the national repository.

The other potential avenue, as alluded to in the Lord Carter of Coles Review of NHS aseptic preparation services, is to concentrate services (i.e., stability testing) in specialised units that would provide stability data back into the system (see https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/931195/aseptic-pharmacy.pdf). While the Cole Review focused on establishing hub-and-spoke models for all aspects of the supply of aseptic preparations (including cancer medicines), this included the conduct of stability testing.

This Review is not proposing the adoption of the same hub-and-spoke model, but that adopting

centralised stability testing be considered as one means of capitalising on scale with respect to generating stability data, which can then be made available throughout the supply chain. Currently, whether or not stability testing is undertaken is a commercial decision based upon anticipated market volume (relative to the cost of undertaking testing). Thus, in the interests of generating centralised data for all molecules, locating such a centralised facility within an existing government agency (e.g., the TGA) or public research facility, would ensure that stability data can be provided without regard to commercial viability.

National Repository	Efficiency	↑	Access	↑	Simplicity	↑	Accountability ↑
Centralised Testing	Efficiency	↑	Access	↑	Simplicity	↑	Accountability ↑

6.3.5 Additional EFC Fee components

Dose repurposing

Analysis by M Ryan and colleagues at the Princess Alexander Hospital in Queensland, estimated that re-labelling of already compounded cancer medicines for repurposing resulted in avoiding disposal of cancer medicines to the value of $1.6 million in 2019. They report that reassigning/repurposing of medicines required approximately 10 minutes of additional administrative and pharmacist processing time, at an estimated cost of approximately $10 per repurposed item.

It is unlikely that the introduction of a $10 payment per re-labelled/repurposed item would alter prescriber behaviour in such a way that it would increase the incidence of repurposing. That is, under current arrangements, pharmacy and clinical administrators schedule patients in such a way as to coordinate medicine and patient availability. It is unlikely that providing a fee for repurposing would diminish such coordinating behaviour, particularly as it is largely motivated by the clinical need for patients to receive treatment and it may not always be the case that it is possible to repurpose a medicine. In addition, given the high unit cost of many medicines supplied via the EFC, the expected loss associated with not appropriately coordinating medicine and patient availability is likely to far outweigh the payment for drug repurposing (a proposed $10 fee).

Two potential means whereby such a fee could be introduced are:

- As a fee attached to repurposing activities. In this situation, a pharmacist would indicate whether the claim related to an instance of drug repurposing at the time of submitting for PBS reimbursement. This would require a change in existing Services Australia PBS claiming systems and provider software. However, implementing an instance-based payment would in

effect result in different DPMA for EFC products, the variance in price depending on whether or not an instance of repurposing was being claimed. Each PBS listed item can only have one DPMA (noting that the payment of any additional fees that is not levied on all instances of use of a medicine, such as the CCPS, sit outside of the PBS and are not attached to the product price).

- As a weighted fee included in the preparation fee. In this situation, there would be an addition to the existing preparation fee to account for the incidence across all items prepared. This approach benefits from: (1) ease of implementation as it does not require a change in existing PBS claiming software; (2) it can be incorporated into the prices proposed by sponsors for initial consideration by the PBAC without requiring assumptions about the extent to which repurposing might occur for a given medicine; and (3) it maintains the principle of one DPMA for each cancer medicine.

Implementation of the repurposing payment as a weighted fee would require evidence on the extent to which repurposing applies across the numerous cancer medicines providers across Australia. Moreover, it would essentially uncouple the payment from the activity (insofar as it would not require practitioners to indicate whether repurposing had occurred in order to access that payment). The decision of mode by which the additional fee should be implemented will depend on the balance between administrative efficiency (as a weighted fee) or accountability (as a specific fee to be claimed).

Dose repurposing fee Efficiency ↑ Access ↑ Simplicity – Accountability ↑

Waste disposal

Several submissions to the Review highlighted the importance of safe disposal of infused cancer medicines, particularly cytotoxic medicines, and the additional requirements disposal imposes on pharmacists compared with other dispensed medications. The need for appropriate and safe disposal of medicines which have been prepared but are not administered to patients is clear, from a patient and occupational health and safety perspective, and in terms of the environmental impact of waste disposal.

None of the submissions to the Review enumerated the activities involved in appropriate waste management and indeed whether the costs associated with those activities are not captured within the existing fees paid under the EFC for medicine preparation. Evidence to inform the extent to which a specific waste disposal fee (or allowance) is required within the EFC payment structure may

be available with the follow-up data collection (see Section 7).

Waste disposal fee Efficiency ➖ Access ➖ Simplicity ➖ Accountability ⬆

Infusion device costs

Submissions to the Review noted that the current EFC remuneration does not include payment for infusion product containers. Such costs are increasing given advances in container technology to improve both sterility and the extent to which all the contents of containers can be extracted (minimising product overage). The use of CSTD is growing, in cancer care, but feedback from submissions is that such containers are expensive.

It is understood that contracts between third-party suppliers (such as TGA-licensed compounders) include specific charges for container use. The specifics of those charges, or comparable costs that might be borne by in-house compounding by hospitals/pharmacists, are not available currently.

Overall, the consideration of whether container costs should be remunerated under EFC arrangements rests on the scope of activity for which the PBS is responsible. The 2013 Review concluded that funding for infusion devices for cancer medicines falls outside of the remit of the PBS (p64), noting that while the costs for such devices are considered by the PBAC in overall deliberations of cost-effectiveness, the responsibility to meet such costs falls within the purview of hospitals and private health insurers (where such devices are listed on the prostheses list). Thus, whether infusion device costs can be factored into EFC fees may rest within the consideration of the broader system wide context (the inter-relationship between PBS funding and the NHRA). Within that context, it should be acknowledged that there is precedent for product delivery devices to be funded under the purview of the Pharmaceutical Benefits Scheme noting the existence of the National Diabetes Service Scheme which funds infusion pumps and monitoring devices (the Government spend on which is reported as part of PBS expenditure, see p. 27, https://www.pbs.gov.au/statistics/expenditure-prescriptions/2019-2020/PBS_Expenditure_and_Prescriptions_Report_1-July-2019_to_30-June-2020.pdf).

Infusion device costs Efficiency ⬆ Access ⬆ Simplicity ➖ Accountability ⬆

6.3.6 *Budgetary implications of alternative payment structures*

Overview of the approach

The potential budgetary implications of a shift to a per-mg basis for drug reimbursement were investigated for three medicines currently funded via the EFC. The aim of this analysis was to model the cost to Government across 5 years from 1 July 2016 to 30 June 2021 under the existing EFC funding arrangement (based on the most efficient combination of vials) compared to an alternative per-mg basis for remuneration. In addition, other scenarios were investigated with respect to possible changes to the impact of EFC fee structures, including applying the existing (s94) private hospital fees to all (s94) public hospital items, and testing various percentage increases in the total quantum of fees (to allow for the potential that additional fees are included subsequent to this Review). All analyses were conducted using observed volumes and net-benefits paid on the PBS at the patient level for the period 1 July 2016 to 30 June 2021. Results are presented in Table 19 and Table 20. Full details of the approach to the analysis and the data utilised are provided in Appendix 9

Three case studies were chosen for assessment in the analysis:

- cabazitaxel for prostate cancer: This medicine was reported by stakeholders to undergo extensive vial-sharing on the PBS.
- avelumab for merkel cell carcinoma: This medicine was included as an example of a recently listed MAb (not a cytotoxic) where use can occur on both mg per kg dosing (as the predominant form of utilisation) and flat based dosing.
- bortezomib for multiple myeloma: This medicine was included as an example of a medicine prescribed on a mg per m^2 basis.

Potential to reduce Government expenditure

From the modelled analysis, it can be observed that adopting a per-mg pricing model resulted in net-costs to Government that were 73%, 69% and 83% of the cost under current EFC arrangements for cabazitaxel, avelumab and bortezomib, respectively (Table 20). This represents a potential reduction in Government spending from adopting per-mg pricing for these three medicines of approximately $36 million over four years. This is broadly consistent with estimates provided in stakeholder submissions to this Review. Ultimately, reductions in Government spending from adopting per mg pricing will depend on the extent to which medicines are prescribed on the basis of flat or weight-based dosing. As noted in Table 20, the potential reductions in expenditure were lower where it was assumed that there was more wastage across infusions (i.e. there was less capacity within the system to vial share).

As alluded to previously, adopting consistent fees across (s94) authorities has minimal impact on the

cost to Government. This can be observed for all three molecules, either under the existing model of remuneration versus shifting to a per-mg pricing model. Similarly, increasing mark-ups has a negligible impact on the cost to Government within a given payment system. However, increasing mark-ups and/or establishing consistent fees between public and private providers would erode some of the reduction in the cost to government from moving to per-mg pricing.

Table 19. Net cost PBS / RPBS based on full calendar year – base case

	2017	2018	2019	2020	Sum at 4 years (million)	Change[1]
Cabazitaxel						
Base case	$4,428,539	$4,674,509	$5,519,221	$6,066,178	$20.69	100%
No public/private distinction	$4,495,729	$4,745,431	$5,602,959	$6,158,215	$21.00	102%
Mark-ups increased by 10%	$4,485,036	$4,734,145	$5,589,633	$6,143,568	$20.95	101%
Mark-ups increased by 25%	$4,569,783	$4,823,598	$5,695,251	$6,259,653	$21.35	103%
Avelumab						
Base case	$0	$0	$15,417,696	$25,768,042	$41.19	100%
No public/private distinction	$0	$0	$15,448,767	$25,819,972	$41.27	100%
Mark-ups increased by 10%	$0	$0	$15,445,975	$25,815,306	$41.26	100%
Mark-ups increased by 25%	$0	$0	$15,488,393	$25,886,200	$41.37	100%
Bortezomib						
Base case	$25,077,466	$24,396,037	$27,211,575	$30,105,403	$106.79	100%
No public/private distinction	$25,782,240	$25,081,660	$27,976,327	$30,951,482	$109.79	103%
Mark-ups increased by 10%	$25,520,287	$24,826,825	$27,692,081	$30,637,008	$108.68	102%
Mark-ups increased by 25%	$26,184,519	$25,473,007	$28,412,839	$31,434,415	$111.50	104%

Abbreviations: PBS, pharmaceutical benefits scheme; RPBS, repatriation pharmaceutical benefits scheme.
Source: Developed for this Review, see Appendix 9
Note: [1] This is the percentage change from base case

Table 20. Net cost PBS / RPBS based on full calendar year – per-mg pricing

	2017	2018	2019	2020	Sum at 4 years (million)	Change[1]
Cabazitaxel						
Base case	$4,428,539	$4,674,509	$5,519,221	$6,066,178	$20.69	100%
Per-mg pricing	$3,215,319	$3,393,905	$4,007,203	$4,404,318	$15.02	73%
Substitution per-mg pricing 95%	$3,275,980	$3,457,935	$4,082,804	$4,487,411	$15.30	74%
Substitution per-mg pricing 90%	$3,336,641	$3,521,965	$4,158,405	$4,570,504	$15.59	75%
Substitution per-mg pricing 80%	$3,457,963	$3,650,025	$4,309,607	$4,736,690	$16.15	78%
Substitution per-mg pricing 70%	$3,579,285	$3,778,086	$4,460,808	$4,902,876	$16.72	81%
No public/private distinction	$3,277,509	$3,459,548	$4,084,709	$4,489,505	$15.31	74%

	2017	2018	2019	2020	Sum at 4 years (million)	Change[1]
and per-mg pricing						
Mark-ups increased by 10% and per-mg pricing	$3,268,940	$3,450,504	$4,074,031	$4,477,769	$15.27	74%
Mark-ups increased by 25% and per-mg pricing	$3,349,372	$3,535,403	$4,174,272	$4,587,944	$15.65	76%
Avelumab						
Base case	$0	$0	$15,417,696	$25,768,042	$41.19	100%
Price per mg	$0	$0	$10,661,514	$17,818,899	$28.48	69%
Substitution per-mg pricing, 95%	$0	$0	$10,905,695	$18,227,005	$29.13	71%
Substitution per-mg pricing, 90%	$0	$0	$11,149,876	$18,635,112	$29.78	72%
Substitution per-mg pricing, 80%	$0	$0	$11,638,237	$19,451,324	$31.09	75%
Substitution per-mg pricing, 70%	$0	$0	$12,126,599	$20,267,537	$32.39	79%
No public/private distinction and per-mg pricing	$0	$0	$10,689,509	$17,865,688	$28.56	69%
Mark-ups increased by 10% and per-mg pricing	$0	$0	$10,687,668	$17,862,610	$28.55	69%
Mark-ups increased by 25% and per-mg pricing	$0	$0	$10,726,898	$17,928,176	$28.66	70%
Bortezomib						
Base case	$25,077,466	$24,396,037	$27,211,575	$30,105,403	$106.79	100%
Price per mg	$20,898,296	$20,330,426	$22,676,753	$25,088,324	$88.99	83%
Substitution per-mg pricing, 95%	$21,107,254	$20,533,707	$22,903,495	$25,339,178	$89.88	84%
Substitution per-mg pricing, 90%	$21,316,213	$20,736,987	$23,130,236	$25,590,032	$90.77	85%
Substitution per-mg pricing, 80%	$21,734,130	$21,143,548	$23,583,718	$26,091,739	$92.55	87%
Substitution per-mg pricing, 70%	$22,152,047	$21,550,109	$24,037,200	$26,593,447	$94.33	88%
No public/private distinction and per-mg pricing	$21,581,751	$20,995,311	$23,418,372	$25,908,810	$91.90	86%
Mark-ups increased by 10% and per-mg pricing	$21,340,084	$20,760,210	$23,156,138	$25,618,689	$90.88	85%
Mark-ups increased by 25% and per-mg pricing	$22,002,766	$21,404,885	$23,875,215	$26,414,236	$93.70	88%

Abbreviations: PBS, pharmaceutical benefits scheme; RPBS, repatriation pharmaceutical benefits scheme.
Source: Developed for this Review, see Appendix 9.
Note: [1] This is the percentage change from base case.
Scenarios which refer to variable substitution allow for the possibility that vial-sharing is not possible and thus that wastage exists in the system.

The base case in the preceding analysis assumed 100% of drug utilisation; there is no wastage of vials. Results from subsequent sensitivity analyses show that there are still potential cost reductions available to Government from adopting a per-mg pricing model, even in the presence of wastage.

The extent to which those reductions can be realised across the full spectrum of medicines available on the EFC will vary depending on the extent to which those medicines are prescribed as a flat dose (such as is the case for many of the new immunotherapies) or that compounders are able to fully utilise available drug.

As noted previously, it was not possible as part of this Review to estimate the extent to which wastage is currently incorporated into utilisation on the PBS. If the relevant information were available to estimate the extent to which vial-sharing occurs within the system, it would be possible to more readily estimate the potential cost reductions applicable to the EFC more broadly from adopting a per-mg pricing model. An hypothetical example of how PBS utilisation data could be used to estimate the extent of vial-sharing (if the relevant data were available) is provided in Appendix 12.

Regardless, the analysis contained herein suggests that by implementing a per-mg pricing model there are potentially significant cost reductions available to Government, regardless of whether the introduction of that model is accompanied by additional changes to EFC fee arrangements.

7 Discussion & recommendations

7.1 Findings and Recommendations

The findings of the Review are consolidated within the following section. These are presented according to the key themes arising from the Review. Subsequent recommendations arising from those findings and the consideration of the evidence to date are presented as they pertain to each theme as per the following classification:

- Short-term: A policy or administrative change which can potentially be enacted, subject to enabling legislative arrangements, within a two-year timeframe.
- Medium-term: A policy or administrative change which may require the collection of additional information and can potentially be enacted, subject to enabling legislative arrangements, beyond a two-year timeframe.
- Long-term: A policy or administrative change which requires additional consultation and/or the collection of data to be analysed prior to implementation (anticipated to occur beyond a two-year timeframe).
- System change: An area requiring further investigation regarding potential broader systems change that would necessitate extensive legislative change.

Each set of recommendations made in relation to a finding is tabulated with that finding, including a cross-reference to the relevant sections in this interim report which present the underlying evidence or analysis which led to that recommendation.

Chemotherapy as a 'specialty service'

The specialty nature of cancer care was highlighted by the stakeholder consultation to the Review. This includes the complex nature of compounding, prescribing and administering cancer medicines. The nature of cancer medicines themselves has changed; from a predominance of cytotoxic drugs at the inception of the EFC to the overwhelming volume and value of EFC services now being associated with the provision of immunotherapy and other biological medicines.

The Review recognizes that the delivery of cancer medicines is one aspect of a more wholistic, yet complex, system of cancer care. Many of the aspects of that care associated with service delivery, care organization, provision of adequate staffing levels and appropriate training, lie outside of the purview of this Review.

1. Short-term: Modify the EFC legislative instrument to recognise that the program funds more than chemotherapy and intravenous cancer medications. Consideration should be

given to the following suggestions: a) 'Efficient Funding of Cancer Medicines'; b) 'Cancer Medicines Funding Program'

2. System change: Investigate system changes with respect to alternative funding mechanisms for the delivery of cancer medicine services that better integrate all aspects of the care pathway (including assessment for treatment, treatment preparation and delivery, and follow-up care).

(see Sections 3.1.1; 3.2.1; 4.1.5)

Service Viability

The Review recognises that the existing PBS arrangements involve a complex interplay of multiple stakeholders in which Government acts as a price-setter for drug reimbursement and reimburses hospitals/pharmacists for drug supplied to patients but does not take receipt of purchased stock. This creates a disconnect in the system between the decision to reimburse drug, the process by which drug is supplied and the impacts therein on the subsequent volumes claimed for reimbursement from Government. In accordance with the recommendations from the WHO, improvements to system efficiency and transparency may be afforded by Government acting as a central procurement agency for all cancer medicines [62]. The WHO noted that where such procurements policies have been pursued, such as in Thailand, Denmark and Norway, there has been a notable decrease in the prices of cancer medicines as well as an increase in the number of patients accessing care (p. 47).

3. System change: Consider the potential for the Commonwealth to purchase medicines directly from manufacturers as a means of increasing system efficiency and reducing pharmacy/hospital exposure to cost pressures associated with purchasing and carrying EFC-listed stock.

(see Sections 3.2.2; 5.1.1; 6.3.6)

EFC remuneration

There was insufficient basis to suggest that the current fee components be amended. Additional fee components could be considered in the longer term to address changes in the provision of cancer medicines and pharmacy practices designed to minimise waste.

4. Short-term: Maintain the EFC's existing fee structure and level as currently legislated, subject to indexing arrangements.

5. Long-term: Consider amending the EFC fee components and levels (subject to an analysis of stakeholders' empirical cost data) to add specific payments with respect to:

    a) Infusion devices (e.g., elastomeric infusors, Cadd devices) required for the administration of the compounded pharmaceutical product;

b) Verification of the distribution fee (in lieu of a specific wholesaler payment);

c) Recognition of the activity required for repurposing/reissue of compounded medicines. Current evidence suggests a payment of $10 per repurposed item. Evidence is required of the proportion of PBS claims to which repurposing might apply to allow this incentive payment to be included on a wighted basis as part of the standard EFC fee arrangements; and

d) Provision of cancer medicines in rural areas, as a means of recognising the additional barriers faced by providers in those areas in maintaining appropriate workforces required to request, dispense and administer cancer medicines, and for the additional logistics costs associated with provision of cancer medicines in rural/regional areas.

6. Long-term: Consider amending the EFC fee level associated with the distribution fee in lieu of a specific wholesaler payment. Further negotiations of the CSO should consider whether the supply of EFC medicines can be captured as a means of simplifying arrangements for the payment of distribution and wholesaler payments.

(see Sections 3.2.2; 4.1.6; 4.3.1; 4.3.2; 4.3.3; 5.1.1; 5.1.2; 6.1.1; 6.1.2; 6.3.5)

Administrative burden

Stakeholders considered that current arrangements for access to medicines on the EFC can be overly complex and associated with high administrative burden, particularly with respect to:

- The need for written and online authorities;
- The impact of PBS authorities on the ability to prescribe the required dose on a per-patient basis;
- Differences between PBS authorities as they apply to medicines funded via the EFC and those funded elsewhere on the PBS; and
- Differences in co-payment arrangements within the EFC and compared with other PBS funded medicines.

7. Short-term: Continue the operation of the Medicare Prescribing chart for online prescribing and claiming.

8. Short-term: Expand the medicines covered under the EFC to include all compounded cancer medicines listed for cancer indications on the PBS.

9. Short-term: Develop an education program targeting all system stakeholders to focus on:

   a) The basis on which the PBAC makes recommendations for cost-effectiveness, including how PBS authority and listing requirements support the principles of cost-effectiveness;

   b) the scope of the existing EFC arrangements, including that EFC funding extends to supportive therapies as covered under Schedule II of the enacting legislative instrument.

(see Sections 3.2.2; 3.2.3; 3.2.4; 4.1.3; 5.1.3; 6.1.1)

Compounding

Compounding is a critical and complex element of the supply chain for cancer medicines. The Review identified that there has been an increase in the use of third-party private sector compounders for the provision of cancer medicines. While this has increased the capacity of some smaller hospitals to provide cancer medicines closer to home and in a timelier manner (particularly in regional and rural areas), overall there has been a reduction in public sector compounding capacity.

Ongoing recognition of the specialised nature of compounding services is essential. However, the changing nature of cancer medicines with an increasing reliance on non-cytotoxic chemotherapies, has blurred the requirements for sterile compounding and cytotoxic safety. Most non-cytotoxic cancer medicines can be compounded in sterile suites used for purposes such as preparation of parenteral nutrition. This means some of this compounding couple be done in smaller hospitals/pharmacies with these facilities, reserving use of third-party compounders for cytotoxic medicines.

For compounding of cytotoxic cancer medicines, hospital stakeholders argued that the distinction between compounding standards for hospitals versus TGA licensed facilities is narrowing with the key difference being the need for auditing and accreditation. Overall, there was no clear rationale to maintain the distinction between TGA-licensed and non-licensed facilities with respect to the payment of compounding fees, if they are undertaking the same activities and provided that the same standards are met.

There was no clear evidence submitted to substantiate a change in the quantum of fees paid for compounding services. Moreover, fees do not appear to vary with scale. The Review recognised the specialised nature of stability testing and its importance for affecting timely access to care for patients.

10. Short-term: It is essential that all compounding sites (TGA and non-TGA licensed) be appropriately recognised for the investment associated with complying with regulatory requirements and good manufacturing practice.

    a) The payment of the CCPS should be expanded to all compounding facilities and made subject to an annual review of compliance with relevant regulatory guidelines and practice (Pharmacy Board Guidelines/USP 797).

    b) Payment of the CCPS fee should be uncoupled from service volume and made on an

annual grant basis.

11. Long-term: Government should investigate the requirements and feasibility of establishing a National Centre for Stability Testing to increase the shelf-life of compounded products under conditions that can be replicated by local compounders.

(see Sections 4.1.1; 4.1.5; 4.3.3; 5.1.1; 6.3.4)

Wastage (and vial-sharing)

The Review identified that the current approach to the remuneration of medicines based on the most efficient combination of vials is associated with inefficiency with respect to what is claimed via the PBS in terms of the 'double-payment' for the amount of drug contained in vials which exceeds what is prescribed on a per-patient basis.

Nonetheless, the use of what is termed 'wastage' for vial-sharing (thereby minimising the quantum of drug which is discarded) is more efficient than would otherwise occur if drug was supplied and claimed on a whole vial basis with the excess discarded and reflects the commercial reality of the existing PBS supply chain.

Reimbursement of drug on a per-mg basis would reduce the extent to which there is 'double-payment' for drug wastage. However, the Review recognizes that adoption of a per mg reimbursement model has broader systemwide implications, particularly for the flow of funds within public hospitals, necessitating that any such change be managed with careful regard to the overall arrangement of public sector hospital funding arrangements.

The Review also recognizes that existing commercial arrangements between Government and manufacturers of cancer medicines necessitate the periodic reconciliation of drugs sold by manufacturers into the supply chain with what is claimed for Government reimbursement via the PBS. Existing data arrangements do not readily support the conduct of those reconciliations.

12. Short-term: Continue the current system of reimbursement on the basis of the most efficient combination of vials.

13. Medium-term: Investigate the introduction of a PBS Dose-Banding chart for cancer medicines to facilitate ease of prescribing within bands (with an aim to reduce wastage on a per-patient basis). Reimbursement would continue to be based on the most efficient combination of vials (ad-interim).

14. Long-term: Adopt a per-mg reimbursement model as the most efficient use of cancer medicines and may support the reconciliation of sales with manufacturers. This is predicated on broader system change with respect to the interface between PBS reimbursement for drug supplied and the flow of funds to states for hospital funding through the Australian

Hospital Agreements. The aim would be to allow hospital-based pharmacies to remain viable in the face of short-term reductions in cash-flow (due to a decline in PBS receipts).

15. Medium-term: Upgrade PBS data collection and reporting systems to ensure information on the form and strength of vials used in estimating the most efficient combination of vials can be readily extracted from the system.

16. Long-term: Serialise vials to facilitate reconciliation of drugs transacted with PBS claims. Feasibility of such an arrangement is subject to requisite infrastructure (e.g., sterility-compliant scanning devices in compounding facilities, pharmacy scanning software) and financial capital investment.

17. System change: Consider the potential for the Commonwealth to purchase medicines directly from manufacturers as a means of increasing system efficiency and more directly align the purchase and reimbursement of PBS medicines.

(see Sections 4.1.1; 4.1.2; 4.2.1; 4.2.2; 4.2.3; 5.1.1; 6.1.2; 6.1.5; 6.3.2; 6.3.4; 6.3.5; 6.3.6)

Patient access and safety

There is an ongoing need to ensure that Australian cancer patients continue to have access to quality cancer medicines. Current co-payment arrangements result in some disparities for cancer patients depending on whether they access care via a public or private hospital setting, or whether they are accessing supportive cancer medicines.

In addition, access to CTG co-payment arrangements is unnecessarily complex and restricts participation in that measure by some Indigenous Australians. The Review recognises the critical nature of ensuring access to quality care for patients living outside of metropolitan areas; current arrangements for the funding and provision of cancer medicines may result in delays in access for patients in rural/remote areas, or increased 'costs' in order to access care. However, many of these issues relate to service provision and are beyond the scope of the Review.

18. Short-term: Remove the distinction between public and private hospital prescribing as a means of rationalising patient co-payments. There should be no distinction between out-of-pocket costs to patients based on the settings in which prescribers are authorised.

19. Short-term: Expand the availability of the Closing the Gap arrangements to all eligible Indigenous peoples accessing cancer medicines listed in Schedule 1 or Schedule 2 of the EFC, irrespective of the setting from which those medicines are prescribed.

20. Short-term: Extend the current co-payment arrangements for EFC Schedule I medicines to Schedule II medicines to ensure patients are not differentially affected by co-payments.

21. Medium-term: Conduct a system wide consultation on the provision of cancer services to consider initiatives that may improve access to care. This will necessitate the combined consultation of State/Territory and Commonwealth Governments, and key health organizations.

(see Sections 3.2.1; 5.2-5.4; 6.3.3)

Standards—Pharmacy

Compliance with international and local standards for compounding, pharmacy and manufacturing practices was cited as critical to the provision of safe, effective and efficient cancer medicines under the EFC. The Review noted that TGA-licensed compounders currently adhere to the PICs standards, as well as numerous State/Territory based standards, and are subject to annual audit of their practices to maintain their TGA licence.

Non-TGA licensed compounders are not required to undergo external audits, but generally adhere to guidelines as set out by the Pharmacy Board of Australia in compliance with the USP 797 standards. The Review heard that overtime the distinction between the USP 797 standards and the PICs standards as they relate to compounding of cancer medicines has narrowed..

22. Short-term: The Review reiterates the findings of the King Review (2017) with respect to the establishment of consistent standards as they apply to the compounding and supply of cancer medicines. There should be a clear and uniform minimum set of standards for all approved cancer medicine compounding facilities. These minimum standards should:

    a) Be developed based upon current Good Manufacturing Practice and the Pharmacy Board of Australia compounding standards, therefore ensuring all TGA-licensed and non-TGA licensed facilities will meet the minimum standards;

    b) Not require that a compounding facility be TGA-licensed to meet minimum requirements;

    c) Reflect the various settings that are appropriate for the preparation of cancer medicines, including 'urgent' preparations in a hospital or community pharmacy setting;

    d) Detail specific and measurable requirements that will be audited to maintain approval to operate as a cancer medicine compounding facility; and

    e) Articulate the distinction in standards required for cytotoxic and non-cytotoxic cancer medicine compounding.

    The Pharmacy Board of Australia, or appropriate regulatory authority, should be adequately resourced to monitor compliance with these national standards.

    (see Sections 4.1.1; 4.1.4; 4.1.6; 4.3.3; 6.3.4)

Public vs private settings

The division in the PBS item numbers currently between (s94) public and private hospital providers

results in unnecessary complexity for providers of cancer medicines. The associated administrative burden has the potential to adversely affect patient access if patients move between the public and private settings (thereby impacting whether scripts are issued as initial or repeat authorities, the former attracting a co-payment, the latter being co-payment free).

Moreover, the Review could not substantiate the basis under which public hospital providers are paid less (with respect to EFC fees) for the provision of cancer medicines relative to either (s90) community pharmacies or (s94) private hospital providers.

23. Short-term: Remove the distinction between (s94) public and private hospital settings with respect to PBS item codes.

24. Short-term: Remove the distinction between (s94) public and private hospital providers with respect to the EFC fees paid for the supply of cancer medicines.

(see Sections 4.1.1; 4.1.5; 5.1.2; 6.3.3)

7.2 Appropriateness and transitional arrangements

As outlined in Section 1.3, the Economic Analysis was structured to address the overarching themes of: (1) Appropriateness—whether the EFC remains an appropriate policy response to the PBS subsidy of cancer medicines; and (2) Transition—to investigate the approach and implications of changing the existing EFC funding arrangements.

As noted in the findings, the Review recognises that the preparation and supply of cancer medicines is a highly specialised service. Moreover, cancer medicines, particularly emergent biological and immunotherapy-based medicines, have high unit prices (resulting in high costs to Government) and are associated with substantial commercial risk to several supply chain stakeholders. Thus, to the extent that the original intent in establishing the EFC as a separate program with the PBS remains, the EFC as a policy response continues to be appropriate. However, the details of the EFC—most notably the manner in which it is implemented via the PBS and its scope (with respect to the range of medicines included) may no longer be appropriate, giving rise to the previous recommendations to consider the addition of new fee elements, the restructuring of how items are listed under the EFC and importantly, the basis upon which cancer medicines are remunerated.

Implementing these recommendations will require further consideration of the interface between the EFC as a program within the PBS, other programs and sections within the PBS, and the interplay between Commonwealth PBS funding and its support for hospital funding via the NHRA. While this Review has estimated that there are potential reductions in Government expenditure from adopting a

per mg reimbursement model, transition to such an arrangement will require detailed consideration with respect to the requisite changes to existing PBS reimbursement processes, the interface with other sections of the PBS (and the potential impact on drug prices where a medicine may be listed in multiple sections), the impact on third-party commercial compounders and hospital facilities.

Similarly, adopting the recommended changes to the components of the EFC fee (e.g., to include payments for infusion devices) and removing the distinction between public and private hospital providers will result in further disparities between funding for cancer medicines and other medicines on the PBS. The existing EFC arrangements already favour access for cancer patients relative to those with other conditions on the PBS (e.g., witness the difference in patient co-payments for cancer medicines which are levied only on the initial script and not repeats as occurs for other PBS listed medications). Transitional arrangements should consider the extent to which further amendments to the EFC further exacerbate those differences.

Overall, it is anticipated by this Review that adopting the changes recommended, including the long-term changes, is likely to result in a less complex system and a reduction in Government spending on EFC medicines (for a given prescription, noting that the total volume of prescriptions is likely to continue to rise) but must be balanced against potential unintended negative impacts on patient access to care which is currently cross-subsidised via the existing EFC arrangements. The recommendations also seek to improve the standard and thus quality of EFC compounding across the system to improve quality of service to patients but this might have unintended consequences for access if some services cannot meet the standards expected for compounding or service provision.

7.3 Further work for the Review

Updating cost information

During the consultation process for the Review it became apparent that the Cancer Services Group (CSG) were undertaking a cost modelling process as a means of informing further discussions about the appropriateness of the existing EFC fee structure and levels with respect to the compounding and provision of infused cancer medicines. It is understood that the CSG process is currently in the data collection phase; results were thus not available for supply to the Review prior to release of this report. Nonetheless, the structure of the data collection form was provided to the Review and is reproduced at Table 21.

It can be observed from this form that detailed data collection is proposed by the CSG, addressing: logistics (freight, storage), waste disposal, compounding resources and software (including labour

resources directly involved in and supporting compounding activities), compounding equipment, compounding maintenance and administration, and overheads. It is not known how specific activities/costs might be attributed to the preparation and supply of EFC medications, or the timeline for reporting of any information that might become available.

Table 21. CSG Data Collection Form

Sub-category	General Ledger (GL) description	Description (inclusions)
	Distribution Charges	Wholesaler freight charges associated with delivery of goods to pharmacy
		Containers
		In process consumables (e.g. syringes & connectors)
		Closed system transfer devices (CSTDs)
		Disposables (e.g. syringes and packaging)
		Cleanroom garments including cleanroom shoes/gowns/overshoes/gloves/goggles +/-with prescriptions/safety glasses/P2 masks/laundering of PJ's
	Waste Disposal	Cytotoxic waste
		General waste
	Cleaning - Sterilisation	Sterilisation costs
	Defects in compounding process	Product discards due to particles etc
	Other compounding materials - pharmacy based costs	Other compounding related costs
Compounding resources and software	Publications Sub & Memberships	Journal subscriptions (and other compounding resource costs)
		Pharmacology monographs
	Stability studies	Stability testings
	IT Costs - Software licensing fees	Compounding software (For protocol and batch sheets)
		Componding Quality Management System(QMS)
Compounding - Direct Labour	Wages - Base & Allowances	Include all Pharmacists (including all quality pharmacists), Technicians, Quality staff, Facility maintenance, Training, Cleaners and Administraion associated with the preparation of compounded chemotherapy
	Professional - Wages	
	Wages - Superannuation	
	Wages - Temporary, Locums & Other	
	Professional - Overtime	
	Professional - Temporary, Locums & Other	
	Wages - Payroll Tax	
	Professional - Payroll Tax	
	Professional - Annual Leave Taken	
	Professional - Superannuation	
	Professional - Long Service Leave Taken	
	Professional - Annual Leave Accrual	
	Professional - Long Service Leave Accrual	
	Support - Wages	
	Support - Overtime	
	Support - Superannuation	
	Support - Long Service Leave Taken	
	Support - Annual Leave Taken	
	Support - Payroll Tax	
	Management - Superannuation	
	Management - Payroll Tax	
	Management - Wages	
	Management - Overtime	
	Management - Temporary, Locums & Other	
	Management - Annual Leave Accrual	
	Management - Long Service Leave Taken	
	Management - Long Service Leave Accrual	
	Management - Annual Leave Taken	
	Workers' Compensation	
Compounding Equipment	IT Costs - Software licensing fees	Building Management System (BMS)/ Environmental Management System (EMS)
	IT Costs - Consultants	External IT support
	IT Costs - Hardware maintenance	IT Links and all IT equipment
	IT Costs - Misc & Other	Miscellaneous IT items
	IT Costs - Software under $300	Software licences
	IT Costs - Software maintenance	Support Agreements / Maintenance for software programs
	Depreciation	Air Handling Units (AHU), cytotoxic drug safety cabinets (CDSC), isolaters, Dehumidifier, Vacuum Systems, Continuous Particle Monitoring (CPM) system, Refrigeration and other devices and equipment
	Depreciation Expense - ROU assets IFRS16	
	Interest on Lease Liability - IFRS16	
	Other equipment - pharmacy based costs	Other equipment related costs
Compounding stock management	Inventory Expenses	Inventory management and procurement
	Stock Losses	Expired stock and temperature deviation write offs
		Other stock costs
Compounding Logistics	Freight	Freight for delivery of compounded medicines to patients
Compounding Maintenance	Quality	Microbiology testing (including consumables such as agar plates)
		Staff Health monitoring including blood tests
		Compliance costs
	Testing & Calibration	Clean room certification
		Equipment certifications
		Operator Validations
	Maintenance	EMS/BMS maintenance
		AHU maintenance
		Clean room / isolator preventative maintenance
		Dehumidifier maintenance
		Continuous Particle Monitoring and Vaccum pump Maintenance
		Refrigeration maintenance
		Equipment maintenance (pumps, sensors, balances etc)
		Micro lab maintenance
	Maintenance Agreements/Service	Other maintenance
Compounding Administration	Fees and Permits	Pharmacy Compounding Licence
	Other	Compliance and audit requirements
Compounding overheads and human resource management	Equipment	Laboratory & cleanroom expenses
	Hire of Plant & Equipment	Hired equipment to support compounding ie Airsamplers
	Rent expense	Rent
	Insurance	Insurance
	Electricity	Electricity
	Telephone	Telephone
	Printing & Stationery	Printing / Stationery
	Compounding costs - General	General costs
	Security Service	Security and alarms
	Cleaning	Pharmacy cleaning
	Storage	Storage of batch sheets, prescriptions and other records
	Consultant and management fees	External Consultants ie Risk assessments and quality
	Compounding Staff Costs - Other	Other staff costs associated with compounding
	Staff Amenities - compounding	General compounding staff amenities
	Other overheads - compounding	Other overheads
	Staff Costs - Recruitment - compounding	Recruitment
	Staff Costs - Training, conf & sem - compounding	Training
Compounding Support Services	Costs of support Services - for compounding only	Finance
		IT
		Human Resources
		Procurement
		WH&S

Source: Excerpt provided by the Cancer Services Group.

Consideration of AHI fees

Further consideration will be given of the available data with respect to the payment of AHI fees for s90 community pharmacies for EFC medicines. In particular, this will consider the extent to which EFC items dispensed by s90 community pharmacies reflected amounts lower than the PBS maximum quantity, resulting in payment of part AHI fees for those items.

Further investigation of patient access

Additional analyses will be undertaken using the PBS line level data with respect to patient access to care. Information on patient and provider location as available from their respective postcodes will be used in geospatial mapping to analyse the travel distances faced by patients accessing cancer medicines in terms of: (1) obtaining a prescription for cancer medicines (as indicated by the difference between patient postcode and prescribing provider postcode); and (2) obtaining the cancer medicines (as indicated by the difference between patient postcode and providing pharmacy postcode.

Consultations will also be undertaken with representatives from Indigenous health providers and peak cancer care organisations to understand the specific issues as they relate to access to cancer medicines among Indigenous peoples. Feedback from those consultations is anticipated to be incorporated as an addendum to the Final Report.

Comparison of standards and quality requirements

A key finding of this Review has been the importance within the cancer supply chain, in particular to the compounding of cancer medicines, of the adherence to operating standards (namely, the PIC/S and USP 797). A mapping of the specific elements of the PIC/S and USP 797 as they relate to EFC activities undertaken by TGA-licensed and non-licensed compounders is provided in Appendix 14. In addition, the Final Report will outline how activities undertaken as part of the cancer medicines supply chain sit with respect to the Australian Commission on Safety and Quality in Health Care (ACSQHC) guidelines.

7.4 Socio-political context of the Review

7.4.1 The COVID-19 pandemic

This Review was conducted during the second year of the COVID-19 pandemic. This is important context within which to view the information provided to the Review and the manner in which it has been interpreted. While the Review team had planned to conduct consultations in a face-to-face

format, including site visits to relevant compounder and hospital care facilities where appropriate, this was not possible given the need to observe social distancing and to ensure the safety of all those participating in the Review. Conduct of consultation interviews via video enabled teleconferencing media was thus utilised. However, it cannot be discounted that the less direct nature of those interactions, coupled with the inevitable interruptions due to technology or other outside interruptions (particularly as many participants in those consultations were also engaged in home schooling duties) had some impact on the engagement of participants in those consultations.

As the majority of the stakeholders participating in the Review are engaged in front-line delivery of health care in some way, many were impacted first-hand by increasing tensions within the health care system due to the pandemic, particularly as it impacted on staff/patient safety and availability. This impacted on the Review in two ways. First, it may have contributed to a general feeling of capacity being squeezed within health care, potentially exacerbating perceptions that EFC remuneration is not sufficient to cover the activities associated with the supply of cancer medicines (e.g., one stakeholder proposed that costs for personal protective equipment related to Covid-19 be captured within the EFC fees). Second, it resulted in there being less capacity within the given timeframe for stakeholders to participate in consultation or to undertake to provide additional data which might have provided further insights to the Review.

7.4.2 Multiple reviews

This Review is the second explicit review of the EFC program (the first conducted in 2013) and the third review since the inception of the EFC to address the funding of cancer medicines. Accordingly, the recommendations from this Review have been tabulated against those of the 2013 Review of the EFC and the King 2017 Pharmacy Review (see Appendix 13). This tabulation has been provided as a means of identifying those issues which have previously been identified as areas for action and which remain so in this Review. This includes:

- the potential adoption of a per-mg funding model for cancer medicines;
- the introduction of serialised (track-and-trace) vials as a means of better reconciling the supply and reimbursement of cancer medicines; and
- the application of consistent standards and fees for the compounding of cancer medicines in relation to the EFC.

Beyond these three reviews there have been a number of other relevant Government reviews and inquiries—most notably, the PBS Pharmaceuticals in Hospitals Review (2017), and Zimmerman Inquiry

into Approval Processes for New Drugs and Medical Technologies (2021)—as well as a range of private sector reports and position papers addressing the complexity of the provision and reimbursement of cancer medicine via the PBS.

There is a commonality in the findings/recommendations made in this report with those arising from previous reviews. That these commonalities exist in some way reflects the structure of the EFC system. It also reflects a system in which there exist multiple stakeholders who may not all benefit to the same degree from changes in the status quo and have therefore been resistant to change.

That there have been multiple reviews of the EFC, and of the PBS and its supporting HTA processes more generally, might also give rise to a sense of 'review fatigue.' With recommendations from previous Reviews not enacted, additional recommendations waiting for a Government response (e.g. Zimmerman Review), and the promise of additional recommendations arising from future reviews affecting cancer medicines funding (as anticipated to occur subsequent to the 2022 HTA Review) participants in this Review may have been less forthcoming with information or participation. Future reviews might well seek to lay out a road-map of policy amendments/change following previous reviews, both as a means of identify those areas for action that remain viable and to engender greater support amongst stakeholders that change is possible if well supported.

Appendix 1. EFC Review Terms of Reference

There are nominal differences between the Terms of Reference (ToR) of the EFC Review published by the Department of Health and the evaluation approach undertaken by CHERE in its Economic Analysis. These differences are elaborated here to bring to light any apparent gaps and to help ensure that the minimum required services provided through CHERE's Economic Analysis align with the expectations of the Department of Health and all stakeholders to the broader EFC Review. Coverage of the ToR's Specific Objectives by CHERE's Research Activities is summarised in Table A1.

Table A1. Coverage of the ToR Specific Objectives by CHERE's Research Activities

	Research Activity undertaken by CHERE											
ToR Specific Objective	1a	1b	1c	1d	2a	2b	2c	3a	4a	4b	5a	6a
1. Activities and experiences of EFC supply chain participants	■	■	■	■		■		■		■		
1a. Prescribing, claims processing, admin burden	■	■	■	■		■		■				
1b. Specific equity considerations	■	■	■	■		■				■		
2. Distribution of costs and remuneration	■	■	■	■		■	■	■				■
3. Outcomes of relevant Commonwealth reviews	■											
4. Patient expectations, priorities and experiences		■	■	■					■	■		
5. Equity, effectiveness of remuneration arrangement:	■	■	■	■		■					■	■
5a. Product and service provision	■	■	■	■		■					■	■
5b. Market competition and innovation	■	■	■	■		■						
6. Describe alternative mechanisms in relevant intl. contexts	■			■							■	■
7. Potential impact of alternatives with respect to equity	■			■							■	■
8. Recommendations to improve transparency of flow/funding							■				■	■
9. Potential impact of new technologies	■			■							■	■
10. Describe EFC item classifications, adjustments to improve:					■							
10a. Patient experience												
10b. Health professional experience												

Note: Darker shading indicates more direct/explicit coverage of the Specific Objective.

Terms of Reference (Department of Health, synopsis)

The Terms of Reference of the EFC Review are summarised below. Language has been modified and some points re-ordered in order to facilitate a more direct comparison with CHERE's Response to Tender and the proposed research activities of the Economic Analysis.

Overall objectives

1. Evaluate the impact and continuing suitability of current EFC arrangements and associated practices within the supply chain to ensure continuing access to these medicines [i.e., how has the EFC addressed the issues identified in the establishment of the mechanism itself and in subsequent reviews?];
2. Examine the extent to which the EFC Program supports patient access to chemotherapy medicines in an efficient and cost-effective manner;
3. Consider whether a new or adjusted reimbursement framework is required to ensure ongoing access to these medicines including the ways in which any changes may encourage innovation and collaboration across the EFC supply chain.

Specific objectives of the Review

1. Describe the activities and experiences of EFC supply chain participants, including:
    a. PBS prescribing, claims processing and the administrative burden associated with providing access to chemotherapy medicines; and
    b. Particular equity considerations with respect to aged Australians, Aboriginal and Torres Strait Islander Peoples, and Australians in Regional and Remote communities.
2. Describe the distribution of costs and current remuneration structures.
3. Consider the outcomes of current Commonwealth reviews into national standards, policies and guidelines of relevance to the EFC.
4. Consider patient expectations, priorities and experiences related to accessing EFC medicines across different States and Territories.
5. Evaluate the equity of remuneration arrangements and their effectiveness in supporting:
    a. product and service provision (within scope of the regulatory requirements); and
    b. market competition and innovation within the EFC supply chain.
6. Describe alternative funding mechanisms in relevant international contexts.
7. Evaluate the potential impact of alternative funding mechanisms with respect to access among identified equity groups.
8. Recommend changes to improve transparency with respect to product flow and funding.
9. Consider the impact of new technologies on the operation of the EFC.
10. Describe the classification of items listed in the EFC Instrument and on the PBS Schedule, including potential adjustments to improve:
    a. patient experience; and
    b. health professional experiences.

Minimum requirements

- Call for public submissions [17 May 2021]
- Consultation with stakeholders on discussion papers and an interim report
- Consideration of approaches to funding of chemotherapy across all jurisdictions
- Analysis of costs incurred in the manufacture, logistics, handling, compounding and dispensing of chemotherapy medicines
- Examination of new and emerging technologies associated with the manufacture, logistics, handling, compounding and dispensing of chemotherapy medicines

Matters considered out of scope

- Considerations relating to ancillary cancer treatment costs (such as travel and accommodation)
- Costs and access arrangements for non-EFC listed cancer treatments (e.g. oral chemotherapy medicines and non-PBS medicines)

[end ToR]

Objectives of the Economic Analysis (CHERE)

The objectives of the Economic Analysis—as outlined in CHERE's Response to Tender—are summarised below. Correspondence between the evaluation objectives and the Specific Objectives of the Review is elaborated throughout.

The objectives of the evaluation are to:

- Identify the key activities (and distribution of costs/remuneration) that participants in the EFC supply chain undertake to support safe patient access to chemotherapy infusions and related pharmaceutical benefits described in the Section 100 EFC legislative instrument [corresponds to ToR Specific Objectives 1, 1a, 1b & 2. ToR specify these 'activities' to include "PBS prescribing, claims processing and administrative burden"; with respect to 'access,' ToR also specify three equity groups: aged Australians, Aboriginal and Torres Strait Islander Peoples, and rural and remote communities];
- Examine whether Government's current EFC remuneration arrangements for the products and services provided by the EFC supply chain support patient access to chemotherapy medicines in a safe and efficient manner [corresponds to ToR Specific Objectives 4 & 5. ToR Specific Objective 4 extends the notion of 'patient access' to include "patient expectations, priorities and experiences", and implies CHERE's analysis will be broken down by

State/Territory, and with explicit attention given to identified equity groups. ToR Specific Objective 5 extends assessment of supply chain participant remuneration to include consideration of "equity" (i.e., appropriateness and effectiveness of remuneration for services)];

- Identify whether alternate models for remunerating EFC arrangements (including any models used in overseas contexts), and new technologies/service delivery approaches for EFC medicines, may drive innovation, collaboration and improve on current service arrangements, including supporting access for Australians in rural and regional areas, Aboriginal and Torres Strait Islander Peoples, and older Australians [corresponds to ToR Specific Objectives 5, 5a, 5b, 6 & 7.];
- Analyse how specified alternate models and/or changes in the framework for EFC arrangements identified during the EFC review process may affect access, safety and cost burdens for key stakeholders, including industry and patients, compared to current arrangements [corresponds to ToR Specific Objectives 6 & 7. CHERE's tender response extended the objectives of the Review to include the potential impact of alternate funding mechanisms on patient safety, as well as the distribution of costs among supply chain participants (including patients) relative to the status quo.]

Other identified gaps between the ToR and CHERE's tender response:

- ToR Specific Objective 3 requires the Review to consider the outcomes of current Commonwealth reviews into national standards, policies and guidelines of relevance to the EFC. While some of these reviews were covered in our literature review, CHERE had not explicitly indicated that it would undertake a critical assessment of the extent to which the recommendations of reviews (undertaken subsequent to the previous EFC review, 2013) have been incorporated within—or otherwise correspond to—the EFC, the extent to which outcomes of those reviews might constrain recommended changes to the EFC, or the ways in which changes to the EFC might directly or indirectly impact extant national standards, policies and guidelines of relevance to the EFC.
- ToR Specific Objective 8 specifies that the Review will make recommendations to improve transparency with respect to product flow and funding—this was not explicitly addressed in CHERE's tender response.
- ToR Specific Objective 9 specifies that the Review will consider the (potential and/or expected) impact of emerging technologies on the operation of the EFC—this was not explicitly addressed in CHERE's tender response (though may be addressed insofar as such

technologies are a part of 'alternative funding mechanisms', i.e., in use in relevant international comparative contexts).

- ToR Specific Objective 10 requires the Review to describe the classification of items listed in the EFC Instrument and PBS Schedule, and to make recommendations for adjustments to these classifications that could improve patient and health care provider experiences—this is not addressed in CHERE's tender response (notwithstanding recommendations that emerged via and assessment of alternative funding mechanisms internationally and through the stakeholder consultations).
- The Minimum Requirements set out in the ToR require an "examination of new and emerging technologies associated with the manufacture, logistics, handling, compounding and dispensing of chemotherapy medicines."—CHERE's tender response did not explicitly address an examination of new and emerging technologies (though this was addressed insofar as such technologies are a part of 'alternative funding mechanisms'; see comments on ToR Specific Objective 9 above).

Appendix 2. Review Governance

Professor Sanchia Aranda, Lead Reviewer

The Department of Health named Professor Sanchia Aranda as Lead Reviewer for the Review. Professor Aranda is a Professor of Health Services Research at the University of Melbourne and an Adjunct Professor in the School of Nursing at UTS, NSW. She is an experienced cancer and health services researcher, who most recently worked in the NSW State Government and the charity sector with a focus on system performance and health policy. Her particular interest lies in the use of administrative data in understanding health disparities and unwarranted clinical variation. Her role in this application is to bring a system and contextual lens to stakeholder engagement and all aspects of analyses within the Review.

CHERE

CHERE's senior team members are internationally recognised for their expertise in health economics, HTA and its application to the area of pharmaceutical reimbursement. The team has extensive combined experience in the conduct of evaluations for the PBAC and MSAC, public health policy review and program evaluation. Team members were selected to leverage CHERE's extensive subject and mixed-methods research expertise. Nominated personnel, roles and key responsibilities are summarised in Table A2.

Table A2. Personnel, roles and key responsibilities

		Key responsibilities													
Name	*Role*	Oversight & risk management	General project management	Ethics application & process	Project workplan	Literature review	Develop interview protocols	Stakeholder recruitment	Stakeholder interviews	Data analysis, qualitative	Cost data access	Model development	Quant data preparation	Data analysis, quantitative	Reporting
A/Prof Richard De Abreu Lourenço	Lead, Chief Investigator	■	■	■	■		■	■	■	■	■	■		■	■
Dr Mark Thomas	Project Manager		■	■	■	■	■	■	■	■					■
A/Prof Professor Ruth Webster	Assoc. Investigator	■	■		■		■		■	■					■
Prof Rosalie Viney	Advisor	■		■	■			■			■				■
Dr Paula Cronin	Advisor				■							■			
Anna Crothers, MA	Research Associate											■	■	■	■
Sopany Saing, MA	Research Associate											■	■	■	■
Milena Lewandowska, MA	Research Associate					■									■
Mussab Fagery, MA	Research Associate												■	■	■
Dr Rebecca Addo	Research Associate									■					■
Nancy Kim, MA	Research Associate						■			■					

Associate Professor Richard De Abreu Lourenço had principal responsibility for the overall carriage of the evaluation. Richard brings a detailed understanding of the methodologies for the evaluation of health care programs and a long history of engagement with the Department of Health, the pharmaceutical sector and health care sector in Australia. He led the team and coordinated all project activities, with a focus on risk management, the productive engagement of stakeholders, stakeholder interviews, quantitative data acquisition, model development, analysis and interpretation of findings and reporting.

Dr Mark Thomas managed the overall conduct of the evaluation. Mark is an experienced health economist with a focus on health equity in Australia. He helped coordinate carriage of the research and contributed to the research planning and design, ethics application, stakeholder communications, logistics, qualitative data analysis, reporting and the timely delivery of all project deliverables.

Associate Professor Ruth Webster provided leadership on the qualitative aspects of the evaluation. Ruth is a medical practitioner with over 15 years of experience in the conduct and reporting of complex, mixed-methods research, including time-and-activity studies to evaluate health service workflows. Ruth conducted stakeholder interviews, guided the interpretation of findings, and provided key input into reporting.

Professor Rosalie Viney provided the evaluation an integral macroeconomic and policy lens. Rosalie is a leading expert in the field of health economics in Australia. As the past Chair of the Economics Sub-Committee to the Pharmaceutical Benefits Advisory Committee (PBAC), she has an intimate knowledge of the pharmaceutical system and the issues affecting drug reimbursement in Australia.

Dr Paula Cronin contributed to the quantitative direction of the evaluation. Paula is an experienced health economist, with a focus on Economic Analysis and applied data analysis. She is a past evaluator for the PBAC and a sitting member of the Economic Sub-Committee to the MSAC.

Anna Crothers, MA contributed principally to the quantitative research design, data analyses and reporting. Anna is an experienced health economist and biostatistician, with over eight years of experience in health technology assessment, program evaluation and public health policy.

Sopany Saing, MA contributed principally to the quantitative analysis of the Review, including data modelling and reporting. Sopany has experience in the systematic review of scientific literature, health economics, evidence-based research methodologies and medical science research.

Milena Lewandowska, MA contributed principally to the literature review, including synthesis of

published data and reporting. Milena is a member of the CHERE's Economic Evaluation team completing evaluations for the PBAC. She has worked on a range of different projects including development and adaptations of economic evaluations to support decision making, Health Technology Assessment of medical devices and surgical procedures as well development and implementation of eHealth initiatives.

Mussab Fagery, MA contributed to the quantitative data analysis of the Review, including data modelling. Mussab is a member of CHERE's Economic Evaluation team. He has experience in conducting cost-effectiveness analyses and is well-versed in Australian government HTA processes for market entry and reimbursement, as well as PBAC and MSAC technical guidelines and requirements for submissions.

Nancy Kim, MA provided the evaluation team with a practical understanding of EFC supply chain processes, assisting in the development of poignant lines of inquiry for interviews. Prior to joining CHERE, Nancy worked for several years as a cancer care pharmacist at a major metropolitan hospital and, more recently, as a content author for the Haematology and Bone Marrow Transplant stream of the Cancer Institute NSW's eviQ program.

Dr Rebecca Addo contributed to the transcription of interviews, qualitative data analysis and reporting. Rebecca has skills in mixed-research methods, including economic modelling, systematic literature reviews, and stakeholder engagement. Her main research interests include priority-setting in health, HTA and its application to health care decisions in developing countries.

Expert Advisory Panel

In consultation with the Lead Reviewer and the Department of Health, CHERE convened an Expert Advisory Panel to provide input on research methods, identify potential stakeholders, support stakeholder recruitment efforts, and provide feedback on CHERE's preliminary findings and draft recommendations.

Members of the Expert Advisory Panel included:

- Ms Kristin Michaels, Society of Hospital Pharmacists
- Dr Deme Karikios, Deputy Chair, Medical Oncology Group of Australia
- Dr Kylie Mason, haematologist, Royal Melbourne Hospital and Peter MacCallum Cancer Centre
- Dr Peter Grimison, oncologist, Chris O'Brien Lifehouse
- Mr David Slade, CEO, Slade Health

- Mr John Stubbs, consumer advocate
- Ms Elizabeth de Somer, CEO, Medicines Australia

Members of the Expert Advisory Panel were provided with the Terms of Reference of the EFC Review, a detailed description of the CHERE's research methodology and the preliminary findings and draft recommendations. Members contributed asynchronous feedback throughout the duration of the evaluation and met independently with CHERE's evaluation management team as required.

Meetings with the Lead Reviewer and Department of Health

The project management team met at least monthly with Lead Reviewer Professor Sanchia Aranda and the Department of Health to discuss the planning and conduct of the Economic Analysis (and broader EFC Review)—including project scope, finalisation of the workplan, identification and engagement of stakeholders, public inquiry, preliminary findings, and reporting of results.

Research ethics

The Review was conducted under the auspices of the UTS Human Research Ethics Committee, ETH21-6108 – "Policy Review and Economic Evaluation of the Efficient Funding of Chemotherapy (EFC) Funding Arrangements."

Appendix 3. Literature Review—Methods and Results

Activities of the Review included a comprehensive review of peer-reviewed and grey literature pertaining to the provision, cost and remuneration of chemotherapeutics in Australia and relevant international contexts. This appendix summarises the methods used in the systematic literature review, and an annotated summary of reviewed publications.

Scope

Publications reviewed included both peer-reviewed and grey literature (e.g., Government reviews, reports, public summary documents, conference papers) published in 2010 or later.

Peer-reviewed literature

Eligible peer-reviewed articles were identified through an online search of the Medline, EMBASE, CINAHL and Cochrane Library databases in June 2021. Stakeholders to the Review also cited a number of peer reviewed publications for consideration. A Preferred Reporting of Items in Systematic Reviews and Meta-analyses (PRISMA) flowchart enumerating the publications identified in the peer-reviewed literature search is provided in Table A3.

Table A3. PRISMA flow chart, peer-reviewed literature

Identification	Records identified: n=9,047	→	Duplicates removed before screening: n=1,182
	↓		
	Records screened: n=7,865	→	Records excluded: n=7,425
	↓		
Screening	Publications sought for retrieval: n=440	→	Publications not retrieved: n=393
	↓		
	Eligibility assessed: n=47	→	Publications excluded: n=24
	↓		
Inclusion	Publications reviewed: n=23		

Search terms and inclusion criteria for the peer-reviewed literature search are presented in Table A4.

Table A4. Literature review method, peer reviewed literature

Search terms	Keywords: 'chemotherapy', 'cancer drug', 'vial sharing', 'pricing, 'remuneration', 'funding', 'payment', 'banding', 'rounding', 'vial sharing', 'named patient', 'activity based funding', 'capitation'
Databases (results)	• Embase (2137) • Pubmed (Medline) (2660)

	• CINAHL (3020) • Cochrane Library (48)
Publication types	(English-language) Peer-reviewed systematic reviews, literature reviews, observational studies, cost studies, time-and-motion studies, retrospective chart reviews, editorials, guidelines.
Search period	Publications after 2010
Inclusion criteria:	Thematically relevant: • Remuneration, payment models for chemotherapy; efficiency, workflow related to supply and administration of chemotherapy • Time-and-motion studies related to the supply and administration of chemotherapy • Safety related to off-label utilisation, drug classification, system administration • Access related to payer status, provider characteristics, system administration, workflow, product flow
Exclusions	• Invalid type of evidence: i.e., clinical evidence (i.e. RCT; case studies; NRCT, clinical safety evaluation), economic evaluation of drug/therapy only (CEA, CUA) • Not oncology • Not in English • Abstract only • Not relevant to the key search terms; otherwise fails to meet inclusion criteria

Abbreviations: CEA, cost-effectiveness analysis; CUA, cost utility analysis; NRCT, non-randomised controlled trial; RCT, randomised controlled trial

Grey literature

For the purporse of the Review, grey literature was defined as a non-peer reviewed or commercial publication, not available through standard distribution means or standard bibliographic controls. The Review utilised a range of sources, including stakeholder websites, web search engines, and online repositories. In addition, conference proceedings and bibliographies of included publications

were scanned manually to identify additional potentially relevant publications. Search terms and inclusion criteria for the grey literature search are presented in Table A5.

Table A5. Literature review method, grey literature

Search terms	Keywords: 'chemotherapy', 'cancer drug', 'vial sharing', 'pricing, 'remuneration', 'funding', 'payment', 'banding', 'rounding', 'vial sharing', 'named patient', 'activity based funding', 'capitation'.
Databases (results)	• Online databases • Web search engines • Web repositories (NICE, CADTH, SMC, PBAC, WHO) • Manual scan of bibliographies
Publication types	(English-language) reviews, reports, guidelines.
Search period	Publications after 2010
Inclusion criteria:	Thematically relevant: • Remuneration, payment models for chemotherapy • Efficiency, workflow related to supply and administration of chemotherapy • Time-and-motion studies related to the supply and administration of chemotherapy • Safety related to off-label utilisation, drug classification, system administration • Access related to payer status, provider characteristics, system administration, workflow, product flow
Exclusions	• Type of evidence: i.e. clinical evidence (i.e. RCT; case studies; NRCT, clinical safety evaluation), economic evaluation of drug/therapy only (CEA, CUA) • Not oncology • Not in English • Abstract only • Not relevant to the key search terms; otherwise fails to meet inclusion criteria

Abbreviations: CADTH, Canadian Agency for Drugs and Technology in Health; HTA, health technology assessment; NICE, National Institute of Health and Care Excellence; NRCT, non-randomised controlled trial; PBAC,

Pharmaceutical Benefits Advisory Committee; RCT**,** randomised controlled trial; SMC**,** Scottish Medicines Consortium; WHO**,** Word Health Organisation

Inclusion/exclusion

Full abstracts of all identified publications were downloaded into EndNote (version X9 3.3; Bld 13966) and independently screened by two reviewers. The full text of publications determined to be potentially relevant was then reviewed for final determination of inclusion/exclusion. Studies that met initial inclusion criteria but were later excluded were documented with reasons for exclusion; disagreements were resolved by a third reviewer.

The following criteria were applied to the titles and abstracts of included citations: publications addressing remuneration and payment models for chemotherapy, or alternatives for improving efficiency and workflow of chemotherapy supply, delivery, and administration; safety issued related to off-label utilisation, drug classification or system administration; and patient access to treatment related to funding, payer status, provider characteristics, or system administration.

Data extraction

Data were extracted from all included studies for incorporation within the analyses of the Review, including citation, setting, method and findings. All data extraction was cross-checked by a second reviewer. An annotated summary of reviewed publications is provided in Table A6.

Table A6. Annotated summary of reviewed publications

Citation	*Setting*	*Design*	*Findings*
Alexander, et al. Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. *Internal Medicine*. 2014; 44(10):1018-26.	Australia	Consensus guidelines developed to address uncertainty and variation of practice relating to the handling of monoclonal antibodies (MAbs) for cancer treatment	The seven recommendations: (i) appropriate determinants for evaluating occupational exposure risk; (ii) occupational risk level compared with other hazardous and non-hazardous drugs; (iii) stratification of risk based on healthcare personnel factors; (iv) waste products; (v) interventions and safeguards; (vi) operational and clinical factors and (vii) handling recommendations.
Bach, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016;352.	US	Analysis of utilisation of the top 20 cancer drugs that are dosed by body size and packaged in single-dose vials, comparing scenarios with vial-sharing and with no vial sharing.	The estimated proportion of drug leftover (unused) in the top 20 cancer drugs was between 1% and 33%. Total revenue associated with discarded drug was $1.8 billion (2016)
Baker & Jones. Rationalisation of chemotherapy services in the university hospital birmingham national health science trust. *Journal of Oncology Pharmacy Practice*. 1998;4(1):10-4.	UK	Prospective audit study of cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) to determine feasibility and cost effectiveness of a centralised service.	Of the 97 courses prescribed in the peripheral out-patient clinic, 13.5% were deferred. All deferred doses were reissued, saving GDP 681.00 over a six-month period. A dose-banding system based on 5% variance from the dose prescribed enabled supply of prefilled syringes, with maximum of two syringes used per dose. The prefilled syringe programme has improved patient waiting times, reduced drug wastage, and enabled rationalisation of chemotherapy services.
Bunnell, et al. High performance teamwork training and systems redesign in outpatient oncology. *BMJ Quality & Safety*. 2013;22(5):405-13	US	A pilot oncology training program followed by prospective observation and interviews of the clinical practice, infusion unit and administrative support to identify areas vulnerable to communication failures; Team training sessions; Modified failure mode and effect analysis.	The rate in the incidence of non-communicated order changes was low at baseline (1.9%) and during follow-up (1.5%). All physicians, nurse practitioners, and physician assistants reported it was easier to communicate change orders and the vast majority had a better understanding of when and how to call for a change order. Infusion nurses reported a decrease in the frequency of non-communicated change orders and more than three-quarters reported a decrease in the

			necessity to page clinicians. Incidence of missing chemotherapy orders for unlinked visits decreased from 30% at baseline to 2% within 2 weeks of implementing the pharmacy screening and email reminder system (p<0.001 Pearson χ2). Improvement in patient's perception of the degree to which your care was well coordinated among doctors and other caregivers (from 93.5% for the 6 moths prior to team training to 97.4% for the 6 months following team training implementation).
Chillari, et al. Assessment of the potential impact of dose rounding parenteral chemotherapy agents on cost savings and drug waste minimization. *Journal of Oncology Pharmacy Practice*. 2018;24(7):507-10.	US	Retrospective chart review of electronic medical records to determine if dose-rounding chemotherapy is an effective cost-containment strategy for an institution with a low-volume oncology clinic.	Cost savings of $22,849 if doses were rounded down by 5% (3.8% difference from the cost of the unrounded doses); cost savings of $30,911 if doses for metastatic diagnoses were rounded down by 10% (5.2% difference from the cost of the unrounded cost).
Chiumente, et al. Preparation of intravenous chemotherapy bags: evaluation of a dose banding approach in an Italian oncology hospital. *Global and Regional Health Technology Assess*. 2021;8:29-34.	Italy	Comparative analysis of three scenarios: current compounding approach used at the IOV, which relies on daily preparation of individualised bags; weekly production of dose-banded bags; purchase of ready-to-use dose banding bags made by an authorised third-party.	Dose banding was predicted to generate savings ranging from €10,998 (−0.84%) for trastuzumab to €169,429.60 (−8.39%) for paclitaxel.
Claus, et al. The impact of logarithmic dose banding of anticancer drugs on pharmacy compounding efficiency at Ghent University Hospital. *European Journal of Hospital Pharmacy*. 2018;25(6):334-6.	Belgium	A 2-week time study provided lead times (between prescription and transfer) for just-in-time and dose banding (DB) preparations. A 'maximal' storage (using all drugs with a relative incidence of ≥2%recurrent monthly prescription) and a 'safe' storage scenario (lowest monthly prescribing pattern) were used to calculate the potential change in full-time equivalent (FTE)	Mean lead times for DB storage and just-in-time preparation were 17.1 min (95% CI 13.5 to 21.0) and 26.5 min (23.3 to 29.8). For 21,164 yearly preparations with 5,292 already in DB (25%); 11,157 and 6, 862 could be batch-produced in advance in maximum storage and safe storage scenarios, respectively. The existing FTE in 2015 of 5.41 could then be reduced to 4.91 and 5.27.
Copur, et al. Potential cost savings by dose down-rounding of monoclonal antibodies in a community cancer center. *Journal of Oncology*	US	Retrospective review of electronic health records. Hypothetical cost savings were calculated based on utilisation of monoclonal	Overall more doses qualified for cost saving at ≤10% dose reduction.

Pharmacy Practice. 2018;24(2):116-20.		antibodies (mABs) on two dose-rounding levels (5% and 10%). The available drug vial sizes(s) and costs per vial and per milligram were noted for each MAb based on average wholesale price; Costs of actual amount prescribed were compared to the costs of theoretically reduced ≤5% and ≤10% doses rounded to the nearest vial sizes; Average dose reduction percentage resulting in cost savings for both groups.	
Dalal, et al. Dosing Patterns and Economic Burden of Palbociclib Drug Wastage in HR+/HER2- Metastatic Breast Cancer. *Advances in Therapy.* 2018;35(6): 768-778.	US	Retrospective analysis of the US claims database reporting dosing patterns. A dose modification was defined as an increase/decrease of at least 25 mg daily compared to the preceding dose. Estimates of drug wastage costs were based on days with overlap in prescription fills for different palbociclib doses.	Dose modification was observed in 17.8%, 31.2%, and 35.0% of patients in first, second, and third line assuming on average 4 months duration of line therapy. Average overlap in prescription fills was 9.2, 9.9, and 5.4 days in first, second, and third line. Potential drug wastage resulted in an average cost of $4,376, $4,740, and $2,592 per patient in first, second, and third line.
Daniels, et al. Adherence to prescribing restrictions for HER2-positive metastatic breast cancer in Australia: A national population-based observational study (2001-2016). *PLOS one*. 2018;13(7).	Australia	Retrospective cohort study based on dispensing records to determine restriction adherence. Group-based trajectory models (GBTMs) used to cluster patients on their patterns of trastuzumab exposure, and then on their patterns of lapatinib and chemotherapy exposure.	The most frequent non-adherent treatments were trastuzumab plus: vinorelbine (24%); capecitabine (24%); anthracycline (10%); and taxane with platinum (TCH; 9%). 193 patients (4%) received non-adherent lapatinib treatment: 165 patients initiated lapatinib as monotherapy; 28 received lapatinib in combination with chemotherapy other than capecitabine. Non-adherent concomitant therapy with trastuzumab and lapatinib was observed in 37 patients (<1%) who had dispensing of lapatinib while continuing trastuzumab.

To be completed for Final Report (n=58)

Appendix 4. Consultations

Written submissions

In May, 2021, the Department of Health released a Discussion Paper inviting submissions to the Review by stakeholders to the EFC supply chain. A total of 40 formal submissions were received. A thematic analysis of these written submissions was conducted to formulate an understanding of EFC supply chain activities, costs and remuneration, and stakeholders' concerns in these areas. This analysis, conducted in collaboration with the Department of Health and Lead Reviewer, also informed the development of interview protocols for the subsequent, in-depth consultation of identified stakeholders.

Face-to-face consultations

The Review team conducted semi-structured interviews with stakeholders involved in the supply, delivery and administration of EFC-funded medicines, including manufacturers, wholesalers and compounders; State and Territory public health services; hospital pharmacists and administrators; health-sector peak bodies; health care professionals involved in cancer treatment and care; and patients. A total of 23 consultations were conducted, including 67 interviewees representing 23 organisations.

Appendix 5. Comparison of Drug Utilisation under the CPAP and EFC

Prior to commencement of the EFC in 2011, extant drugs subsequently listed on the EFC were supplied on the PBS via the Chemotherapy Product Access Program (CPAP) for public hospitals, with parallel listings under s100 and the General Benefits section of the PBS for private hospital access. Under pre-EFC funding arrangements, drugs were reimbursed on the basis of the full pack quantity, rather than the minimum combination of vials required to provide the prescribed dose. To assess the impact of shifting to remuneration on the basis of the efficient combination of vials, an historical analysis of aggregate PBS services volumes and benefit value was conducted.

Molecules used as the basis for this comparison and their corresponding PBS indications are listed in Table A7. Molecules were included if previously funded via the CPAP, with at least two years of PBS service and benefit value data prior to the commencement of the EFC. All non-IV formulations (i.e., tablets) were excluded from the analysis. To mitigate confounding, the molecules rituximab, trastuzumab, doxorubicin and methotrexate were excluded, as these drugs have PBS-approved IV formulations for non-EFC indications.

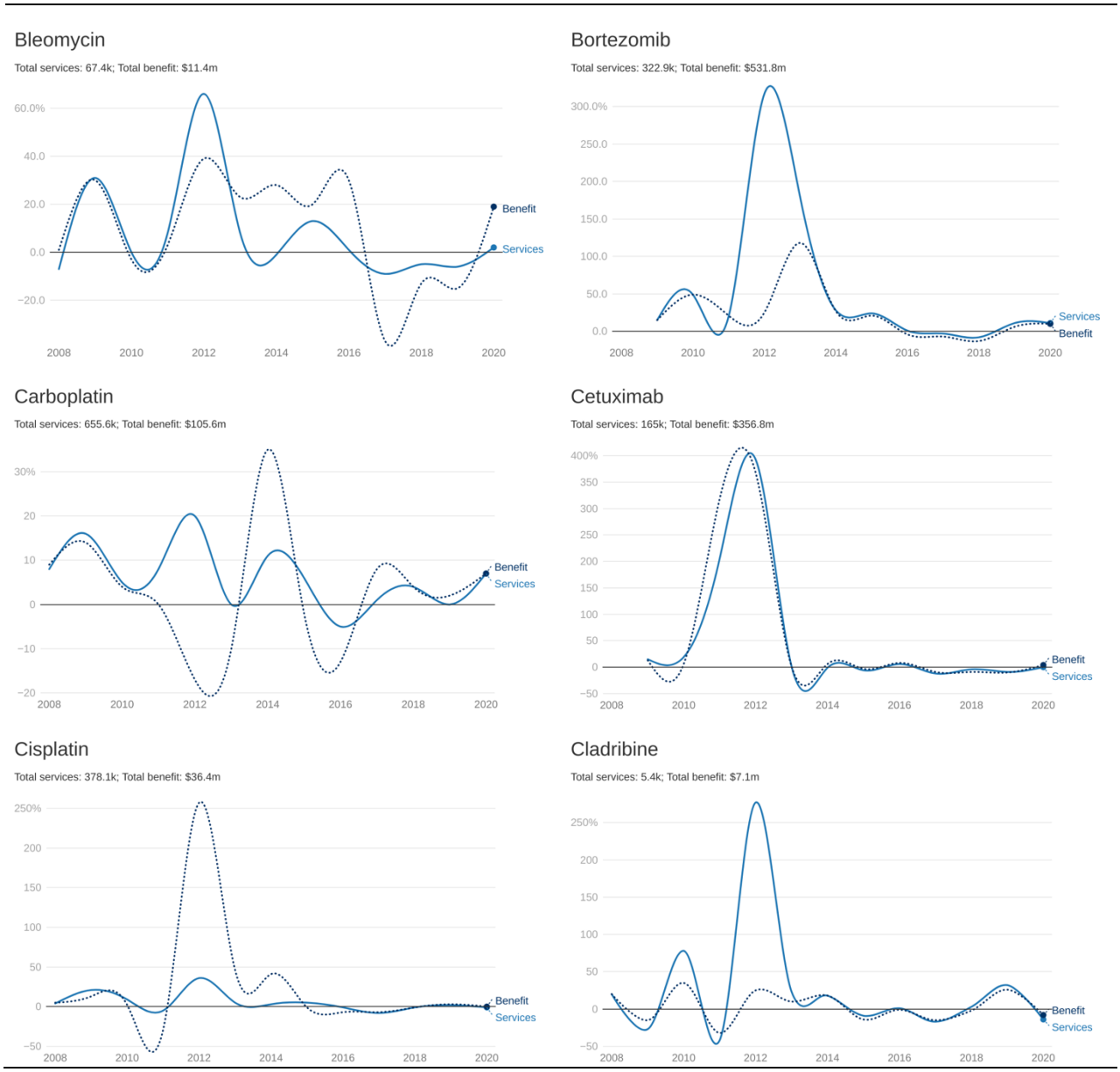
Table A7. Select EFC-listed drugs by PBS indication

Molecule	*PBS indication (intravenous formulations only)*
Bleomycin	Germ cell neoplasm
Bortezomib	Multiple myeloma
Carboplatin	Not restricted (NR)
Cetuximab	Stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx
Cisplatin	NR
Cladribine	Hairy cell leukaemia
Cyclophosphamide	NR
Cytarabine	NR
Docetaxel	NR
Epirubicin	NR
Etoposide	NR
Fludarabine	NR
Fluorouracil	NR
Fotemustine	Metastatic malignant melanoma
Gemcitabine	NR
Idarubicin	Acute myelogenous leukaemia
Ifosfamide	NR
Irinotecan	NR
Oxaliplatin	NR
Paclitaxel	NR
Raltitrexed	Advanced colorectal cancer
Topotecan	NR
Vinblastine	NR
Vincristine	NR
Vinorelbine	NR

Each drug's corresponding PBS item codes active under the CPAP and EFC periods were used to

derive historical PBS service volumes and benefit values for the periods immediately before (2008-2011) and after the introduction of the EFC (2012-2020).[1] For each molecule, the year-on-year growth rate (i.e., percent change) in PBS service volume and benefit value was calculated and plotted to assess whether the introduction of the EFC corresponded with an apparent change in utilisation. Results are presented in Figure A1.

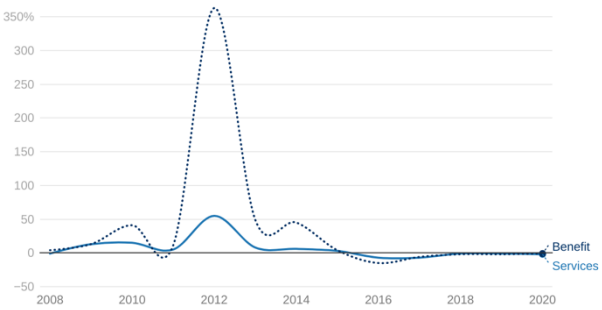
Figure A1. Annual percent change, PBS service volume and benefit value by molecule (2008-2020)



[1] Services Australia. (2021). Pharmaceutical benefits schedule item reports. Australian Government. Accessed online 1 November 2021 at http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp.

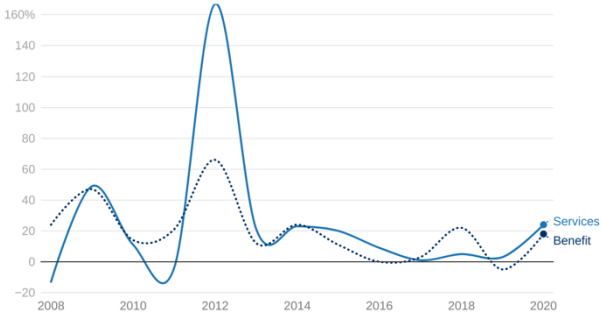
Cyclophosphamide

Total services: 1.4m; Total benefit: $148.8m



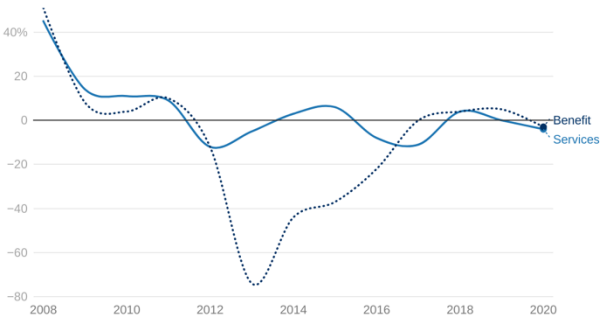
Cytarabine

Total services: 101k; Total benefit: $23.9m



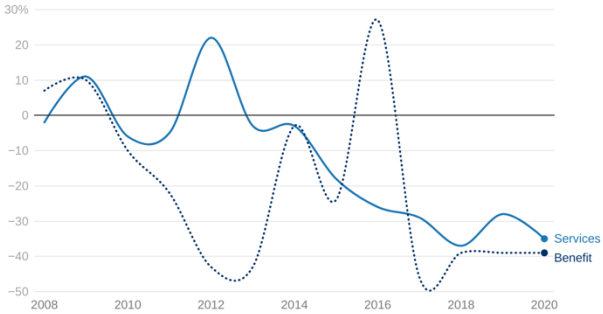
Docetaxel

Total services: 398k; Total benefit: $321.4m



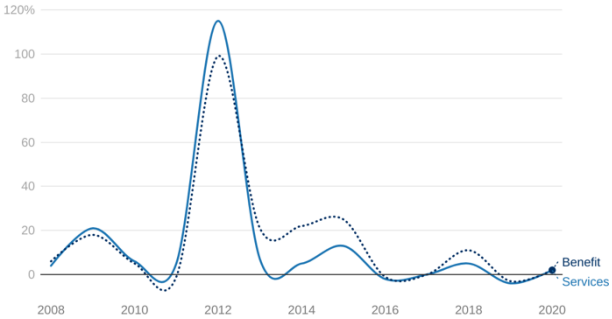
Epirubicin

Total services: 150k; Total benefit: $60.1m



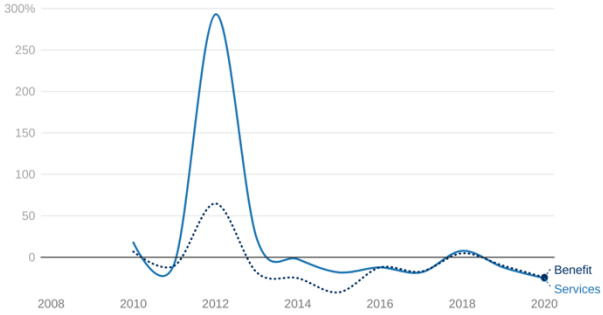
Etoposide

Total services: 384k; Total benefit: $64.6m



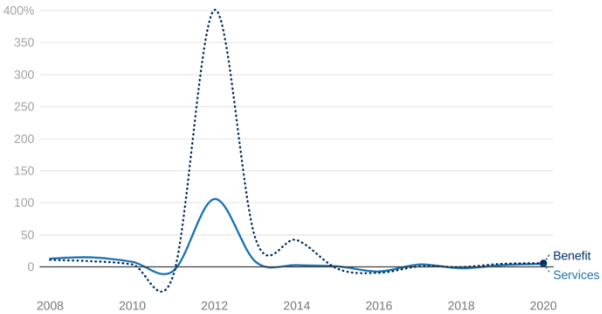
Fludarabine

Total services: 42k; Total benefit: $12m



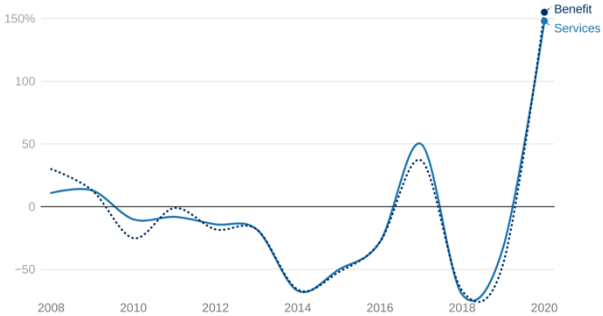
Fluorouracil

Total services: 1.7m; Total benefit: $182m



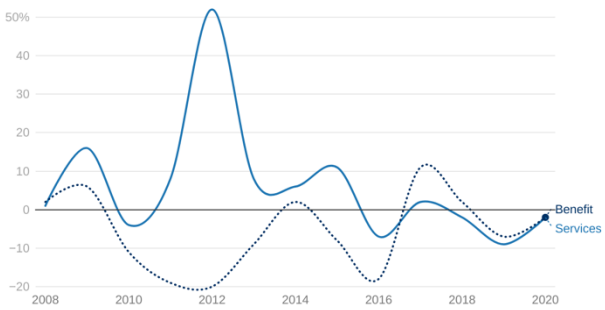
Fotemustine

Total services: 6k; Total benefit: $8.3m



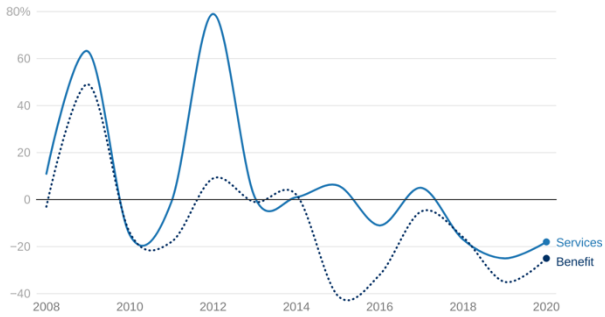
Gemcitabine

Total services: 690k; Total benefit: $158.9m



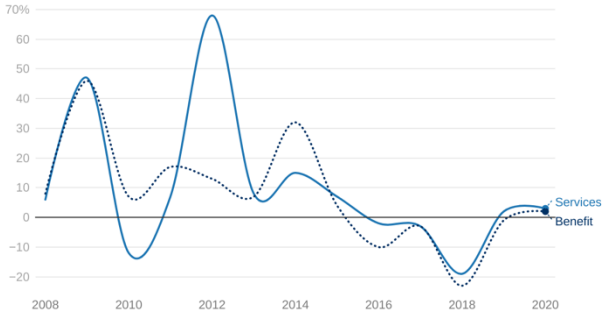
Idarubicin

Total services: 5k; Total benefit: $3.5m



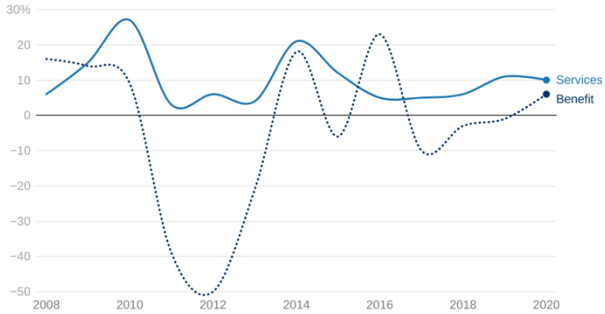
Ifosfamide

Total services: 44k; Total benefit: $14.1m



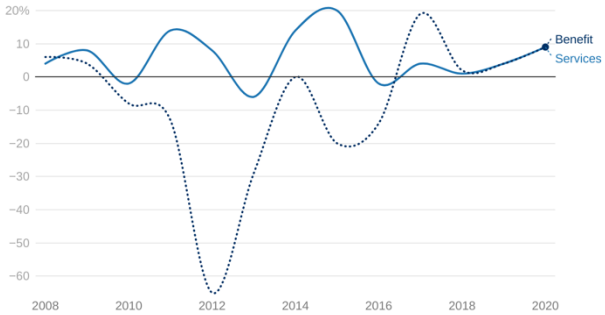
Irinotecan

Total services: 358k; Total benefit: $112m



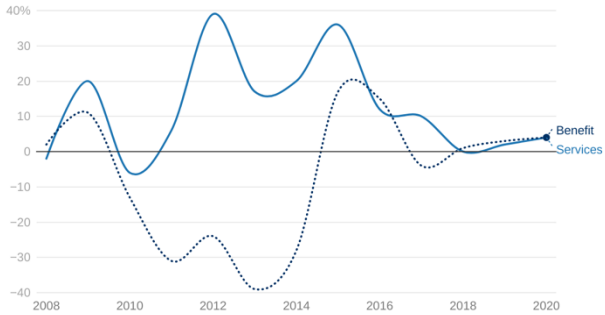
Oxaliplatin

Total services: 533k; Total benefit: $220.8m



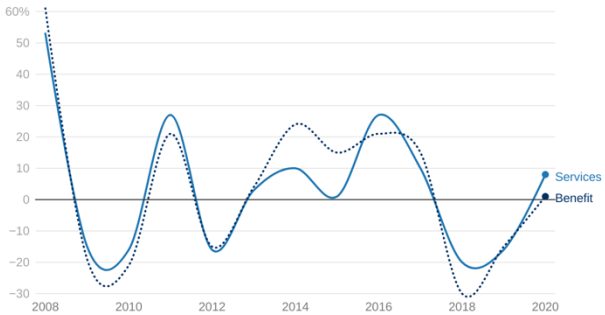
Paclitaxel

Total services: 747k; Total benefit: $256m



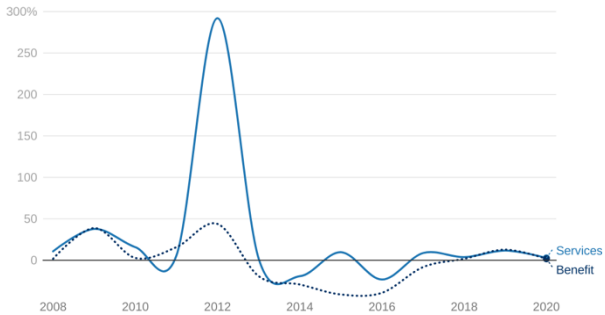
Raltitrexed

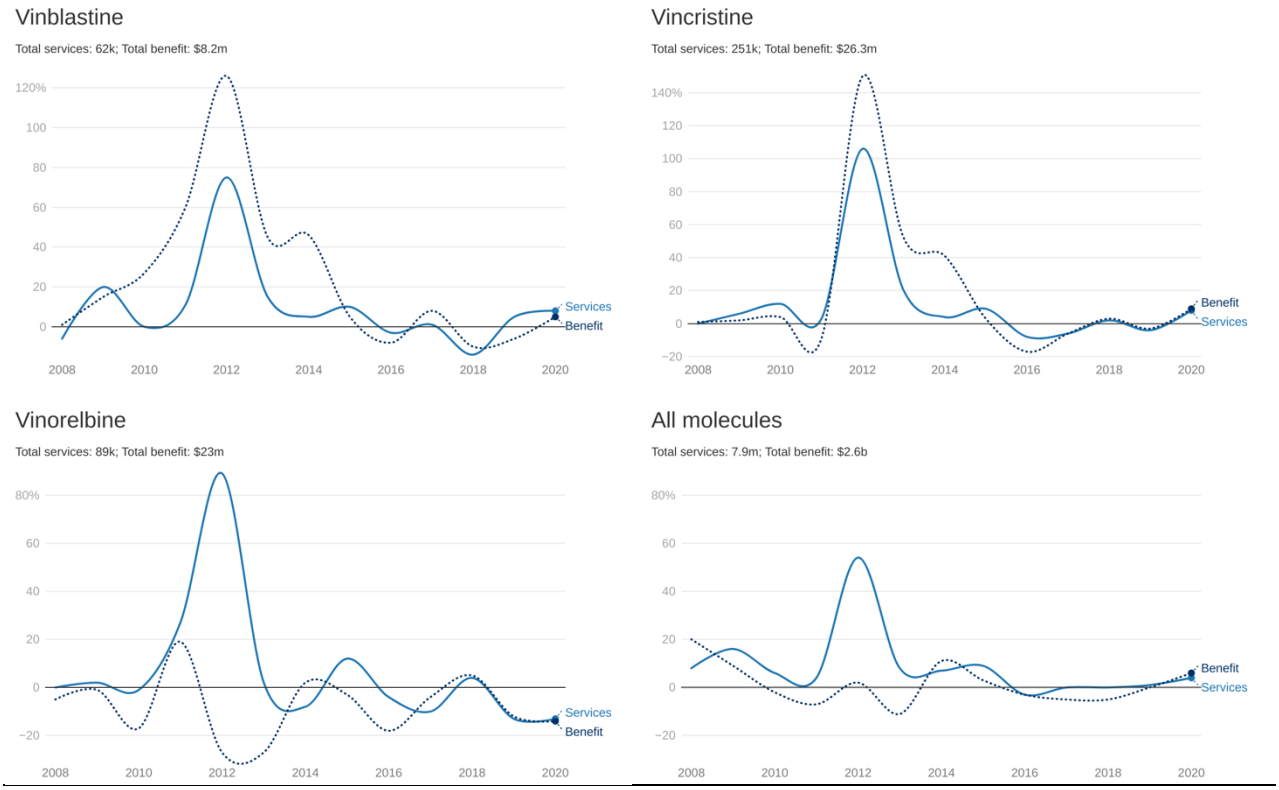
Total services: 4k; Total benefit: $3.5m



Topotecan

Total services: 14k; Total benefit: $6.2m





Across all molecules analysed, aggregated annual service volumes increased 54% in the year following the introduction of the EFC (i.e., in the calendar year ending December 2012). In the same period, aggregated benefit values increased by only 2%, representing greater overall service provision at reduced per-unit cost to government over the previous year (i.e., percent growth in service volume was greater than percent growth in benefit value in 2012).

For the majority of molecules (88%), introduction of the EFC coincided with a year-on-year increase in PBS service volume in the year ending December 2012, with only docetaxel, fotemustine and raltitrexed experiencing a decline in the number of services relative to 2011 (-12%, -14% and -16%, respectively). For around one-third of molecules (36%), the introduction of the EFC corresponded with a substantial increase (+100%) in the number of PBS services provided in the year to December 2012, including bortezomib (317%), cetuximab (393%), cladribine (277%), cytarabine (167%), etoposide (115%), fludarabine (293%), fluorouracil (106%), topotecan (292%) and vincristine (106%).

Notwithstanding the potential impacts of changed reimbursement arrangements introduced with the EFC, increased service volumes in 2012 may be linked to new recommended indications for approved drugs. To further contextualise changes in service volumes, public summary documents were analysed for new recommendations made by the Pharmaceutical Benefits Advisory Committee (PBAC)

in the period 2008-2012 for all EFC-listed molecules previously available under CPAP arrangements. In the period 2008-2012, PBAC recommended additional indications for bortezomib—for first-line treatment of patients with multiple myeloma in combination with melphalan or cyclophosphamide and corticosteroids (Jul 2009), for initial treatment of symptomatic multiple myeloma in newly diagnosed patients who have severe acute renal failure (Jul 2011), and for treatment in combination with chemotherapy of a patient with newly diagnosed symptomatic multiple myeloma who is eligible for high-dose chemotherapy and a primary stem cell transplant (Mar 2012); cetuximab—for treatment of metastatic colorectal cancer (Jul 2010); docetaxel—for neoadjuvant treatment of squamous cell carcinoma (Jul 2008), and for adjuvant treatment of operable breast cancer in combination with cyclophosphamide (Nov 2009); and fludarabine—for treatment of B-cell chronic lymphocytic leukaemia in combination with an alkylating agent, where the patient has advanced disease (Binet Stage B or C) or evidence of progressive disease (Mar 2008).[2]

Year-on-year service volume growth in the year ending December 2012 was not necessarily commensurate with changes in drugs' corresponding benefit values. For 17 of the molecules analysed (68%), the year following the introduction of the EFC coincided with greater overall service provision at reduced per-unit cost to government. Drugs with increased service volume at lower per-service cost in the year ending December 2012 included bleomycin, bortezomib, carboplatin, cetuximab, cladribine, cytarabine, epirubicin, etoposide, fludarabine, gemcitabine, idarubicin, ifosfamide, irinotecan, oxaliplatin, paclitaxel, topotecan, and vinorelbine.

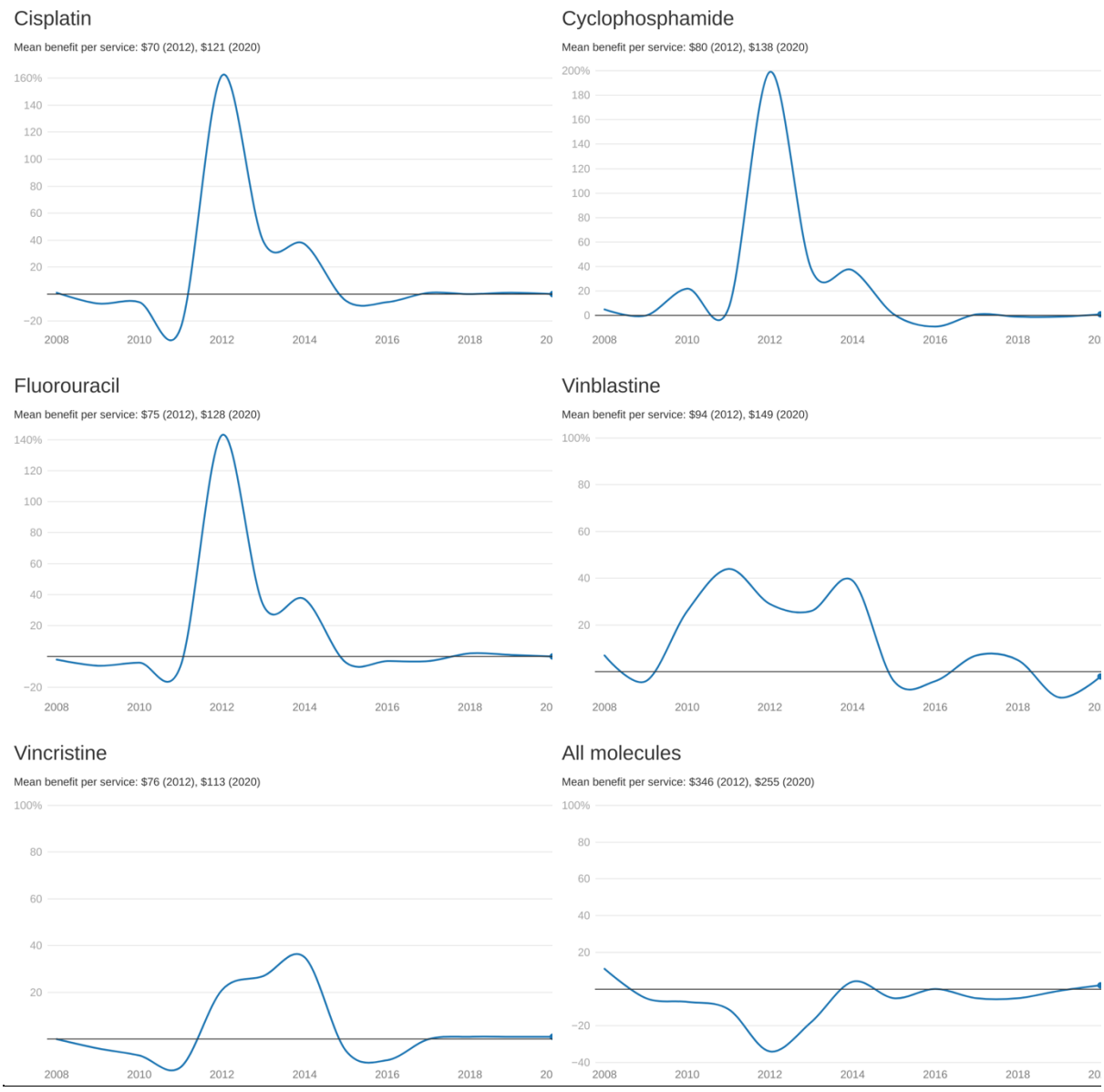
Evident reductions in per-unit costs to government may have been impacted by statutory price reductions due to price disclosure or introduction of generic or biosimilar competitors. Among analysed drugs with greater overall service provision at reduced per-unit cost to government in the year ending December 2012, statutory price reductions were enacted in the period 2008-2012 for fludarabine, irinotecan (2008); gemcitabine, oxaliplatin, paclitaxel, vinorelbine (2009); carboplatin, epirubicin, oxaliplatin and docetaxel (2012).[3]

[2] Department of Health. (2021). Public summary documents by product. Accessed online 16 November 2021 at https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/public-summary-documents-by-product.

[3] Department of Health. (2021). Price Reduction Outcomes from EAPD Cycles [Archived]. Accessed online 16 November 2021 at https://www.pbs.gov.au/info/industry/pricing/eapd.

In a limited number of cases, introduction of the EFC coincided with an increase in benefit value, but without a commensurate increase in service volume, indicating a greater per-unit cost to government for services in the period. Drugs demonstrating higher growth in benefit value relative to service volume for the year ending December 2012 included cisplatin, cyclophosphamide, fluorouracil, vinblastine and vincristine (see Figure A2). On a mean benefit-per-service basis, year-on-year cost growth to December 2012 was substantial (+100%) for cisplatin (162%), cyclophosphamide (199%) and fluorouracil (143%). Across all drugs previously funded under CPAP arrangements, mean benefit-per-service fell 34% in the year immediately following the introduction of the EFC. Over the full time horizon of this analysis, the mean overall cost-per-service to government for EFC drugs previously funded under CPAP arrangements fell 62%, from $666 (2008) to $255 (2020).

Figure A2. Annual percent change, mean PBS benefit-per-service by molecule (2008-2020)



Overall, transition to the EFC was associated with an increase in PBS service volumes and benefit values for drugs previously available under the CPAP arrangements. While the present analysis has not determined this relationship to be causal—both service volumes and benefit values are a function of multiple inter-related factors, including underlying clinical demand and relative prices—evidence suggests that reimbursement of infusible chemotherapies based on the efficient combination of vials has generally promoted access to these drugs at a reduced per-unit cost to government relative to previous arrangements under the CPAP.

Appendix 6. Analysis of Cancer Medicines Supplied via the PBS

The purpose of this analysis was to examine the utilisation of cancer medicines listed on the EFC by patient demographics, such as age, sex and state. Additionally, this analysis sought to examine patient access using metrics such as out-of-pocket costs and remoteness (the distribution of patients geographically as compared with that of their prescribing clinician and dispensing pharmacy.

PBS data

Prescription data for cancer medicines listed on the PBS were provided by the Department of Health based on items dispensed for the period 1 July 2016 to 30 June 2021. Data were extracted in September 2021 and comprise information on Schedule 1 and Schedule 2 medicines (see Table A8 and Table A9, respectively). The supplied data comprised 6,303,730 dispensing records, across 27,676 unique patient records. Patient-level analyses and counts of patients supplied with EFC medicines were conducted using person-specific numbers (non-identifying) in the data.

Table A8. PBS item codes and presentations by EFC item, Schedule 1

Molecule	*PBS item codes*	*Presentations*
Arsenic	04371C; 07241D; 10691Q; 10699D	10 mg/10 mL injection
Atezolizumab	11277M; 11284X; 11297N; 11309F; 11792P; 11801D; 11802E; 11807K; 11926Q; 11927R; 11928T; 11929W; 11930X; 11931Y; 11940K; 11957H; 12076N; 12078Q; 12097Q; 12098R; 12155R; 12159Y; 12163E; 12164F; 12167J; 12168K; 12171N; 12174R	1.2 g/20 mL injection, 20 mL vial 840 mg/14 mL injection, 14 mL vial
Avelumab	11671G; 11679Q; 11685B; 11695M	200 mg/10 mL injection, 10 mL vial
Bendamustine	10760H; 10763L	100 mg injection, 1 vial 25 mg injection, 1 vial
Bevacizumab	04400N; 07243F; 10114H; 10115J; 10120P; 10121Q; 10881Q; 10885X; 11727F; 11731K; 11745E; 11749J; 11791N; 11803F; 11809M; 11811P; 12165G; 12166H; 12479T; 12508H	400 mg/16 mL injection, 16 mL vial 100 mg/4 mL injection, 4 mL vial
Bleomycin	04433H; 07244G; 11701W; 11704B	15 000 international units injection, 1 vial
Blinatumomab	11115B; 11116C; 11117D; 11118E; 11119F; 11120G; 11814T; 11850Q; 11867N	38.5 microgram injection [1 vial] (&) inert substance solution [10 mL vial], 1 pack
Bortezomib	04403R; 04429D; 04706Q; 04712B; 04713C; 04725Q; 04732C; 07238Y; 07268M; 07269N; 07271Q; 07272R; 07274W; 07275X; 12219D; 12227M	1 mg injection, 1 vial 3 mg injection, 1 vial 3.5 mg injection, 1 vial
Brentuximab Vedotin	10166C; 10171H; 10172J; 10180T; 11067L; 11073T; 11079D; 11080E; 11086L; 11087M; 11089P; 11096B; 11651F; 11660Q; 11661R; 11664X	50 mg injection, 1 vial
Cabazitaxel	04376H; 07236W	60 mg/1.5 mL injection [1.5 mL vial] (&) inert substance diluent [4.5 mL vial

Molecule	*PBS item codes*	*Presentations*
Carboplatin	04309T; 07222D	150 mg/15 mL injection, 15 mL vial
		450 mg/45 mL injection, 45 mL vial
Carfilzomib	11229B; 11230C; 12243J; 12244K	10 mg injection, 1 vial
		30 mg injection, 1 vial
		60 mg injection, 1 vial
Cetuximab	04312Y; 04435K; 04436L; 04731B;	500 mg/100 mL injection, 100 mL vial
	07223E; 07240C; 07242E; 07273T;	100 mg/20 mL injection, 20 mL vial
	10262D; 10265G	
Cisplatin	04319H; 07224F	50 mg/50 mL injection, 50 mL vial
		100 mg/100 mL injection, 100 mL vial
Cladribine	04326Q; 07225G	10 mg tablet
		10 mg/10 mL injection, 10 mL vial
		10 mg/5 mL injection, 5 mL vial
Cyclophosphamide	04327R; 07226H	50 mg tablet, 50
		500 mg injection, 1 vial
		1 g injection, 1 vial
		2 g injection, 1 vial
Cytarabine	04357H; 07227J	100 mg/5 mL injection, 5 x 5 mL vials
Daratumumab	12220E; 12221F; 12225K; 12226L;	1.8 g/15 mL injection, 15 mL vial
	12228N; 12229P; 12230Q; 12231R	100 mg/5 mL injection, 5 mL vial
		400 mg/20 mL injection, 20 mL vial
Docetaxel	10148D; 10158P	160 mg/16 mL injection, 16 mL vial
		80 mg/4 mL injection, 4 mL vial
		80 mg/8 mL injection, 8 mL vial
		160 mg/8 mL injection, 8 mL vial
Doxorubicin	04361M; 07229L	200 mg/100 mL injection, 100 mL vial
		50 mg/25 mL injection, 25 mL vial
Doxorubicin Hydrochloride (As Pegylated Liposomal)	04364Q; 07230M	50 mg/25 mL injection, 25 mL vial (as pegylated liposomal)
		20 mg/10 mL injection, 10 mL vial (as pegylated liposomal)
Durvalumab	11911X; 11915D	500 mg/10 mL injection, 10 mL vial
		120 mg/2.4 mL injection, 2.4 mL vial
Epirubicin	04375G; 07231N	200 mg/100 mL injection, 100 mL vial
		100 mg/50 mL injection, 50 mL vial
		50 mg/25 mL injection, 25 mL vial
Eribulin	10140Q; 10144X; 11199K; 11212D	1 mg/2 mL injection, 2 mL vial
Etoposide	04428C; 07237X	50 mg capsule, 20
		100 mg capsule, 10
		100 mg/5 mL injection, 5 x 5 mL vials
		100 mg/5 mL injection, 5 mL vial
Fludarabine	04393F; 07233Q	10 mg tablet, 20
		50 mg/2 mL injection, 5 x 2 mL vials
		50 mg injection, 1 vial
Fluorouracil	04394G; 04431F; 07234R; 07239B	5% cream, 20 g
		5 g/100 mL injection, 100 mL vial
		2.5 g/50 mL injection, 50 mL vial
		1 g/20 mL injection, 20 mL vial
		500 mg/10 mL injection, 10 mL vial
Fotemustine	04437M; 07245H	208 mg injection [1 vial] (&) inert substance diluent [4 mL ampoule], 1 pack
Gemcitabine	04439P; 07246J	1 g/26.3 mL injection, 26.3 mL vial
		2 g/52.6 mL injection, 52.6 mL vial
Idarubicin	04440Q; 07247K	5 mg/5 mL injection, 5 mL vial
Ifosfamide	04448D; 07248L	1 mg injection, 1 vial

Molecule	*PBS item codes*	*Presentations*
Inotuzumab Ozogamicin	11668D; 11673J; 11674K; 11680R; 11696N	·1 mg injection, 1 vial
Ipilimumab	02638W; 02641B; 02643D; 02663E; 11628B; 11641Q; 11644W; 11647B; 12304N; 12322M; 12324P	·200 mg/40 mL injection, 40 mL vial ·50 mg/10 mL injection, 10 mL vial
Irinotecan	04451G; 07249M	·500 mg/25 mL injection, 25 mL vial ·100 mg/5 mL injection, 5 mL vial ·40 mg/2 mL injection, 2 mL vial
Methotrexate	04502Y; 04512L; 07250N; 07251P	·10 mg tablet ·50 mg/2 mL injection, 2 mL vial ·7.5 mg/0.3 mL injection, 4 x 0.3 mL syringes ·15 mg/0.6 mL injection, 4 x 0.6 mL syringes ·20 mg/0.8 mL injection, 4 x 0.8 mL syringes ·10 mg/0.4 mL injection, 4 x 0.4 mL syringes ·7.5 mg/0.15 mL injection, 0.15 mL syringe ·5 mg/2 mL injection, 5 x 2 mL vials ·25 mg/0.5 mL injection, 0.5 mL syringe ·2.5 mg tablet, 30 ·20 mg/0.4 mL injection, 0.4 mL syringe ·50 mg/2 mL injection, 5 x 2 mL vials ·10 mg/0.2 mL injection, 0.2 mL syringe ·15 mg/0.3 mL injection, 0.3 mL syringe ·25 mg/mL injection, 4 x 1 mL syringes ·1 g/10 mL injection, 10 mL vial ·500 mg/20 mL injection, 20 mL vial ·5 g/50 mL injection, 50 mL via
Mitozantrone	04514N; 07252Q	25 mg/12.5 mL injection, 12.5 mL vial 20 mg/10 mL injection, 10 mL vial
Nanoparticle Albumin-Bound Paclitaxel	04531L; 07270P; 10150F; 10165B	100 mg injection, 1 vial
Nivolumab	10745M; 10748Q; 10764M; 10775D; 11143L; 11150W; 11152Y; 11153B; 11157F; 11158G; 11159H; 11160J; 11411N; 11425H; 11434T; 11435W; 11532Y; 11543M; 11626X; 11627Y; 11631E; 11635J; 11636K; 11642R; 11900H; 11906P; 12315E; 12323N	40 mg/4 mL injection, 4 mL vial 40 mg/4 mL injection, 4 mL vial
Obinutuzumab	10407R; 10418H; 11455X; 11456Y; 11457B; 11458C; 11460E; 11462G; 11468N; 11473W; 12193R; 12204H	1 g/40 mL injection, 40 mL vial
Ofatumumab	10236R; 10237T; 10239X; 10240Y; 10249K; 10252N	20 mg/0.4 mL injection, 0.4 mL pen device
Oxaliplatin	04542C; 07253R	·100 mg/20 mL injection, 20 mL vial ·200 mg/40 mL injection, 40 mL vial
Paclitaxel	04567J; 07254T	·300 mg/50 mL injection, 50 mL vial ·30 mg/5 mL injection, 5 mL vial ·150 mg/25 mL injection, 25 mL vial ·100 mg/16.7 mL injection, 16.7 mL vial
Panitumumab	10069Y; 10082P; 10508C 10513H	·100 mg/5 mL injection, 5 mL vial ·400 mg/20 mL injection, 20 mL vial
Pembrolizumab	10424P; 10436G; 10475H; 10493G; 11330H; 11352L; 11492W; 11494Y; 11632F; 11646Y; 12119W; 12120X; 12121Y; 12122B; 12123C; 12124D;	·100 mg/4 mL injection, 4 mL vial

Molecule	*PBS item codes*	*Presentations*
	12125E; 12126F; 12127G; 12128H; 12129J; 12130K	
Pemetrexed	04600D; 07255W; 10267J; 10268K; 10308M; 10309N; 10333W; 10334X	·500 mg injection, 1 vial
		·100 mg injection, 1 vial
		·1 g injection, 1 vial
Pralatrexate	11271F; 11272G; 11278N; 11293J	·20 mg/mL injection, 1 mL vial
Raltitrexed	04610P; 07256X	·2 mg injection, 1 vial
Rituximab	04613T; 04614W; 04615X; 07257Y;	·1.4 g/11.7 mL injection, 11.7 mL vial
	07258B; 07259C; 10179R; 10193L;	·100 mg/10 mL injection, 2 x 10 mL vials
	11935E; 11936F	·500 mg/50 mL injection, 50 mL vial
Topotecan	04617B; 07260D	4 mg injection, 5 vials
		·4 mg/4 mL injection, 5 x 4 mL vials
Trastuzumab	04632T; 04639E; 04650R; 04703M;	·600 mg/5 mL injection, 5 mL vial
	07264H; 07265J; 07266K; 07267L;	·150 mg injection, 1 vial
	10381J; 10383L; 10391X; 10401K;	·60 mg injection, 1 vial
	10402L; 10423N; 10575N; 10581X;	420 mg injection, 1 vial
	10588G; 10589H; 10595P; 10597R	
Trastuzumab Emtansine	10281D; 10282E; 11951B; 11956G	·160 mg injection, 1 vial
		·100 mg injection, 1 vial
Vinblastine	04618C; 07261E	·10 mg/10 mL injection, 5 x 10 mL vials
Vincristine	04619D; 07262F	·1 mg/mL injection, 5 x 1 mL vials
Vinorelbine	04620E; 07263G	·20 mg capsule, 1
		·10 mg/mL injection, 1 mL vial
		·50 mg/5 mL injection, 5 mL vial

Source: PBS website—compiled for the Review

Table A9. PBS item codes and presentations by EFC item, Schedule 2

Item	*PBS Item Code*	*Presentations Available*
Aprepitant	02550F	165 mg capsules
Folinic Acid	05890B; 05870Y; 01904F; 05904R; 01899Y; 05886T; 05863N	oral liquid (400 grams)
Fosaprepitant	11103J	150 mg injection, 1 vial
Granisetron	05899L; 05898K	
Interferon Alfa-2a	05945X; 05946Y; 05997P; 05996N;	1.5 mL injection, 4 x 1.5 mL cartridges
	05998Q; 05949D; 05948C; 05953H;	0.5 mL injection, 12 x 0.5 mL pen devices
	05956L	0.5 mL injection, 12 x 0.5 mL syringes
		0.5 mL injection, 4 x 0.5 mL syringes
Interferon Beta-1B	08101J	250 mg injections (15 x 1.2 mL syringe)
Mesna	05961R; 05960Q	400 mg/4 mL injection, 15 x 4 mL ampoules
		1 g/10 mL injection, 15 x 10 mL ampoules
Mycobacterium Bovis (Bacillus Calmette And Guerin (Bcg)) Tice Strain	05902P	500 million CFU injection, 3 vials
Netupitant + Palonosetron	10714X	netupitant 300 mg + palonosetron 500 microgram capsule

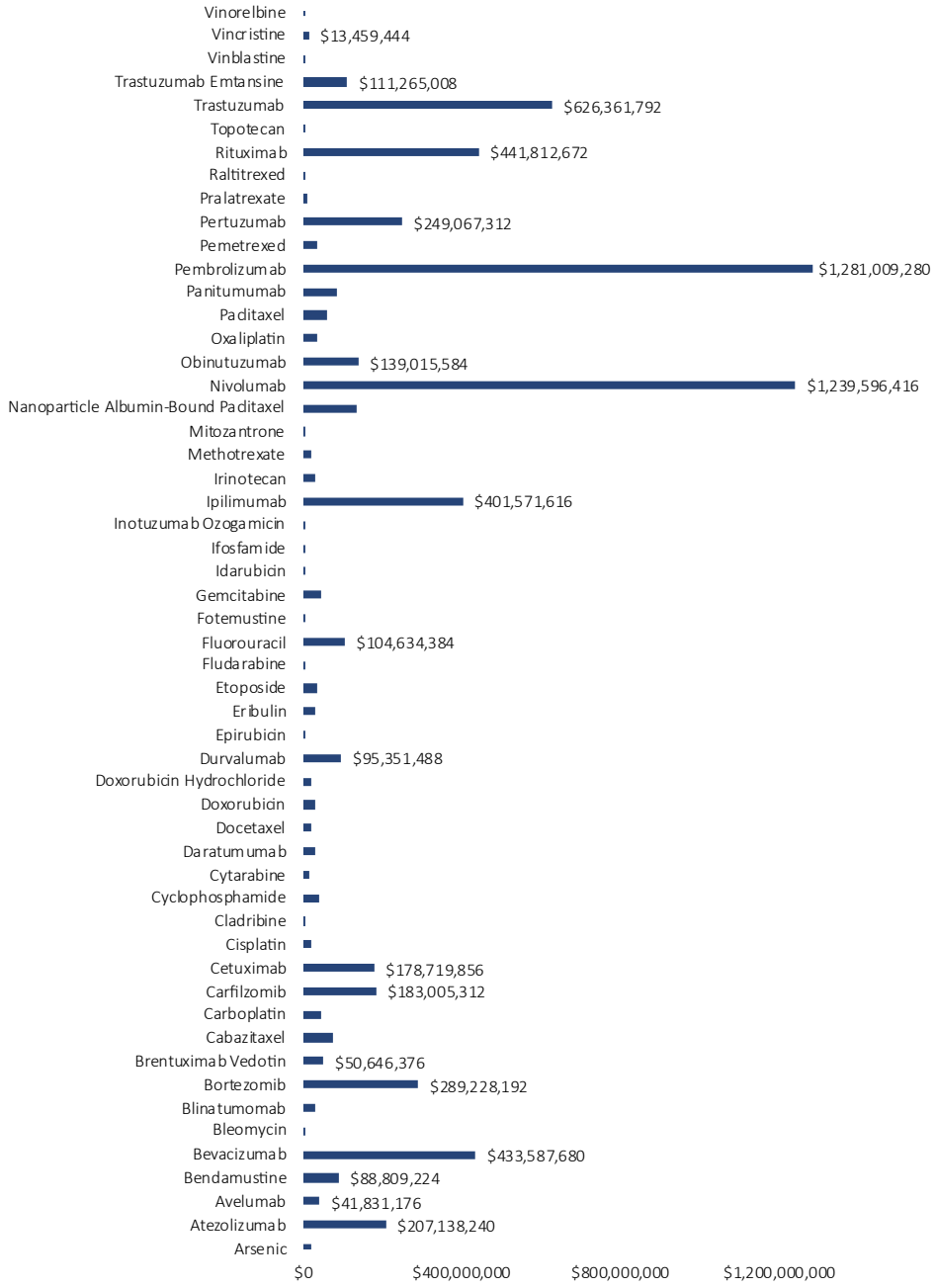
Item	*PBS Item Code*	*Presentations Available*
Ondansetron	05968D; 05848T; 05857G; 05858H; 05967C; 05970F; 05969E; 05972H; 05971G	8 mg wafer, 4 8 mg orally disintegrating tablet, 4 4 mg tablet, 10 8 mg wafer, 10 4 mg orally disintegrating tablet, 10 4 mg orally disintegrating tablet, 4 8 mg orally disintegrating tablet, 10 8 mg tablet, 4 4 mg tablet, 4 8 mg tablet, 10 4 mg wafer, 4 4 mg wafer, 10 4 mg/5 mL oral liquid, 50 mL
Palonosetron	05853C	250 microgram/5 mL injection, 5 mL vial
Rituximab	10710Q; 10741H; 10720F; 10708N; 11942M	·1.4 g/11.7 mL injection, 11.7 mL vial ·100 mg/10 mL injection, 2 x 10 mL vials ·500 mg/50 mL injection, 50 mL vial
Trastuzumab	10743K; 10817H; 10744L; 10829Y; 10811B	600 mg/5 mL injection, 5 mL vial 150 mg injection, 1 vial 60 mg injection, 1 vial 420 mg injection, 1 vial
Tropisetron	05987D	5 mg/5 mL injection, 5 mL ampoule

Source: Information from the PBS Website – compiled for this Review.

PBS expenditure on the EFC

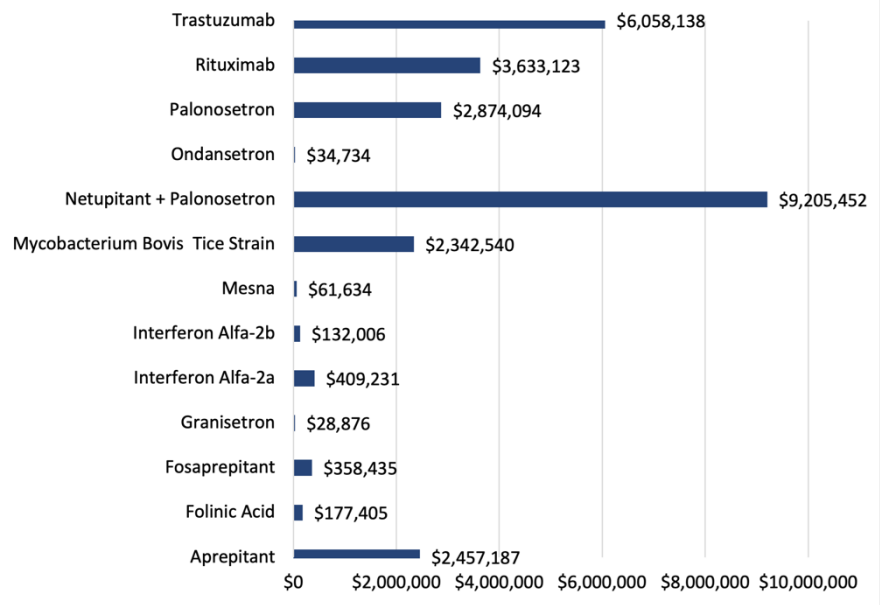
A summary of total Government expenditure for EFC Schedule 1 and Schedule 2 medicines is presented in Figure A3 and Figure A4, respectively. Overall, total Government expenditure for the period July 2016 to June 2021 was $7,100,970,748 ($7,073,197,870 for Schedule 1 medicines and $27,772,878 for Schedule 2 medicines, excluding the payment of the CCPS and other administrative fees, which fall outside of the PBS benefit).

Figure A3. PBS spending by EFC item, Schedule 1 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

Figure A4. PBS spending by EFC item, Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

PBS per annum expenditure and script volume for EFC-listed items are detailed in **Error! Not a valid bookmark self-reference.** and Table A11, respectively.

Table A10. PBS spending on EFC by schedule and item (July 2016 - June 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
			Schedule 1 Medicines				
Arsenic	$1,649,416	$2,922,527	$3,304,897	$4,256,043	$4,596,804	$2,069,707	$18,799,394
Atezolizumab	-	-	$15,512,122	$41,923,748	$90,559,720	$59,142,644	$207,138,240
Avelumab	-	-	-	$11,494,113	$19,905,486	$10,431,575	$41,831,176
Bendamustine	$6,823,934	$16,974,108	$17,664,850	$18,797,334	$18,646,948	$9,902,049	$88,809,224
Bevacizumab	$42,787,848	$85,416,088	$84,587,160	$82,266,032	$92,808,608	$45,721,948	$433,587,680
Bleomycin	$750,150	$1,061,686	$944,570	$815,784	$972,955	$490,878	$5,036,023
Blinatumomab	-	$3,158,481	$7,214,214	$4,997,769	$9,189,041	$4,074,092	$28,633,596
Bortezomib	$32,886,088	$58,885,912	$53,739,108	$57,155,188	$63,012,956	$23,548,936	$289,228,192
Brentuximab Vedotin	$1,338,673	$8,339,322	$11,518,501	$10,592,789	$12,564,556	$6,292,536	$50,646,376
Cabazitaxel	$12,172,889	$12,934,946	$13,158,070	$15,336,579	$16,879,614	$4,236,722	$74,718,824
Carboplatin	$3,732,065	$8,072,468	$8,447,373	$8,789,125	$9,401,576	$4,828,159	$43,270,768
Carfilzomib	-	-	$48,302,312	$52,898,980	$56,633,612	$25,170,406	$183,005,312
Cetuximab	$20,979,912	$38,488,364	$35,864,496	$33,349,322	$33,444,922	$16,592,838	$178,719,856
Cisplatin	$2,058,491	$3,759,051	$3,823,924	$3,980,342	$3,873,989	$1,976,796	$19,472,592
Cladribine	$231,745	$498,722	$487,690	$583,296	$583,864	$344,569	$2,729,886
Cyclophosphamide	$4,104,160	$7,970,324	$7,975,681	$7,903,521	$7,708,152	$3,630,611	$39,292,448
Cytarabine	$1,119,184	$2,468,151	$2,798,025	$2,738,060	$3,268,729	$1,904,543	$14,296,692
Daratumumab	-	-	-	-	-	$28,309,288	$28,309,288
Docetaxel	$1,939,331	$3,872,206	$4,168,203	$4,379,428	$4,170,718	$2,137,177	$20,667,062
Doxorubicin	$2,425,309	$5,262,150	$6,051,998	$6,133,349	$6,162,071	$3,066,423	$29,101,298
Doxorubicin-Hydrochloride	$2,942,616	$4,633,545	$4,183,014	$4,212,530	$4,280,403	$2,077,103	$22,329,210
Durvalumab	-	-	-	-	$61,052,512	$34,298,976	$95,351,488
Epirubicin	$1,078,835	$1,312,686	$812,466	$493,515	$307,674	$146,062	$4,151,238
Eribulin	$3,296,375	$7,602,102	$8,765,378	$5,218,889	$4,934,953	$2,014,677	$31,832,372
Etoposide	$3,470,119	$6,926,292	$7,719,367	$7,601,632	$7,600,078	$3,722,598	$37,040,084
Fludarabine	$279,514	$525,854	$537,862	$479,054	$373,976	$164,861	$2,361,121
Fluorouracil	$9,840,593	$19,645,970	$20,241,096	$21,295,834	$22,346,438	$11,264,455	$104,634,384

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
Fotemustine	$51,122	$141,494	$29,924	$24,151	$62,510	$11,365	$320,565
Gemcitabine	$4,251,385	$9,024,637	$9,402,586	$8,808,929	$8,745,547	$4,523,351	$44,756,436
Idarubicin	$68,855	$143,737	$115,509	$69,746	$62,884	$38,137	$498,868
Ifosfamide	$664,868	$1,344,422	$1,030,765	$1,055,518	$1,079,449	$668,015	$5,843,039
Inotuzumab Ozogamicin	-	-	-	$1,736,799	$3,411,223	$2,257,400	$7,405,423
Ipilimumab	$16,388,846	$64,371,608	$72,696,320	$92,794,360	$101,482,920	$53,837,556	$401,571,616
Irinotecan	$3,033,522	$5,512,638	$5,565,256	$5,488,779	$5,788,423	$3,004,142	$28,392,758
Methotrexate	$1,646,906	$3,957,485	$4,118,106	$3,556,944	$3,315,467	$1,632,339	$18,227,246
Mitozantrone	$69,014	$101,667	$78,144	$65,367	$56,784	$24,574	$395,550
NAB Paclitaxel	$13,655,600	$27,420,772	$27,237,908	$26,676,470	$27,612,604	$13,813,467	$136,416,816
Nivolumab	$3,765,645	$96,914,280	$252,392,144	$293,468,544	$397,628,096	$195,427,696	$1,239,596,416
Obinutuzumab	$2,645,379	$8,761,236	$11,359,069	$33,272,362	$50,581,164	$32,396,380	$139,015,584
Ofatumumab	$1,063,206	$2,076,581	$1,355,957	$622,434	-	-	-
Oxaliplatin	$3,005,568	$6,724,713	$7,025,102	$7,418,237	$8,038,657	$4,273,548	$36,485,824
Paclitaxel	$5,851,141	$11,170,748	$11,467,172	$11,986,310	$12,353,789	$6,181,280	$59,010,440
Panitumumab	$7,257,805	$19,904,150	$19,640,552	$15,381,979	$14,180,276	$6,007,912	$82,372,672
Pembrolizumab	$66,367,576	$141,935,808	$166,311,792	$282,645,152	$408,762,784	$214,986,128	$1,281,009,280
Pemetrexed	$14,092,767	$9,786,756	$2,232,138	$2,164,847	$3,539,618	$2,032,366	$33,848,492
Pertuzumab	$16,482,725	$39,918,368	$47,184,100	$53,806,256	$61,439,788	$30,236,084	$249,067,312
Pralatrexate	-	-	$1,369,737	$2,393,528	$3,150,300	$1,455,407	$8,368,971
Raltitrexed	$199,613	$398,908	$294,255	$242,467	$259,974	$105,125	$1,500,340
Rituximab	$60,385,536	$114,978,432	$98,464,568	$81,208,864	$62,446,560	$24,328,712	$441,812,672
Topotecan	$94,700	$195,224	$192,489	$233,315	$241,910	$189,303	$1,146,939
Trastuzumab	$76,020,232	$151,128,048	$146,616,288	$124,766,216	$91,467,368	$36,363,640	$626,361,792
Trastuzumab Emtansine	$9,443,633	$18,485,434	$17,948,440	$17,346,378	$28,750,990	$19,290,136	$111,265,008
Vinblastine	$475,623	$1,015,444	$903,305	$880,308	$912,916	$442,342	$4,629,938
Vincristine	$1,284,393	$2,576,051	$2,713,966	$2,627,876	$2,829,968	$1,427,191	$13,459,444
Vinorelbine	$607,504	$1,169,286	$1,226,754	$1,083,368	$945,790	$391,905	$5,424,608
Total Schedule 1	*$464,780,407*	*$1,039,888,878*	*$1,276,794,718*	*$1,479,517,755*	*$1,854,428,113*	*$962,906,126*	*$7,073,197,870*
			Schedule 2 Medicines				
Aprepitant	$618,019	$938,585	$663,353	$223,016	$7,892	$6,322	$2,457,187
Folinic Acid	$22,063	$46,638	$38,690	$29,951	$29,226	$10,838	$177,405
Fosaprepitant	-	$34,672	$33,645	$96,434	$133,745	$59,938	$358,435
Granisetron	$5,998	$5,711	$5,166	$5,539	$4,965	$1,497	$28,876

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
Interferon Alfa-2a	$43,160	$99,798	$147,761	$79,852	$35,620	$3,039	$409,231
Interferon Alfa-2b	$21,985	$65,573	$44,449	-	-	-	$132,006
Mesna	$6,222	$12,001	$9,370	$14,181	$10,676	$9,185	$61,634
Mycobacterium Bovis BCG Tice Strain	$222,836	$477,745	$571,373	$492,118	$353,545	$224,924	$2,342,540
Netupitant + Palonosetron	$39,180	$647,836	$1,601,119	$2,396,746	$2,994,023	$1,526,549	$9,205,452
Ondansetron	$21,597	$6,790	$1,988	$1,327	$2,249	$783	$34,734
Palonosetron	$354,409	$668,935	$603,264	$515,966	$497,813	$233,707	$2,874,094
Rituximab	$24,150	$359,751	$850,513	$899,503	$1,105,934	$393,272	$3,633,123
Trastuzumab	$199,699	$862,968	$1,140,425	$892,043	$1,945,642	$1,017,360	$6,058,138
Tropisetron	-	-	$18	-	-	$5	$23
Total Schedule 2	*$1,579,317*	*$4,227,004*	*$5,711,134*	*$5,646,675*	*$7,121,329*	*$3,487,418*	*$27,772,878*
Schedule 1 & 2 Medicines	*$465,296,518*	*$1,042,039,301*	*$1,281,149,895*	*$1,484,541,996*	*$1,861,549,442*	*$966,393,544*	*$7,100,970,748*

Source: Prepared for this Review using PBS patient-level data.

Table A11. PBS service volume by EFC item and schedule (July 2016 - June 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
			Schedule 1 Medicines				
Arsenic	2,418	4,131	4,785	5,793	6,875	4,020	28,022
Atezolizumab			2,034	5,496	12,172	7,932	27,634
Avelumab				1,859	3,107	1,643	6,609
Bendamustine	4,380	10,769	11,310	12,043	11,934	6,392	56,828
Bevacizumab	19,337	38,106	37,775	37,946	45,206	23,979	202,349
Bleomycin	3,403	6,257	6,096	5,779	5,754	2,759	30,048
Blinatumomab		56	96	67	127	56	402
Bortezomib	21,403	39,202	38,021	42,409	46,919	28,679	216,633
Brentuximab Vedotin	87	494	718	727	888	433	3,347
Cabazitaxel	2,186	4,105	4,333	5,116	5,623	2,834	24,197
Carboplatin	27,618	56,994	59,446	60,640	64,440	33,282	302,420

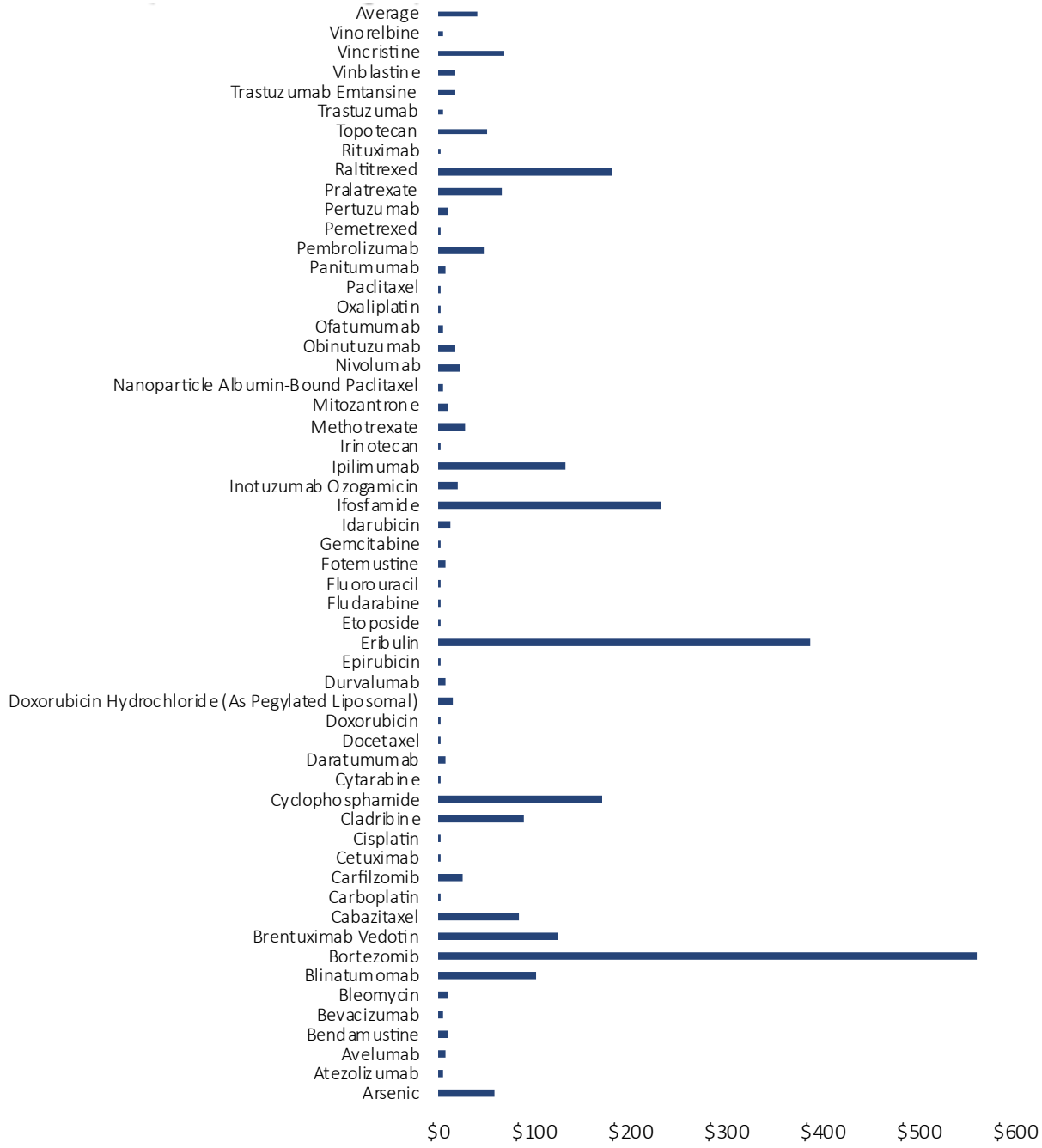
Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
Carfilzomib			19,967	22,984	24,397	10,550	77,898
Cetuximab	9,356	16,648	16,416	15,424	14,772	7,227	79,843
Cisplatin	17,340	31,567	32,029	33,174	31,874	16,101	162,085
Cladribine	222	467	492	596	561	352	2,690
Cyclophosphamide	29,398	56,734	57,678	57,860	55,790	26,201	283,661
Cytarabine	5,600	11,388	11,708	12,377	15,637	9,266	65,976
Daratumumab						3,617	3,617
Docetaxel	14,827	27,003	29,038	29,113	27,511	14,063	141,555
Doxorubicin	21,220	43,217	44,191	44,554	44,311	22,099	219,592
Doxorubicin-Hydrochloride	2,425	4,916	5,191	5,361	5,392	2,678	25,963
Durvalumab					9,409	5,343	14,752
Epirubicin	4,474	6,692	4,294	3,150	2,076	988	21,674
Eribulin	2,527	5,733	6,621	6,878	6,756	2,783	31,298
Etoposide	19,207	38,489	40,502	39,702	39,385	19,119	196,404
Fludarabine	1,740	3,608	3,778	3,307	2,534	1,133	16,100
Fluorouracil	77,750	159,257	160,848	168,095	174,356	87,932	828,238
Fotemustine	35	119	24	23	58	11	270
Gemcitabine	32,695	64,781	64,426	59,418	58,404	30,096	309,820
Idarubicin	233	529	418	300	289	157	1,926
Ifosfamide	2,160	4,329	3,513	3,685	3,798	2,333	19,818
Inotuzumab Ozogamicin				68	122	101	291
Ipilimumab	515	2,044	2,343	3,680	4,097	2,230	14,909
Irinotecan	16,609	33,441	36,965	41,144	44,373	22,941	195,473
Methotrexate	13,461	33,380	33,436	28,671	26,203	12,925	148,076
Mitozantrone	394	618	465	391	338	140	2,346
NAB Paclitaxel	14,061	27,957	27,592	27,287	30,080	15,540	142,517
Nivolumab	748	19,322	50,664	54,659	51,673	24,354	201,420
Obinutuzumab	485	1,607	2,085	6,100	9,263	6,072	25,612
Ofatumumab	319	619	410	184			1,532
Oxaliplatin	23,860	47,878	49,953	52,768	56,710	29,306	260,475
Paclitaxel	42,200	87,527	89,368	92,959	95,262	47,769	455,085
Panitumumab	1,976	5,378	5,360	5,726	5,894	2,527	26,861
Pembrolizumab	7,847	16,736	19,662	32,197	46,630	24,966	148,038

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
Pemetrexed	4,774	9,097	9,608	12,147	20,005	10,853	66,484
Pertuzumab	4,956	11,992	14,275	16,308	18,665	9,423	75,619
Pralatrexate			408	754	895	413	2,470
Raltitrexed	196	380	321	261	299	118	1,575
Rituximab	20,469	39,374	37,489	35,369	33,995	16,964	183,660
Topotecan	543	1,268	1,237	1,513	1,552	1,341	7,454
Trastuzumab	25,016	49,372	50,596	53,047	53,929	25,797	257,757
Trastuzumab Emtansine	2,153	4,177	4,035	3,965	6,413	4,332	25,075
Vinblastine	3,161	6,151	5,384	5,828	6,125	2,969	29,618
Vincristine	11,528	23,296	24,340	23,476	25,020	12,588	120,248
Vinorelbine	4,333	7,890	8,097	7,066	6,181	2,573	36,140
Total Schedule 1	*521,645*	*1,065,095*	*1,139,841*	*1,189,444*	*1,264,079*	*650,300*	*5,830,404*
			Schedule 2 Medicines				
Aprepitant	7,874	12,719	9,722	3,503	204	154	34,176
Folinic Acid	4,894	9,878	9,827	8,829	7,140	3,146	43,714
Fosaprepitant		475	460	1,303	1,774	810	4,822
Granisetron	5,674	7,998	3,643	3,204	2,906	1,585	25,010
Interferon Alfa-2a	112	248	404	237	104	10	1,115
Interferon Alfa-2b	36	122	80				238
Mesna	419	563	607	787	647	429	3,452
Mycobacterium Bovis BCG Tice Strain	874	1,934	2,594	2,945	2,054	1,102	11,503
Netupitant + Palonosetron	514	8,636	21,446	32,518	40,387	20,747	124,248
Ondansetron	9,731	13,742	9,683	7,114	4,373	1,496	46,139
Palonosetron	20,924	39,857	36,424	31,483	29,871	15,173	173,732
Rituximab	9	134	349	429	658	234	1,813
Trastuzumab	72	311	433	423	1,230	706	3,175
Tropisetron		26	69	36	37	21	189
Total Schedule 2	*51,133*	*96,643*	*95,741*	*92,811*	*91,385*	*45,613*	*473,326*
			Total				
Schedule 1 & 2 Medicines	*572,778*	*1,161,738*	*1,235,582*	*1,282,255*	*1,355,464*	*695,913*	*6,303,730*

PBS price per unit

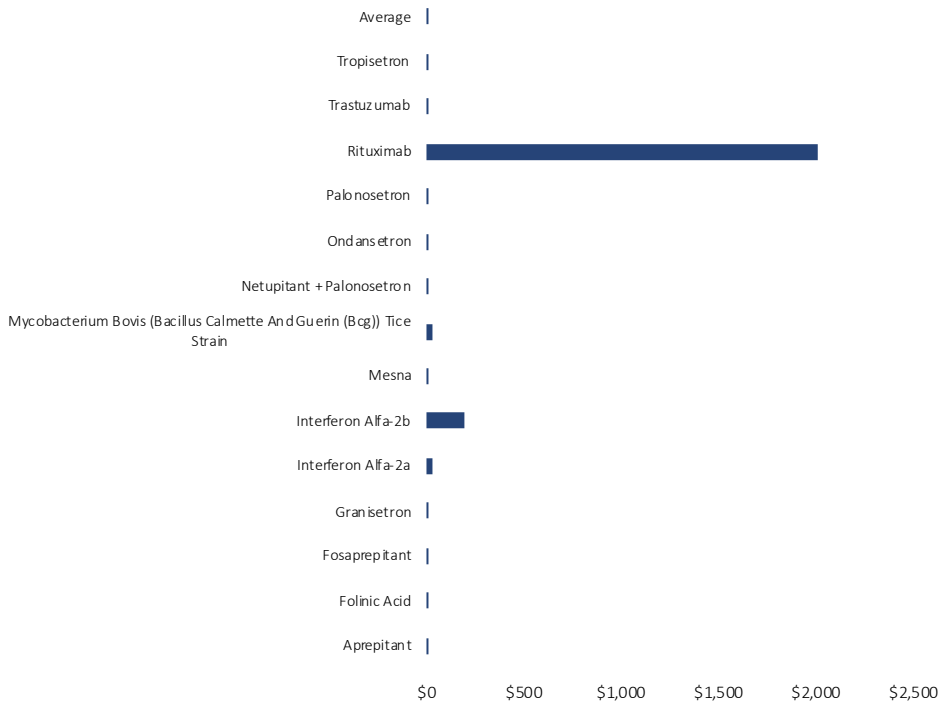
A summary of the average price paid per unit (mg, mcg or international unit) by the Government for cancer medicines from July 2016 to June 2021 is presented in Figure A5 and Figure A6. Overall, the average price paid per unit was $39.63 for Schedule 1 medicines and $8.21 for Schedule 2 medicines. For this analysis, the price per unit is estimated based on the benefit paid divided by the number of units dispensed per claim. The number of units per PBS claim has been estimated based on the reported Regulation 24 quantity dispensed as an indicator of dose, modified by the reported presentation strength (where the information reported under Regulation 24 related to the number of packs dispensed rather than the dose dispensed). An annual breakdown of the average price paid per unit is provided in Table A12.

Figure A5. Mean PBS price per unit by item, Schedule 1 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

Figure A6. Mean PBS price per unit by item, Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

Table A12. Mean price per unit by item (July 2016 - June 2021)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*2016-2021*
			Schedule 1 Medicines				
Arsenic	$61.48	$60.40	$65.88	$60.32	$55.74	$46.14	$58.24
Atezolizumab	-	-	$6.38	$6.36	$6.14	$6.10	$6.19
Avelumab	-	-	-	$10.87	$7.72	$7.72	$8.61
Bendamustine	$9.36	$9.41	$9.87	$9.44	$9.47	$9.52	$9.53
Bevacizumab	$4.81	$4.89	$4.86	$4.41	$3.66	$3.21	$4.31
Bleomycin	$12.30	$9.82	$7.95	$6.85	$8.26	$8.94	$8.77
Blinatumomab		$77.05	$105.14	$105.24	$105.76	$106.03	$101.56
Bortezomib	$636.39	$625.37	$589.58	$563.64	$568.90	$347.30	$559.02
Brentuximab Vedotin	$121.67	$123.57	$154.64	$115.96	$111.14	$109.36	$123.40
Cabazitaxel	$144.68	$82.66	$81.61	$82.55	$85.80	$44.63	$84.33
Carboplatin	$0.44	$0.50	$0.54	$0.49	$0.49	$0.53	$0.50
Carfilzomib			$25.47	$23.52	$23.50	$23.45	$24.01
Cetuximab	$3.68	$3.67	$3.47	$3.31	$3.31	$3.32	$3.46
Cisplatin	$2.12	$1.93	$1.91	$1.97	$2.01	$2.05	$1.98
Cladribine	$90.39	$97.35	$86.47	$90.39	$87.10	$87.83	$89.87
Cyclophosphamide	$182.68	$175.02	$179.96	$167.98	$156.16	$164.14	$170.67
Cytarabine	$2.09	$1.77	$2.15	$2.32	$2.49	$2.59	$2.25
Daratumumab	-	-	-	-	-	$7.43	$7.43
Docetaxel	$1.16	$1.22	$1.29	$1.41	$1.35	$1.41	$1.31
Doxorubicin	$1.93	$2.00	$2.22	$2.04	$2.01	$1.97	$2.04
Doxorubicin-Hydrochloride	$21.52	$16.60	$14.36	$13.91	$13.92	$13.98	$15.23
Durvalumab	-	-	-	-	$8.50	$8.78	$8.60
Epirubicin	$2.54	$2.06	$2.00	$1.79	$1.73	$1.96	$2.07
Eribulin	$501.97	$501.83	$500.39	$287.77	$279.42	$276.76	$386.60
Etoposide	$1.10	$1.20	$1.22	$1.17	$1.15	$1.15	$1.17
Fludarabine	$3.56	$3.28	$3.24	$3.10	$3.23	$3.51	$3.27
Fluorouracil	$0.23	$0.17	$0.13	$0.12	$0.11	$0.11	$0.14
Fotemustine	$22.12	$6.67	$7.08	$6.44	$5.77	$5.34	$8.44
Gemcitabine	$0.16	$0.12	$0.10	$0.10	$0.11	$0.19	$0.12
Idarubicin	$14.44	$13.03	$12.77	$10.41	$10.48	$12.79	$12.33
Ifosfamide	$106.53	$108.14	$99.71	$92.47	$260.22	$948.79	$231.80

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*2016-2021*
Inot. Ozogamicin (mcg)	-	-	-	$16.86	$17.40	$23.72	$19.47
Ipilimumab	$130.58	$131.05	$130.50	$134.42	$131.59	$131.49	$131.99
Irinotecan	$0.69	$0.64	$0.56	$0.50	$0.50	$0.52	$0.55
Methotrexate	$23.06	$19.86	$23.74	$28.05	$34.87	$38.60	$26.91
Mitozantrone	$9.10	$9.05	$8.99	$8.34	$8.19	$8.77	$8.79
NAB Paclitaxel	$5.49	$5.42	$5.43	$5.47	$5.13	$5.06	$5.34
Nivolumab	$22.22	$22.16	$22.10	$22.97	$22.56	$21.65	$22.40
Obinutuzumab	$73.25	$38.96	$49.42	$18.87	$6.33	$17.58	$18.81
Ofatumumab	$3.66	$3.75	$3.74	$3.78	-	-	$3.73
Oxaliplatin	$1.15	$1.03	$1.06	$1.01	$1.08	$1.00	$1.05
Paclitaxel	$1.00	$0.94	$0.96	$0.96	$1.00	$1.00	$0.97
Panitumumab	$8.71	$9.06	$8.34	$6.26	$5.59	$5.60	$7.21
Pembrolizumab	$51.63	$51.65	$51.26	$49.33	$44.13	$40.86	$46.90
Pemetrexed	$3.63	$1.38	$0.27	$0.21	$0.21	$0.23	$0.63
Pertuzumab	$19.73	$8.44	$7.87	$9.80	$9.21	$8.16	$9.52
Pralatrexate	-	-	$65.60	$67.22	$66.13	$65.93	$66.34
Raltitrexed	$194.19	$195.67	$182.19	$165.65	$169.70	$168.51	$180.78
Rituximab	$4.17	$4.10	$3.69	$3.27	$2.62	$2.05	$3.40
Topotecan	$53.72	$44.75	$46.13	$48.34	$51.97	$55.97	$49.88
Trastuzumab	$7.06	$7.03	$6.62	$5.32	$3.82	$3.17	$5.54
Trastuzumab Emtansine	$18.43	$18.47	$18.54	$18.62	$18.47	$18.06	$18.43
Vinblastine	$16.83	$17.84	$17.80	$16.98	$17.47	$17.43	$17.44
Vincristine	$66.06	$65.58	$68.18	$67.42	$68.70	$68.96	$67.51
Vinorelbine	$3.51	$3.70	$3.70	$3.66	$3.77	$3.68	$3.68
Average Schedule 1	*$45.54*	*$41.78*	*$39.44*	*$38.13*	*$38.46*	*$34.44*	*$39.63*
			Schedule 2 Medicines				
Aprepitant	$0.48	$0.45	$0.41	$0.39	$0.23	$0.25	$0.44
Folinic Acid	$0.02	$0.01	$0.01	$0.01	$0.01	$0.01	$0.01
Fosaprepitant	-	$0.49	$0.49	$0.49	$0.50	$0.49	$0.50
Granisetron	$0.28	$0.19	$0.35	$0.40	$0.35	$0.21	$0.28
Interferon Alfa-2a	$30.45	$29.06	$23.86	$22.69	$22.83	$23.15	$25.33
Interferon Alfa-2b	$203.56	$185.51	$192.72	-	-	-	$190.66
Mesna	$3.54	$4.12	$3.17	$2.99	$3.12	$4.15	$3.44
Mycobacterium Bovis BCG Tice Strain	$28.71	$28.67	$25.83	$23.72	$23.74	$23.83	$25.42

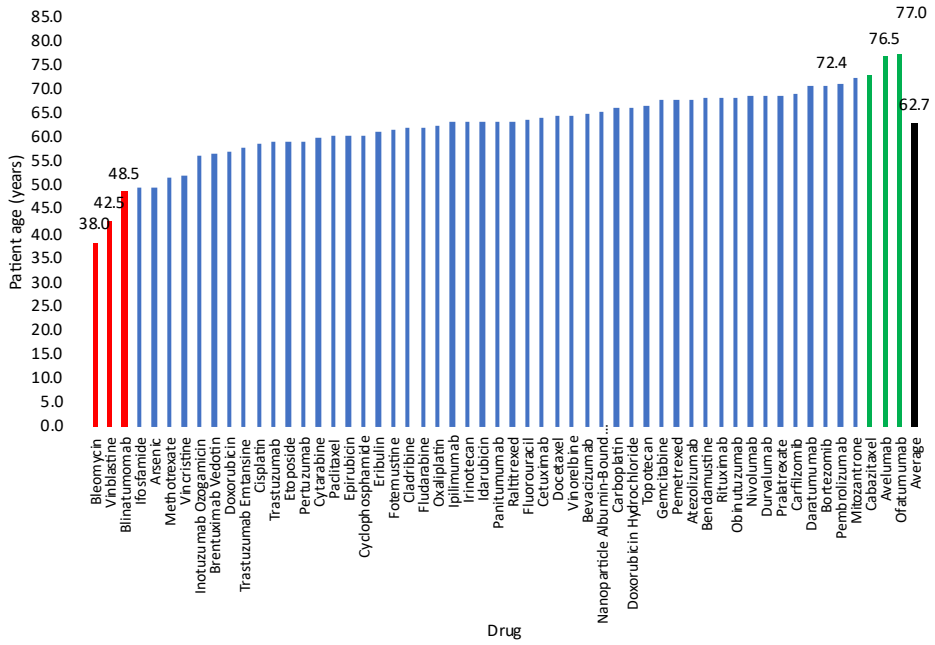
Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*2016-2021*
Netupitant + Palonosetron	$0.25	$0.25	$0.25	$0.25	$0.25	$0.25	$0.25
Ondansetron	$0.27	$0.06	$0.01	$0.01	$0.06	$0.05	$0.09
Palonosetron	$0.07	$0.07	$0.07	$0.07	$0.07	$0.06	$0.07
Rituximab	$2,683.31	$2,684.71	$2,437.00	$2,095.98	$1,680.75	$1,680.65	$2,003.65
Trastuzumab	$4.62	$4.62	$4.39	$3.51	$2.64	$2.40	$3.18
Tropisetron	-	-	$0.05	-	-	$0.04	$0.02
Average Schedule 2	*$1.40*	*$4.80*	*$10.05*	*$10.67*	*$12.91*	*$9.45*	*$8.21*

Source: Prepared for the Review using PBS patient-level data.

Patient age

Patients' age at the date of dispensing was calculated by deducting year of birth from the date of supply. The mean age of patients at the date of dispensing was calculated for each drug and overall for the period, July 2016 to June 2021. The mean age of patients at dispensing was 62.7 years for Schedule 1 medicines (see Figure A7), with 72% of medicines use being in patients over 60 years. Bleomycin, vinblastine and blinatumomab were dispensed to the youngest patients (mean age ranged from 38.0 to 48.5 years), which was unsurprising given that these medicines are used to treat acute leukemias and lymphomas, which predominately occur in children and young adults. Cabazitaxel, avelumab and ofatumumab were dispensed to the oldest patients (mean age ranged from 72.4 to 77.0 years). These medicines are used to treat prostate cancer, merkel cell carcinoma and chronic lymphocytic leukemia respectively.

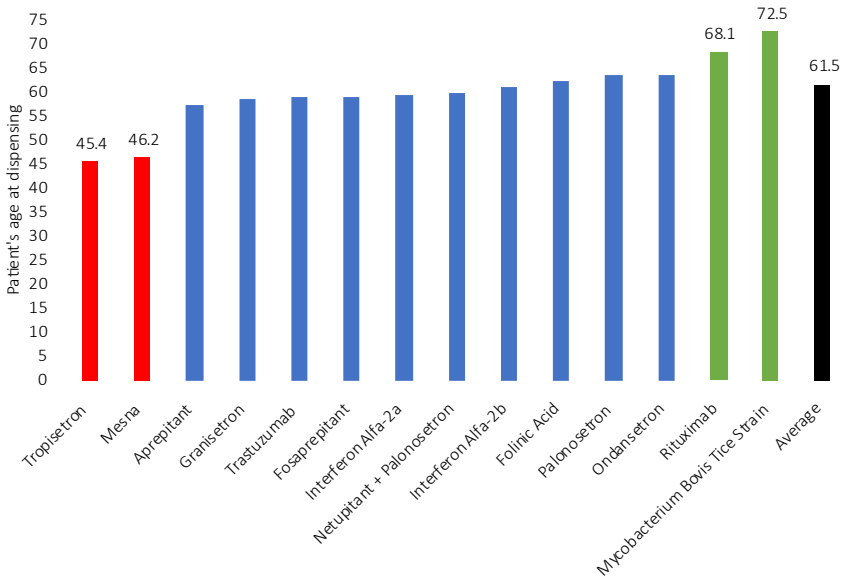
Figure A7. Mean patient age at dispensing by EFC item, Schedule 1 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

For Schedule 2 items, the mean patient age at dispensing was 61.5 years (see Figure A8). Tropisetron, which is used to treat vomiting and nausea during cytotoxic chemotherapy and mesna, which counteracts urothelial toxicity were dispensed to the youngest patients (mean age ranged from 45.4 to 46.2 years). Rituximab, which is to treat autoimmune conditions and blood cancers; and mycobacterium bovis (Bacillus Calmette and Guerin (BCG)) Tice strain, which treats superficial urothelial carcinoma of the bladder were dispensed to the oldest patients (mean age 68.1 to 72.5 years).

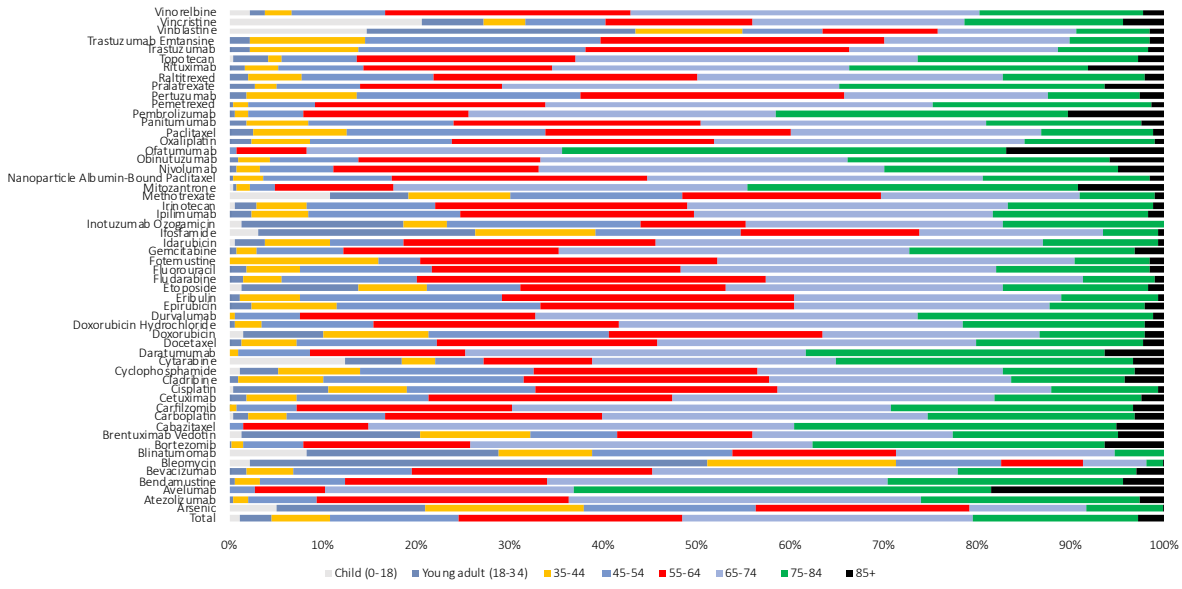
Figure A8. Mean patient age at dispensing by EFC item, Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

The age distribution for patients dispensed each of the Schedule 1 medicines is summarised in Figure A9. Overall, the largest age cohort for utilisation of EFC medicines was patients aged 65-74 years (31%), followed by patients aged 55-64 years (24%). Children (0-18 years) and young adults (18-34 years) made up approximately 4% of all dispensed items of Schedule 1 medicines.

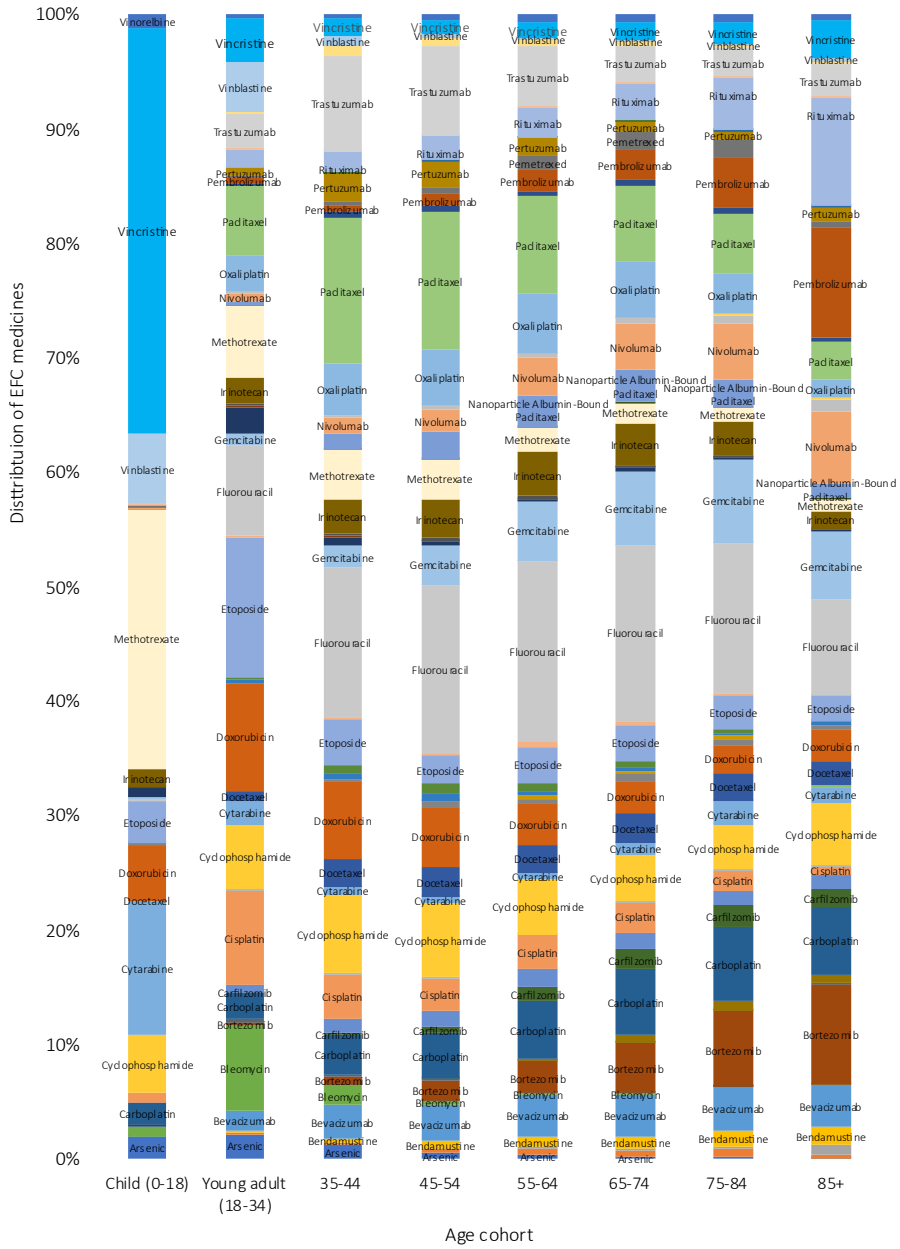
Figure A9. Distribution of patient ages by EFC item, Schedule 1 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.

A summary of the most commonly used medicines in each age cohort is provided in Figure A10. In children, the most commonly used medicines were vincristine (35%), methotrexate (23%) and cytarabine (11.7%). These medicines are commonly used for leukemias and lymphomas. In young adults, the most commonly used medicines are etoposide (12%), doxorubicin (9%) and cisplatin (8%), which are used to treat a variety of cancers. In the 35-44, 45-54, 55-64 and 65-74 age cohorts, the most commonly used medicines were fluorouracil, paclitaxel, gemcitabine and trastuzumab. These medicines are commonly used in the treatment of hormone-sensitive cancers such as colorectal, ovarian, uterine, testicular and breast cancers. In patients aged 85 years and over, the most commonly used medicines were pembrolizumab (10%), rituximab (9%), bortezomib (9%), used to treat a variety of solid tumours and blood cancers respectively.

Figure A10. Distribution of EFC items by age cohort, Schedule 1 (July 2016 - June 2021)



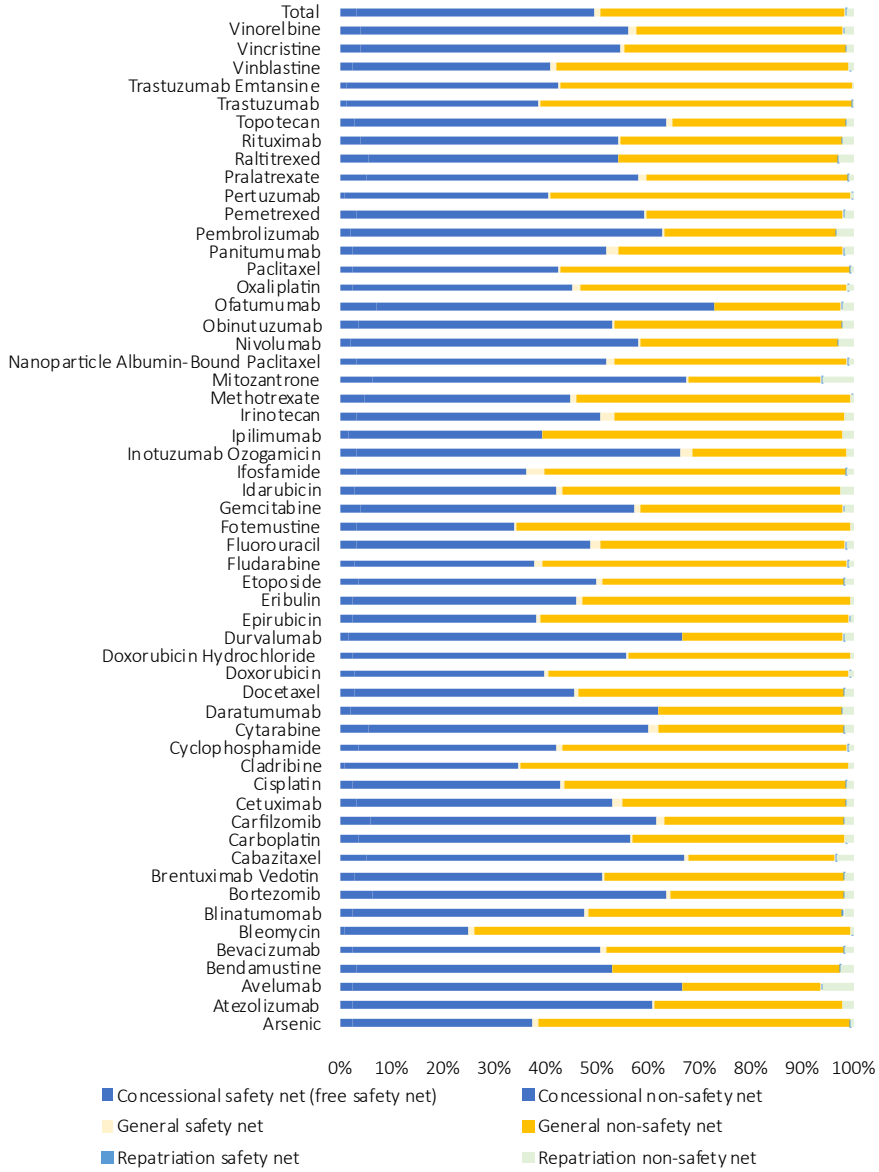
Source: Prepared for this Review using PBS patient-level data.

PBS concession status

Patient concession status for the payment of co-payments is classified as general patients, who pay the standard co-payment fee (currently $42.50), or concessional patients (co-payment of $6.80). For all PBS items, the co-payment amounts are reduced once annual out-of-pocket expenditure caps are reached: for general patients the current safety net is $1,542.10, beyond which the co-payment amount reverts to the concessional amount of $6.80; and for concessional patients, the current safety net is $326.40, beyond which there is no patient co-payment. Payment of co-payments for EFC

medicines is restricted to the initial prescription item only (not repeats). Prescriptions provided to patients under the Repatriation Pharmaceutical Benefits Scheme (RPBS) are subject to co-payments as per the concessional patient schedule. A breakdown of the patient categories under which prescriptions of Schedule 1 medicines were provided is depicted in Figure A11. Overall, general patients accounted for half of all patients accessing cancer medicines, the remainder being concessional (< 2% were covered under the RPBS).

Figure A11. Utilisation by item and patient concession status (July 2016 - June 2021)

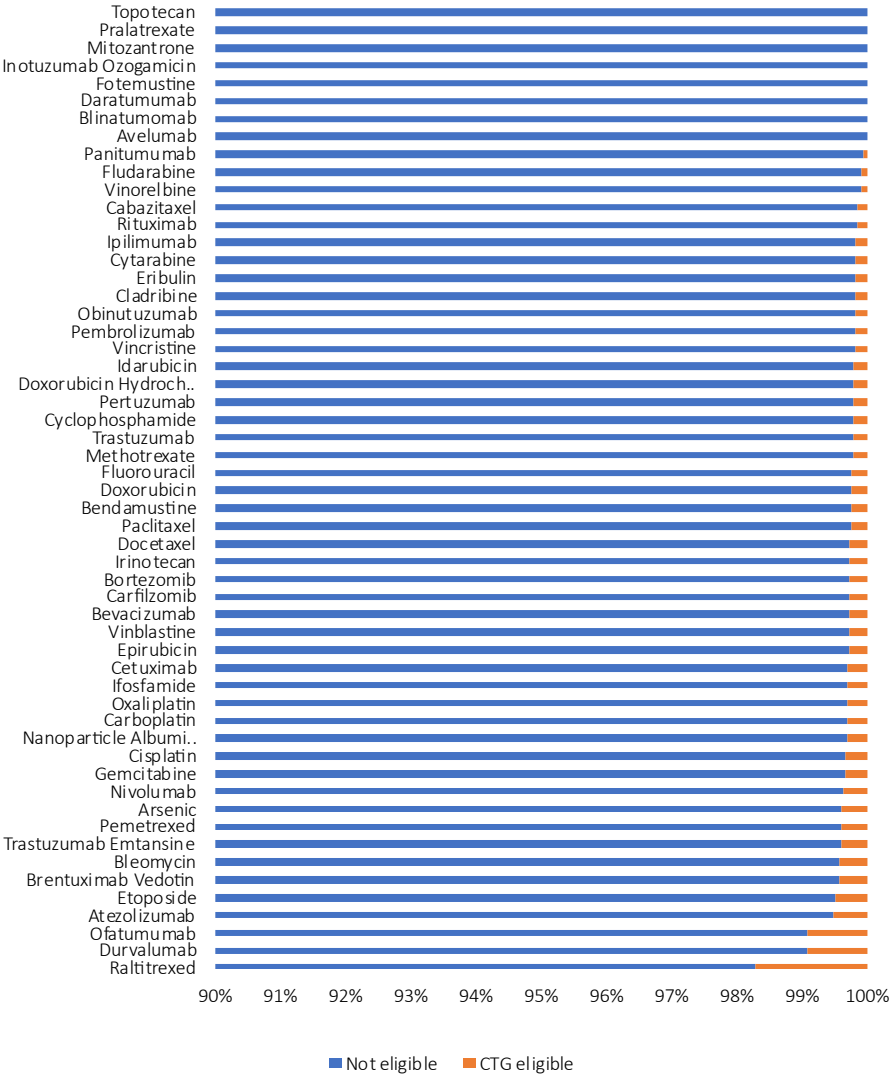


Source: Prepared for this Review using PBS patient-level data.

Utilisation by 'Close the Gap' (CTG) eligibility

A summary of Schedule 1 utilisation by CTG eligibility is provided in Figure A12. Overall, less than 0.3% of all PBS items dispensed for Schedule 1 medicines claimed the CTC benefit. Raltitrexed (1.7%), durvalumab (0.9%) and ofatumumab (0.9%), which are used to treat chest cancer and chronic lymphocytic leukemia, had the highest incidence of CTG claim. Daratumumab (0%), pralatrexate (0%) (which are used to treat blood cancers) and topotecan (0%) (used to treat ovarian cancer) had the lowest incidence of CTG claim.

Figure A12. Utilisation by item and CTG eligibility, Schedule 1 (July 2016 - June 2021)

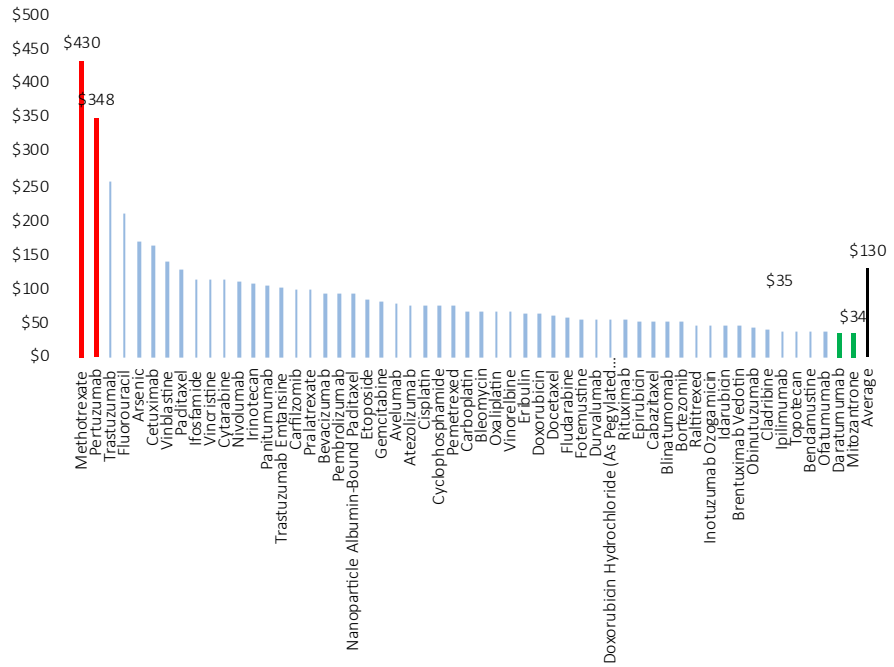


Source: Prepared for this Review using PBS patient-level data.

Patient out-of-pocket costs

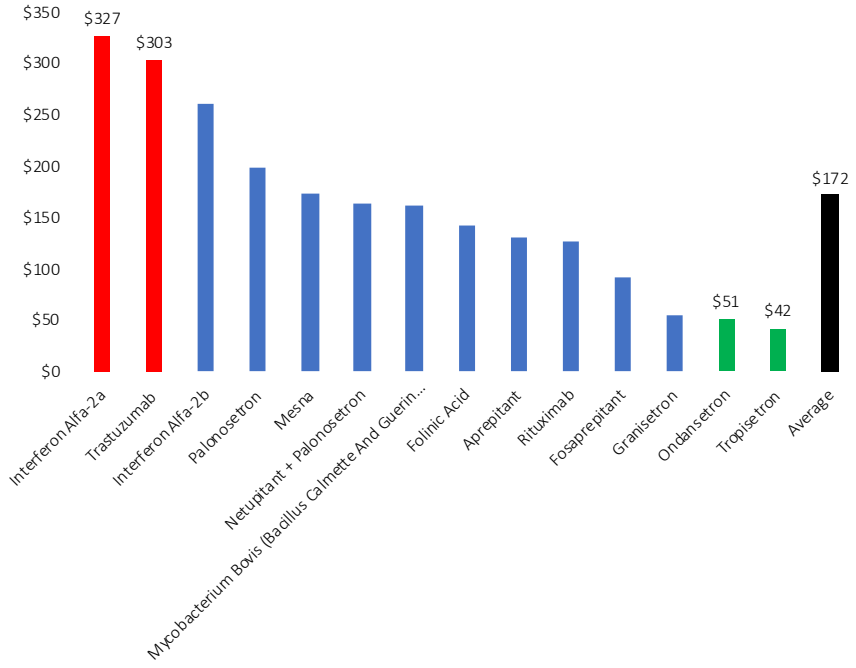
A summary of the average total out-of-pocket costs for Schedule 1 and Schedule 2 medicines is provided in Figure A13 and Figure A14, respectively. Methotrexate and pertuzumab had the highest average total out-of-pocket costs for Schedule 1 medicines. Interferon Alfa-2a and trastuzumab had the highest average total out-of-pocket costs for Schedule 2 medicines. A summary of the average total out-of-pocket costs per year is provided in Figure A15 and indicates that, overall, patients had a total average out-of-pocket totalling $342 over the 5 years (July 2016 to June 2021).

Figure A13. Mean patient out-of-pocket costs by EFC item, Schedule 1 (July 2016 - June 2021)



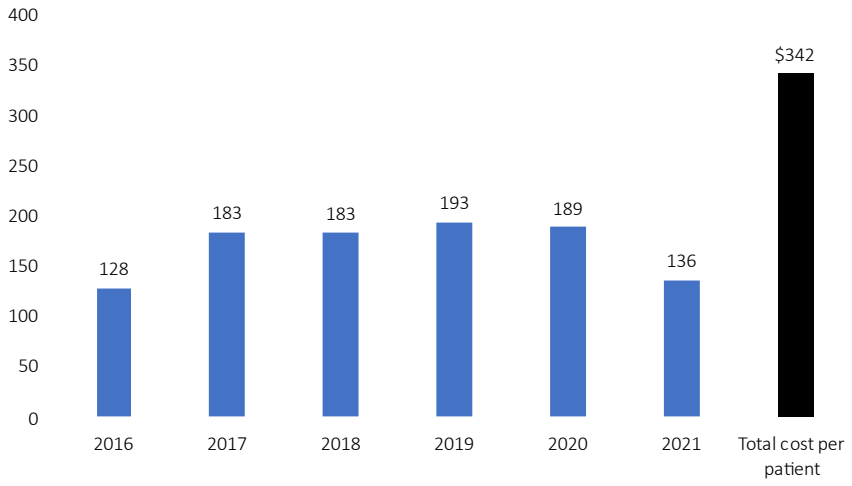
Source: Prepared for this Review using PBS patient-level data.
Note: Based on reported PBS patient co-payments.

Figure A14. Mean patient out-of-pocket costs, Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.
Note: Based on reported PBS patient co-payments.

Figure A15. Mean out-of-pocket costs (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.
Note: Based on reported PBS patient co-payments.

Utilisation by State and Territory

EFC drug (in grams) and service volumes over the period July 2016 to June 2021 are summarised by State and Territory in Table A13 and Table A14, respectively. Overall, states with the largest populations had the greatest consumption of EFC medicines.

Table A13. Quantity supplied (grams) by State and Territory, Schedule 1 (July 2016 - June 2021)

Drug Name	*ACT*	*NSW*	*NT*	*QLD*	*SA*	*TAS*	*Vic*	*WA*
Arsenic	-	101	2	80	35	8	78	39
Atezolizumab	64	10,400	250	5,779	3,057	579	8,447	4,426
Avelumab	21	2,117	31	1,655	283	211	796	337
Bendamustine	69	2,827	32	2,495	1,083	287	1,635	1,021
Bevacizumab	325	30,600	683	21,400	9,614	2,096	26,900	13,600
Bleomycin	3,140	208,000	5,569	161,000	50,500	14,400	171,000	75,900
Blinatumomab	-	94	-	36	18	11	110	16
Bortezomib	1,749	168,000	2,032	111,000	39,000	14,100	127,000	55,100
Brentuximab	1	154	-	61	31	11	133	46
Cabazitaxel	6	251	4	208	104	22	208	122
Carboplatin	424	42,800	722	29,900	12,000	2,822	31,200	13,600
Carfilzomib	24	2,407	20	1,939	537	238	1,858	728
Cetuximab	236	18,100	454	9,996	3,528	1,451	12,500	6,292
Cisplatin	34	3,828	99	2,939	1,041	236	2,629	2,353
Cladribine	0	10	0	6	3	1	8	3
Cyclophosph…	1,803	90,200	1,348	70,100	24,900	6,559	76,700	33,000
Cytarabine	42	20,000	40	29,500	2,286	471	7,714	5,061
Daratumumab	11	1,449	5	982	340	156	1,261	415
Docetaxel	161	5,326	107	3,872	1,137	424	4,250	2,618
Doxorubicin	98	5,696	99	3,861	1,609	398	4,417	1,940
Doxorubicin-Hydrochloride	5	479	4	252	117	40	292	299
Durvalumab	-	3,763	28	2,499	872	340	2,190	1,535
Epirubicin	49	710	14	483	367	62	514	387
Eribulin	0	23	0	21	6	2	17	13
Etoposide	110	11,900	182	8,357	2,672	807	7,234	4,264
Fludarabine	4	168	5	303	42	14	174	42
Fluorouracil	6,843	582,000	11,600	448,000	178,000	45,900	514,000	281,000
Fotemustine	-	22	2	2	4	2	6	11
Gemcitabine	4,489	159,000	2,186	105,000	42,200	9,731	109,000	71,200
Idarubicin	-	4	-	28	3	0	5	3
Ifosfamide	100	21,600	158	18,500	7,107	726	4,385	10,100
Inotuzumab	-	128	-	66	21	28	183	18
Ipilimumab	18	962	18	761	144	85	723	428
Irinotecan	123	16,800	332	11,100	5,162	1,581	14,600	7,239
Methotrexate	138	7,264	10	10,100	3,085	676	3,564	2,702
Mitozantrone	1	14	-	15	1	2	10	6
NAB Paclitaxel	99	7,219	117	5,857	2,142	688	6,179	3,821
Nivolumab	231	17,300	325	13,900	3,864	1,308	11,700	8,691
Obinutuzumab	223	8,345	66	6,380	2,480	507	5,034	2,375
Ofatumumab	33	195	26	659	325	13	86	86
Oxaliplatin	146	12,800	329	8,576	3,585	1,036	9,672	5,398
Paclitaxel	316	20,900	458	15,800	6,403	1,428	16,500	7,452
Panitumumab	23	3,416	75	3,053	1,672	348	1,655	1,566
Pembrolizumab	102	9,400	266	6,390	2,217	667	6,083	2,773
Pemetrexed	242	18,900	314	11,800	5,164	1,288	13,500	6,330
Pertuzumab	114	9,812	365	6,188	2,817	732	8,957	3,652
Pralatrexate	-	42	-	34	11	1	26	15
Raltitrexed	0	4	-	2	1	0	1	1
Rituximab	520	38,000	340	30,600	10,400	2,558	36,700	12,600
Topotecan	-	4,693	96	13,000	1,725	1,093	3,208	1,726
Trastuzumab	771	33,600	867	24,600	9,524	2,161	31,500	11,300
Trastuzumab-Emtansine	25	2,092	40	1,217	522	145	1,470	570
Vinblastine	2	76	2	67	22	6	85	32
Vincristine	1	52	1	53	17	4	60	27
Vinorelbine	6	364	6	368	168	43	354	247
Total (000s)	*22,9*	*1,604*	*29.7*	*1,211*	*444*	*119*	*1,289*	*665*

Source: Prepared for this Review using PBS patient-level data.

Note: Based on the reporting of dispensed amounts under PBS Regulation 24 (may underreport total grams supplied where the unit of reporting was packs and the PBS database does not reflect the actual pack strength provided).

Table A14. EFC service volume by State and Territory, Schedule 1 (July 2016 - June 2021)

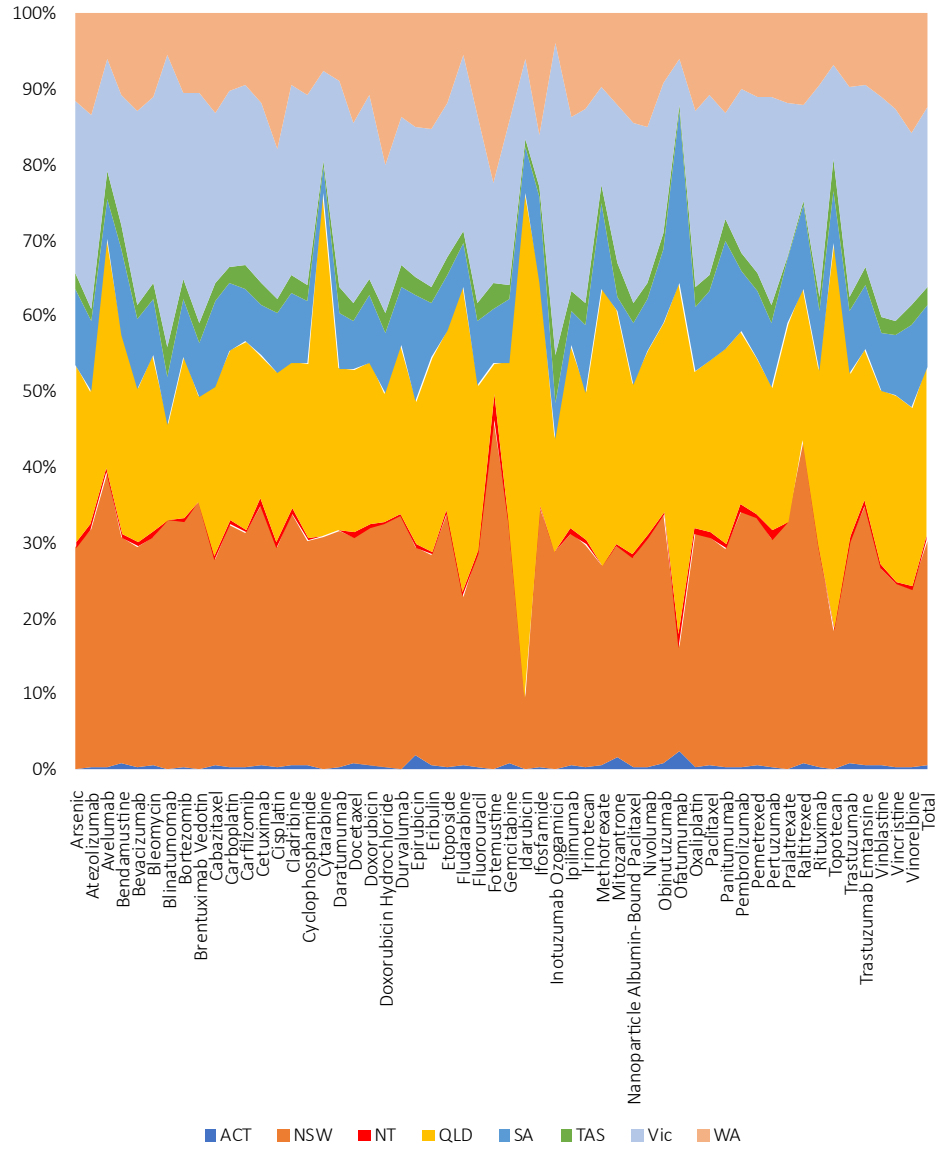
Drug Name	*ACT*	*NSW*	*NT*	*QLD*	*SA*	*TAS*	*Vic*	*WA*
Arsenic	-	8088	202	6588	2723	691	6434	3296
Atezolizumab	53	8573	208	5207	2510	477	6949	3657
Avelumab	33	2586	45	1923	367	266	995	394
Bendamustine	391	16997	180	14643	6471	1798	10334	6014
Bevacizumab	675	58374	1231	39661	18293	4152	53655	26308
Bleomycin	141	8924	224	6846	2216	646	7844	3207
Blinatumomab	-	131	-	53	26	15	154	23
Bortezomib	746	70060	753	45989	15984	5934	54479	22688
Brentuximab	4	1184	-	459	255	82	1009	354
Cabazitaxel	140	6565	94	5235	2821	606	5561	3175
Carboplatin	895	92872	1579	70092	26533	6944	73127	30378
Carfilzomib	322	24179	168	19582	5202	2271	19126	7048
Cetuximab	370	24952	621	14640	4447	1892	22508	10413
Cisplatin	389	46988	1130	37780	12761	2948	32839	27250
Cladribine	14	862	15	503	276	57	710	253
Cyclophosph…	1697	77613	1235	68149	22774	5425	75602	31166
Cytarabine	236	20948	545	18187	1974	1136	17852	5098
Daratumumab	9	1150	4	764	245	110	989	346
Docetaxel	1224	41237	811	31406	8612	3341	34049	20875
Doxorubicin	1124	72484	1056	44668	18016	4775	52212	25257
Doxorubicin-Hydrochloride	71	8323	62	4167	2169	704	5407	5060
Durvalumab	-	4967	34	3185	1143	426	2965	2032
Epirubicin	369	6002	89	3602	3740	428	4223	3221
Eribulin	146	8765	121	7890	2260	699	6705	4712
Etoposide	647	62988	1007	46405	15604	4221	40323	25209
Fludarabine	91	3581	103	6343	893	277	3923	889
Fluorouracil	2996	229641	4597	175934	68787	18174	216488	111621
Fotemustine	-	129	7	10	17	9	37	61
Gemcitabine	2431	96866	1325	64754	25729	6119	68769	43827
Idarubicin	-	188	7	1245	111	18	224	133
Ifosfamide	30	6584	46	6280	1953	264	1419	3242
Inotuzumab	-	78	-	44	12	13	138	6
Ipilimumab	79	4566	78	3428	752	396	3511	2099
Irinotecan	393	57228	1121	37823	17607	5471	50870	24960
Methotrexate	104	87163	173	12379	8821	23127	10420	5889
Mitozantrone	33	670	2	702	39	101	521	278
NAB Paclitaxel	567	39098	564	31954	11364	3670	34842	20458
Nivolumab	908	61015	1132	47662	13093	4348	41068	32194
Obinutuzumab	223	8379	66	6423	2490	509	5136	2386
Ofatumumab	36	210	26	706	342	14	98	100
Oxaliplatin	837	79015	1870	53445	21882	6551	62750	34125
Paclitaxel	2167	138586	2849	104887	42001	9561	110905	44129
Panitumumab	49	7701	180	6823	3714	767	3867	3760
Pembrolizumab	566	50744	1299	33712	11464	3556	31989	14708
Pemetrexed	270	21817	366	13458	5986	1549	15759	7279
Pertuzumab	262	22681	842	14357	6538	1704	20751	8484
Pralatrexate	-	780	-	642	196	14	557	281
Raltitrexed	12	682	-	311	162	10	195	203
Rituximab	724	52278	444	41706	14112	3539	53364	17493
Topotecan	-	1331	39	3383	702	257	1162	580
Trastuzumab	1691	75646	1996	55701	21017	4504	71398	25804
Trastuzumab-Emtansine	110	8689	177	4932	2100	613	6120	2334
Vinblastine	177	7360	151	6658	2379	607	8928	3358

Drug Name	*ACT*	*NSW*	*NT*	*QLD*	*SA*	*TAS*	*Vic*	*WA*
Vincristine	399	28489	279	29159	9875	2449	33515	16083
Vinorelbine	124	8477	148	8359	3910	932	8710	5480
Total (000s)	25	1775.5	31.3	1270.8	475.5	149.2	1403.5	699.7

Source: Prepared for this Review using PBS patient-level data.

The consumption of EFC medicines by state is proportional to the size of the population (see Figure A16); New South Wales and Victoria had the greatest consumption of PBS listed cancer medicines, whilst the Northern Territory and the Australian Capital Territory had the smallest consumption of medicines.

Figure A16. PBS distribution by EFC item and State and Territory, Schedule 1 (July 2016 - June 2021)



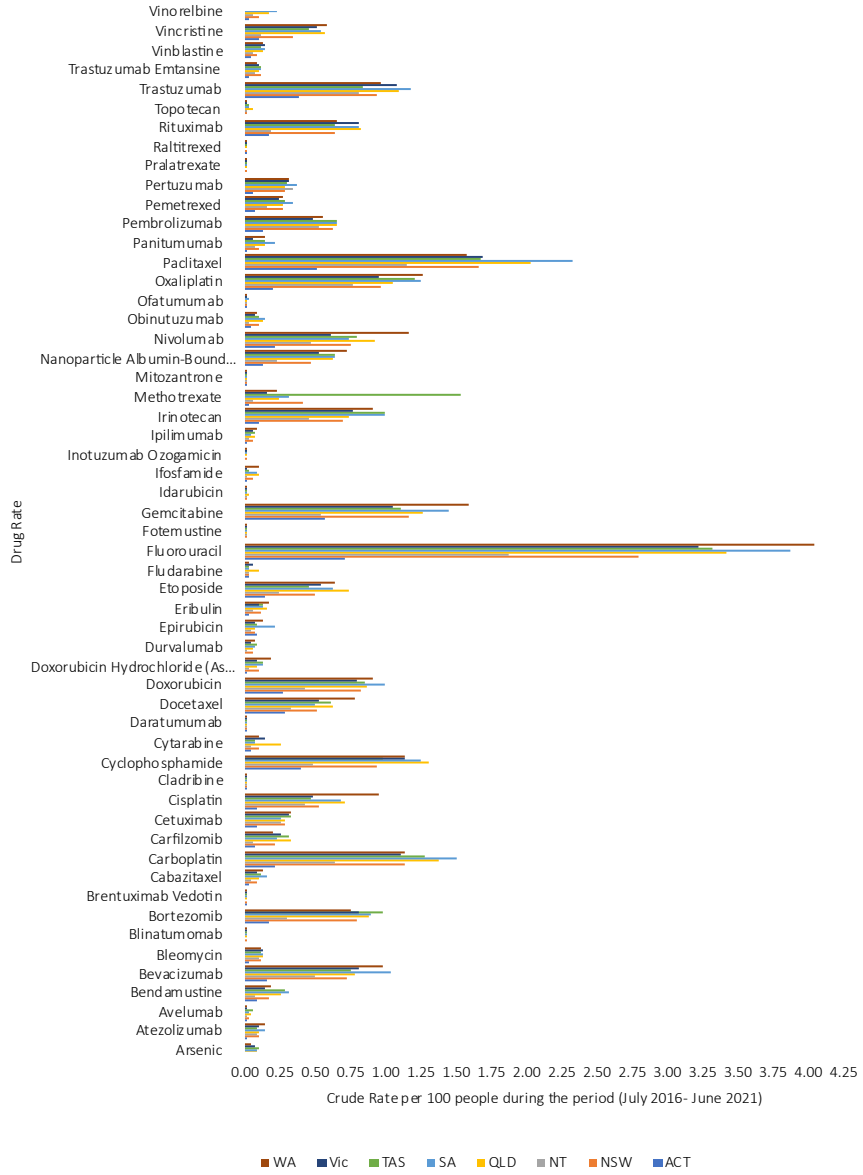
Source: Prepared for this Review using PBS patient-level data.
Note: Based on the reporting of dispensed amounts under PBS Regulation 24 (may underreport total grams supplied where the unit of reporting was packs and the PBS database does not reflect the actual pack

strength provided).

After adjusting for the size of the population in each state, the crude rates of Schedule 1 medicine use per 100 people differs between states and by drugs (see Figure A17). The medicines with the highest crude rates of use per 100 people in each state were fluorouracil, gemcitabine, paclitaxel and carboplatin. The three most commonly prescribed drugs in any state are summarised in Figure A18. After adjusting for population size, Western Australia had the highest crude rate of fluorouracil and gemcitabine use per 100 people. South Australia had the highest crude rate of carboplatin, paclitaxel and trastuzumab use per 100 people, while Tasmania had the highest crude rate of methotrexate use.

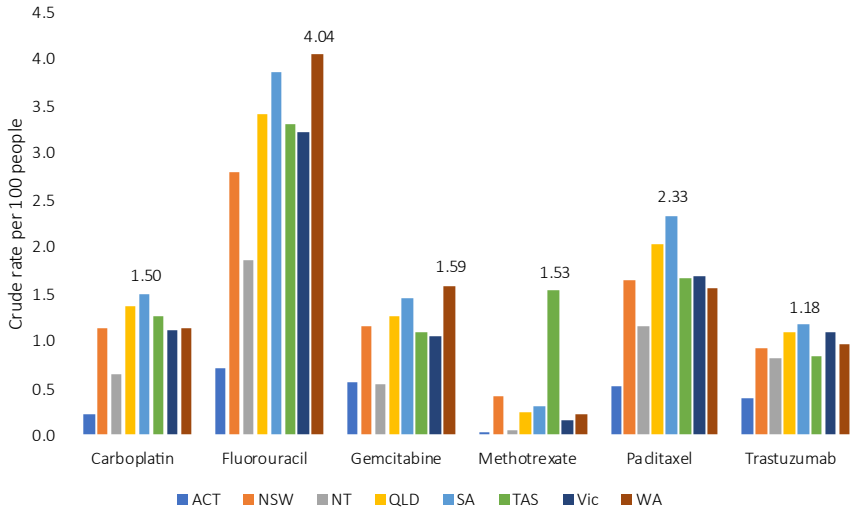
Figure A17. Use per 100 people (crude rate) by EFC item and State and Territory, Schedule 1 (July 2016 - June

2021)



Source: Prepared for this Review using PBS patient-level data.

Figure A18. Most common EFC items by State and Territory, Schedule 1 (July 2016 - June 2021)

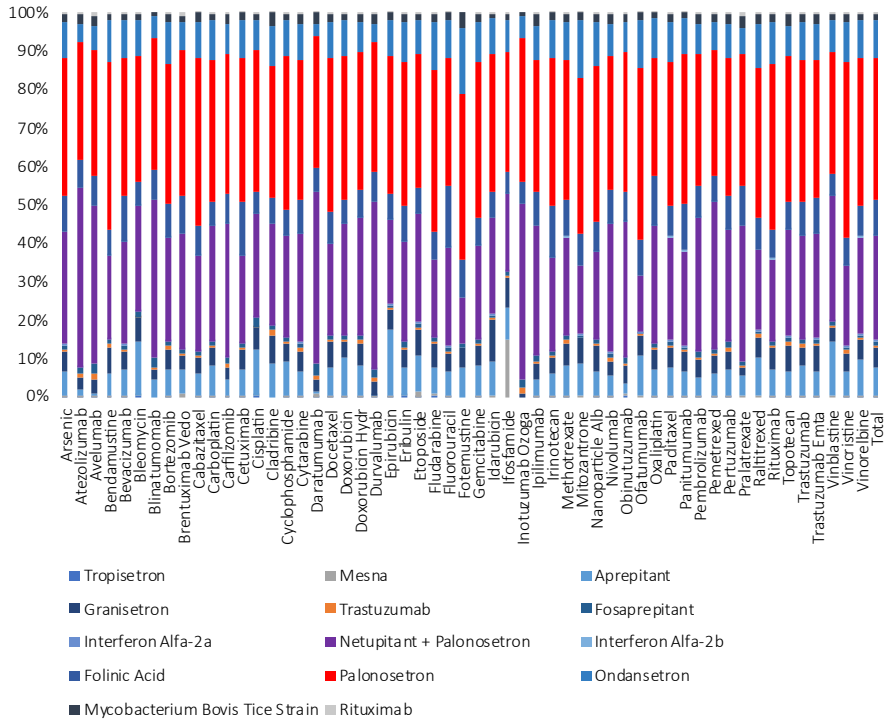


Source: Prepared for this Review using PBS patient-level data.

Utilisation of Schedule 2 medicines

A summary of the utilisation of Schedule 2 medicines (Related Benefit Items) according to concomitant Schedule 1 medicine use is provided in Figure A19. Overall, netupitant + palonosetron and palonosetron were the most commonly prescribed EFC-related items. These medicines reduce nausea and vomiting associated with cytotoxic chemotherapy.

Figure A19. Utilisation of Schedule 2 medicines by concomitant Schedule 1 medicine (July 2016 - June 2021)

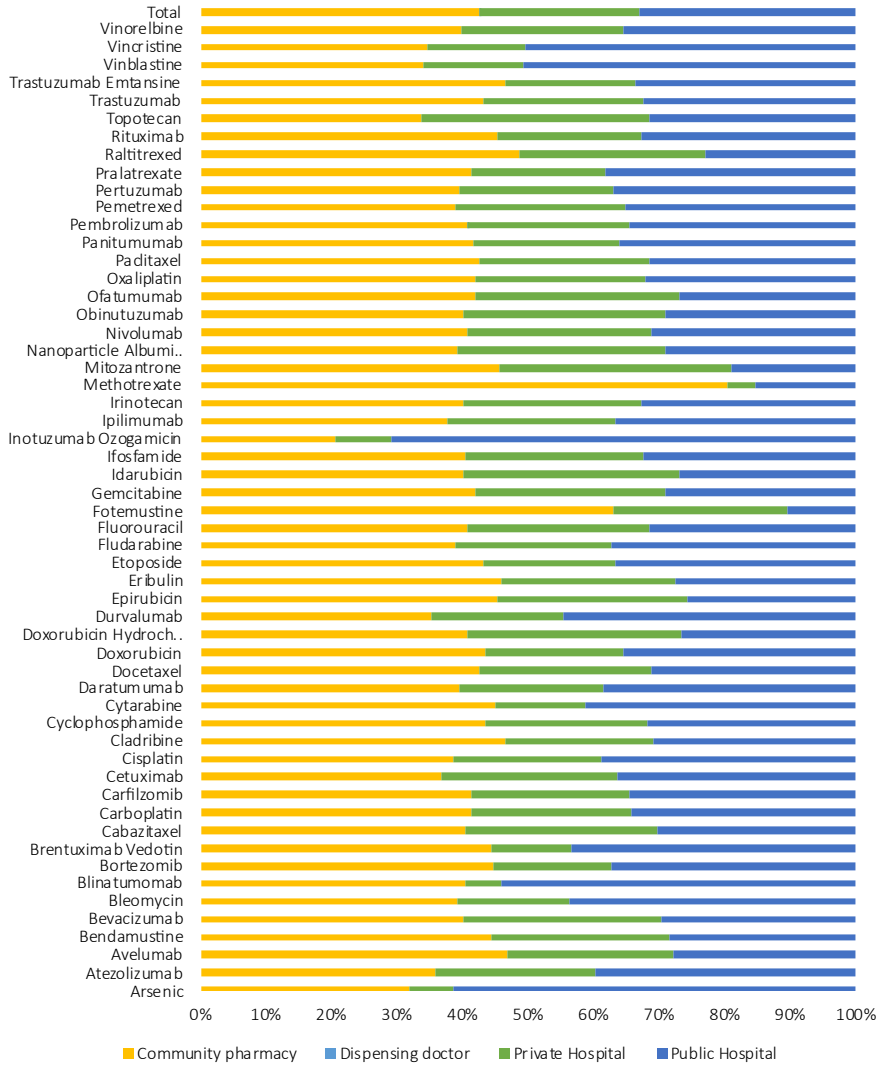


Source: Prepared for this Review using PBS patient-level data.

Utilisation by Pharmacy Approval Type

Under the PBS, claims may be lodged according to the following pharmacy types: s94 Participating public hospital; s94 Non-participating public hospital; s90 Approved community pharmacy; s90 Dispensing doctor; s90 Approved community pharmacy (flagged as a friendly society); s94 Private hospital. A summary of the utilisation of Schedule 1 medicines by pharmacy approval types is provided in Figure A20. The majority of patients (58%; 33% public and 25% private hospitals) received their Schedule 1 medicines from an s94 approved facility with the remainder receiving them from a community pharmacy (see Figure A20). In accordance with the underlying legislation, all Schedule 2 medicines were supplied via s94 public hospital facilities.

Figure A20. Distribution by EFC item and pharmacy setting, Schedule 1 (July 2016 - June 2021)

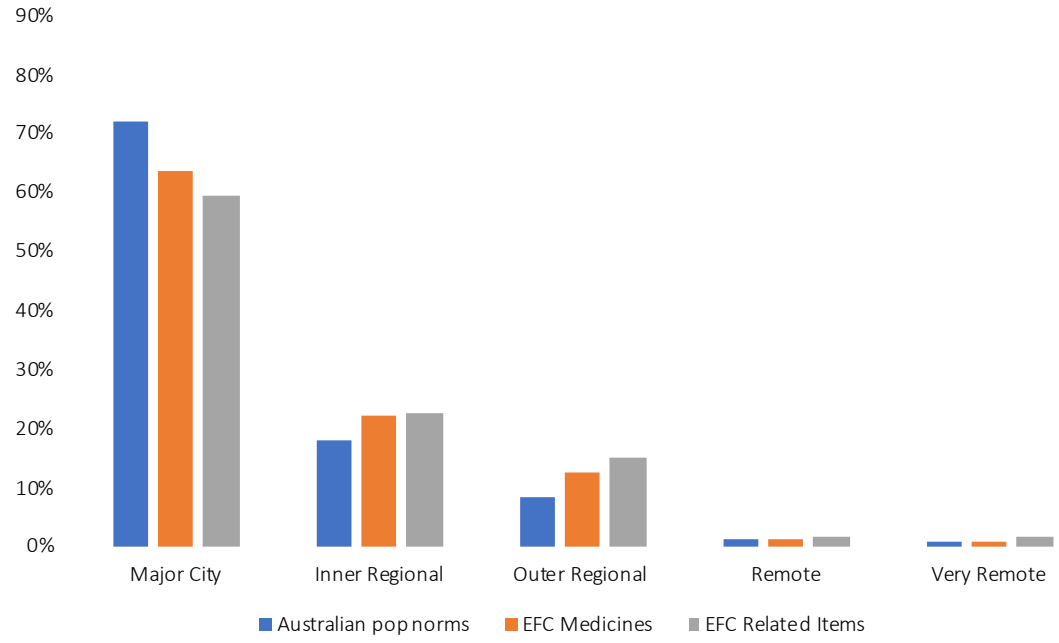


Source: Prepared for this Review using PBS patient-level data.

Access by remoteness

The distribution of patients accessing EFC listed medicines according to their ARIA score compared with Australian population norms is presented in Figure A21. From these data it can be observed that EFC patients tend to live in more rural and remote locations than the general Australian population.

Figure A21. EFC patient distribution by ARIA score (July 2016 - June 2021)

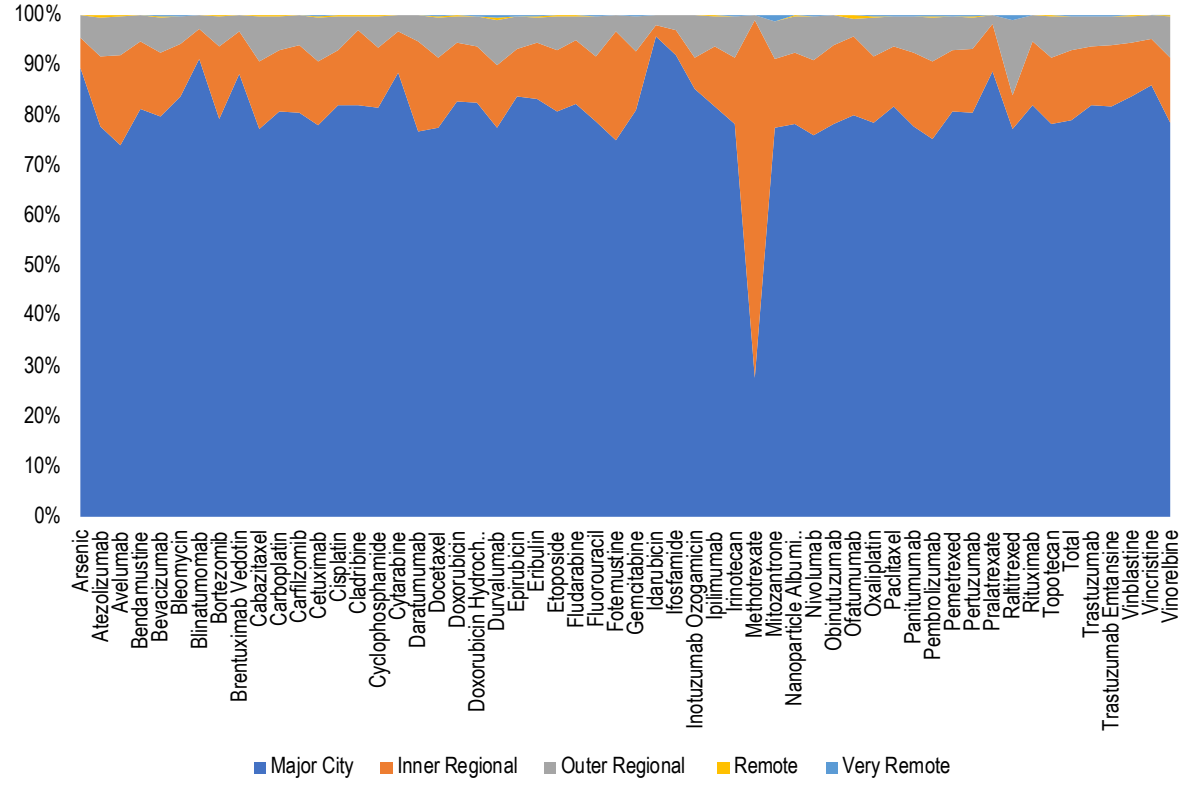


Source: Prepared for this Review using PBS patient-level data; AIHW, 2019 [69].
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

A summary of the distribution of EFC Schedule 1 medicine utilisation by ARIA score is provided in Figure A22. Overall, fotemustine and blinatumomab had the highest proportion of patients living in cities (70-71%), inotuzumab ozogamicin and avelumab had the highest proportion of patients living in inner regional areas (32-30%) while raltitrexed and ofatumumab had the highest proportion of patients living in outer regional areas (23-18%) and remote and very remote areas (4-3%), respectively.

Figure A22. Patient distribution by EFC item and remoteness of residence (ARIA), Schedule 1 (July 2016 - June

2021)

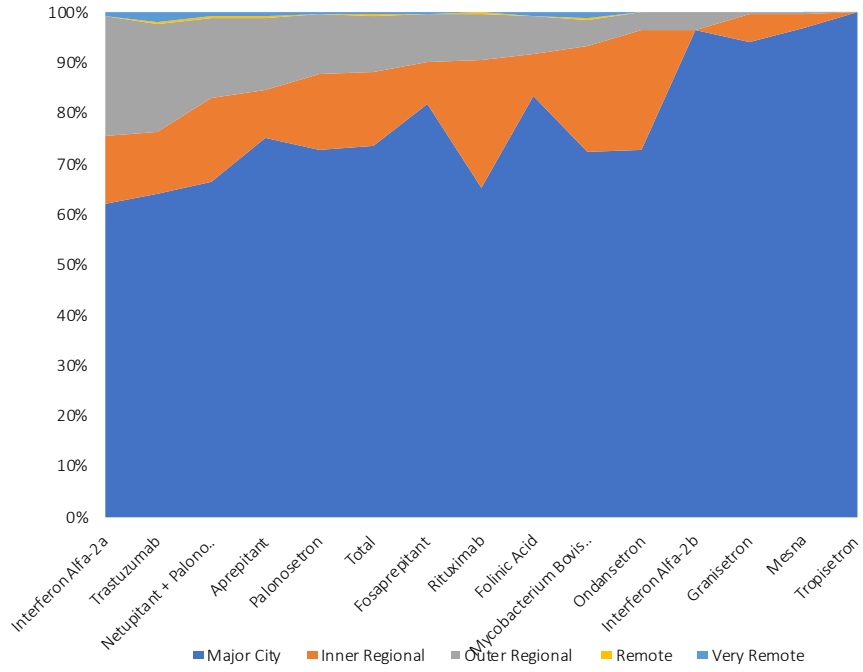


Source: Prepared for this Review using PBS patient-level data.
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

A summary of the utilisation of EFC Schedule 2 medicines by patients' ARIA scores is provided in Figure A23. Overall, interferon Alfa-2b and tropisetron had the highest proportion of patients living in major cities (75-85%), ondansetron and mycobacterium bovis had the highest proportion of patients living in inner regional areas (26-36%), fosaprepitant and mesna had the highest proportion of patients living in outer regional areas (10-15%), and aprepitant and fosaprepitant had the highest proportion of patients living in remote and very remote areas (5%).

Figure A23. Patient distribution by EFC item and remoteness of residence (ARIA), Schedule 2 (July 2016 - June

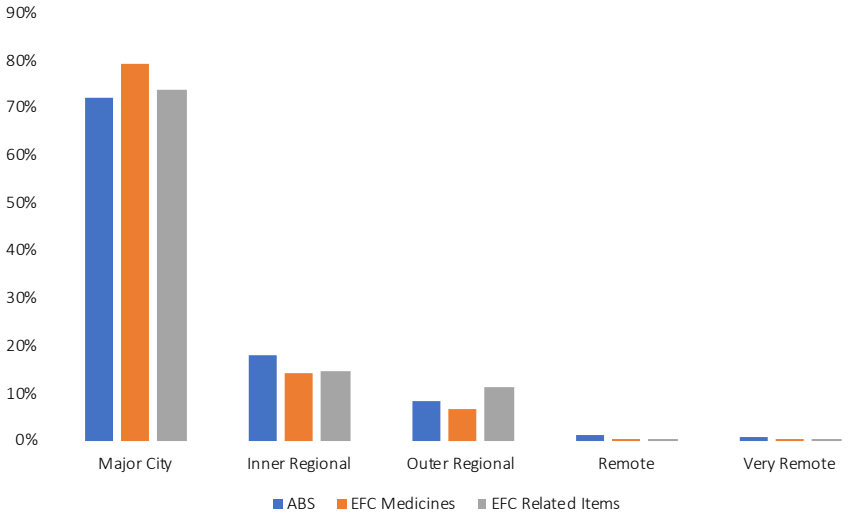
2021)



Source: Prepared for this Review using PBS patient-level data.
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

The distribution of pharmacies and hospitals dispensing EFC medicines by ARIA scores is compared with Australian population norms [48] in Figure A24. Overall, more pharmacies and hospitals dispensing EFC medicines were located in urban areas than Australian population norms.

Figure A24. Distribution of dispensing pharmacy by remoteness (ARIA) and service type (July 2016 - June 2021)

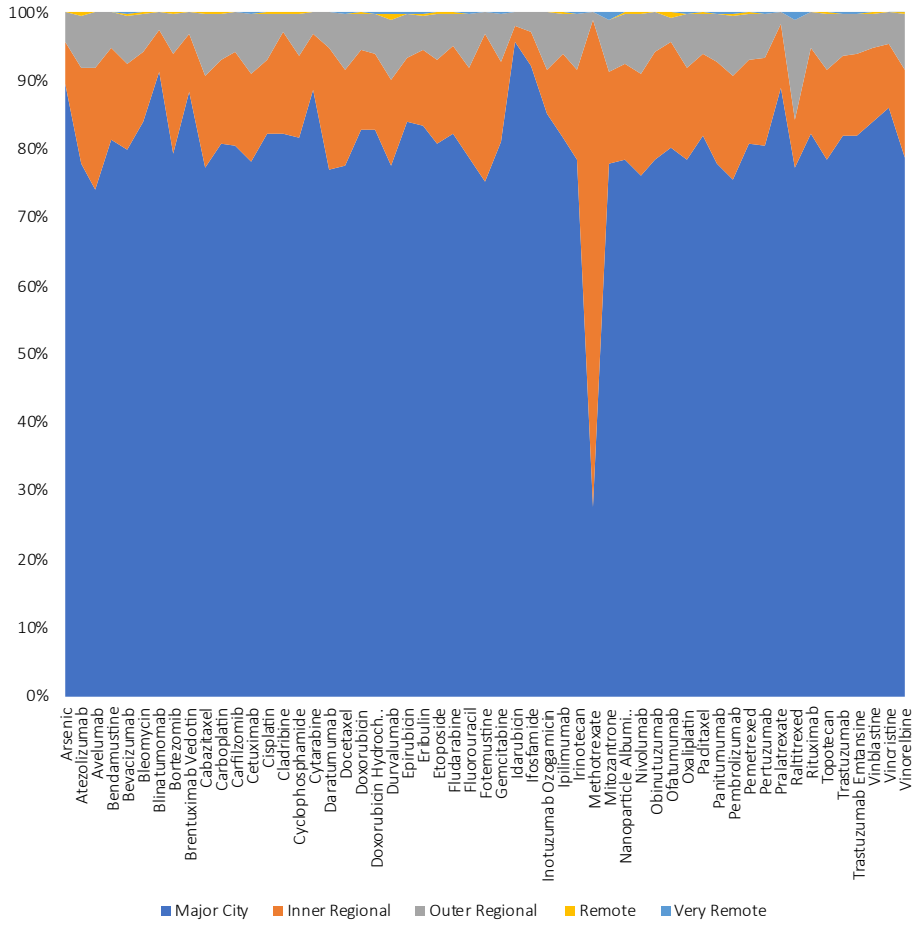


Source: Prepared for this Review using PBS patient-level data.

Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

The distribution of pharmacies and hospitals dispensing Schedule 1 medicines by ARIA score and medicine is provided in Figure A25. Overall, idarubicin and ifosfamide had the highest proportion of hospitals and pharmacies located in cities (96-92%%), methotrexate and fotemustine had the highest proportion of hospitals and pharmacies located inner regional areas (21%-71%%), while raltitrexed and cabazitaxel had the highest proportion of hospitals and pharmacies located in outer regional areas (9-15%).

Figure A25. Distribution of dispensing pharmacy by EFC item and remoteness (ARIA), Schedule 1 (July 2016 - June 2021)

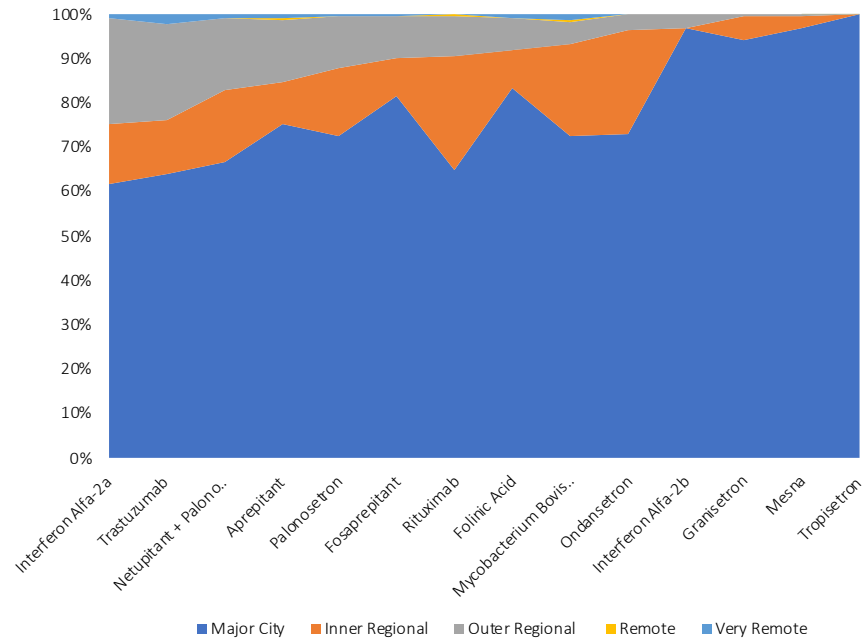


Source: Prepared for this Review using PBS patient-level data.
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

The distribution of pharmacies and hospitals dispensing Schedule 2 medicines is provided in Figure A26. Tropisetron and mesna had the highest proportion of hospitals and pharmacies located in cities

(97-100%), rituximab and ondansetron had the highest proportion of hospitals and pharmacies located inner regional areas (24-25%), with interferon Alfa-2a and trastuzumab having the highest proportion of hospitals and pharmacies located in outer regional areas (21-24%).

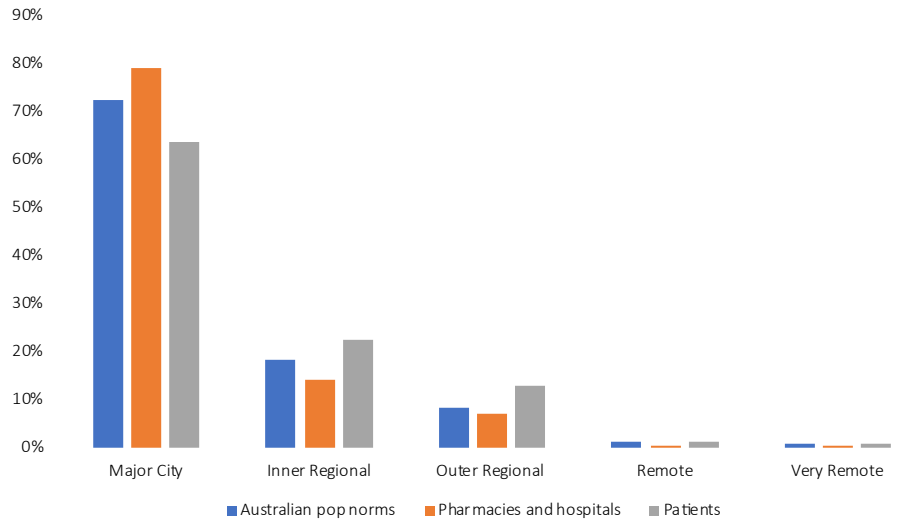
Figure A26. Distribution of dispensing pharmacy by EFC item and remoteness (ARIA), Schedule 2 (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

Whilst patients accessing cancer medicines are located in more rural locations than Australian population norms, hospitals and pharmacies dispensing these medicines are located in more urban areas than Australian population norms (see Figure A27).

Figure A27. Distribution of EFC patients and dispensing pharmacies by remoteness (ARIA) (July 2016 - June 2021)



Source: Prepared for this Review using PBS patient-level data.
Note: PBS reported patient post codes were converted to ABS ARIA classifications using a publicly available mapping algorithm.

Comparison of PBS claims and in-market sales

The purpose of this analysis was to compare PBS claims for cancer medicines via the EFC with in-market sales for those same medicines. Additionally, this analysis sought to determine the extent to which sales data can be used to reconcile claims for PBS use. This included a comparison of the price per mg as observed through the PBS claims data with that estimated from the in-market sales data.

In-market sales data were obtained from IQVIA as explained in the associated appendix to this Review. In summary, the data reflected in-market sales (manufacturer, wholesaler, third-party compounders, pharmacist and hospital entities) for cancer medicines (see Table A15.) sold during the period January 2016 to December 2021.

Table A15. Pack types by EFC item

Drug	*Pack Types*
Arsenic	PHENASEN COMP SOLN; PHENASEN IV INFUSION 10 MG 10 X 10 ML; ARSENIC TRIOXIDE JUNO VIAL 10 MG 10 X 10 ML
Atezolizumab	TECENTRIQ VIAL 1200 MG 20 ML; TECENTRIQ COMP SOLN; TECENTRIQ VIAL 840 MG 14 ML
Avelumab	BAVENCIO COMP SOLN; BAVENCIO VIAL 200 MG 10 ML
Bendamustine	RIBOMUSTIN COMP SOLN; RIBOMUSTIN VIAL 25 MG; RIBOMUSTIN VIAL 100 MG
Bevacizumab	AVASTIN COMP SOLN; AVASTIN VIAL 100 MG 4 ML; AVASTIN VIAL 400 MG 16 ML
Bleomycin	BLEOMYCIN SULPH VIAL 15 K; BLEO VIAL 15 K; BLEO COMP SOLN; BLEOMYCIN DBL COMP SOLN; WILLOW BLEOMYCIN COMP SOLN; BLEOMYCIN COMP SOLUTION; BLEOMYCIN CIPLA COMP SOLN; BLEOMYCIN CIPLA 15K VIAL; BLEOMYCIN FOR INJECTION USP COMP SOLN; BLEOMYCIN FOR INJECTION USP VIAL 15 U

Drug	*Pack Types*
Blinatumomab	BLINCYTO VIAL AND SOLUTION STABILISER 38.5 Y; BLINCYTO COMP SOLN
Bortezomib	VELCADE COMP SOLN; VELCADE PDR VIAL 3.5 MG; VELCADE PDR VIAL 1 MG; VELCADE PDR VIAL 3 MG
Brentuximab Vedotin	ADCETRIS VIAL 50 MG; ADCETRIS COMP SOLN
Cabazitaxel	JEVTANA VIAL 60 MG /1.5 1.83 ML; JEVTANA COMP SOLN
Carboplatin	DBL CARBOPLATIN VIAL 150 MG 15 ML; CARBOPLATIN KABI COMP SOLN; DBL CARBOPLATIN COMP SOLN; CARBACCORD VIAL 450 MG 45 ML; DBL CARBOPLATIN VIAL 450 MG 45 ML; DBL CARBOPLATIN VIAL 50 MG 5 ML; CARBACCORD VIAL 150 MG 15 ML; CARBOPLATIN EBEWE COMP SOLN; CARBOPLATIN VIAL 450 MG 45 ML; CARBOPLATIN COMP SOLN; CARBACCORD COMP SOLN; CARBOPLATIN VIAL 50 MG 5 ML; CARBOPLATIN ACCORD COMP SOLN; CARBOPLATIN ACCORD VIAL 450 MG 45 ML
Carfilzomib	KYPROLIS VIAL 60 MG; KYPROLIS VIAL 30 MG; KYPROLIS COMP SOLN; KYPROLIS VIAL 10 MG
Cetuximab	ERBITUX COMP SOLN; ERBITUX VIAL 500 MG 100 ML; ERBITUX VIAL 100 MG 20 ML
Cisplatin	CISPLATIN EBEWE VIAL 100 MG 100 ML; CISPLATIN VIAL 50 MG 50 ML; CISPLATIN COMP SOLN; CISPLATIN VIAL 100 MG 100 ML; CISPLATIN EBEWE COMP SOLN; CISPLATIN ACCORD COMP SOLN; CISPLATIN ACCORD CONCENTRATED INJECTION VIAL 50 MG 50 ML; CISPLATIN ACCORD CONCENTRATED INJECTION VIAL 100 MG 100 ML
Cladribine	LITAK VIAL 10 MG 5 ML; LEUSTATIN VIAL 10 MG 10 ML LITAK COMP SOLN LEUSTATIN COMP SOLN
Cyclophosphamide	ENDOXAN VIAL 2 G; ENDOXAN VIAL 1 G; ENDOXAN VIAL 500 MG; ENDOXAN COMP SOLN; CYCLOBLASTIN TABLETS 50 MG 50
Cytarabine	CYTARABINE FOT VIAL 100 MG 5 X 5 ML; CYTARABINE FOT COMP SOLN; CYTARABINE FOT VIAL 1000 MG /10M 10 ML; CYTARABINE COMP SOLN; CYTARABINE VIAL 2000 MG 20 ML; CYTARABINE VIAL 1000 MG 10 ML; CYTARABINE FOT VIAL 2000 MG /20M 20 ML; CYTOSAR U VIAL 1 G
Docetaxel	ONCOTAXEL VIAL 80 MG 4 ML; ONCOTAXEL VIAL 140 MG 7 ML; DBL DOCETAXEL VIAL 20 MG 2 ML; DBL DOCETAXEL COMP SOLN; DBL DOCETAXEL VIAL 80 MG 8 ML; ONCOTAXEL VIAL 20 MG 1 ML; DBL DOCETAXEL VIAL 160 MG 16 ML; TAXOTERE COMP SOLN; ONCOTAXEL COMP SOLN; TAXOTERE VIAL 20 MG 1 ML; AS-DOCETAXEL COMP SOLN; DOCETAXEL SANDOZ COMP SOLN; DOCETAXEL SUN VIAL 80 MG; DOCETAXEL SUN COMP SOLN; DOCETAXEL ACCORD COMP SOLN; DOCETAXEL ACCORD VIAL 160 MG 8 ML; DOCETAXEL ACCORD VIAL 80 MG 4 ML; DOCETAXEL ACCORD VIAL 20 MG 1 ML
Doxorubicin	CAELYX VIAL 50 MG 25 ML; ACCORD DOXORUBICIN COMP SOLN; CAELYX COMP SOLN; ADRIAMYCIN SOLN VIAL 50 MG 25 ML; L-DOXORUBICIN SUN VIAL 20 MG 10 ML; DOXORUBICIN MYX COMP SOLN; DOXORUBICIN VIAL 10 MG 5 ML; DOXORUBICIN VIAL 50 MG 25 ML; L-DOXORUBICIN SUN VIAL 50 MG 25 ML; CAELYX VIAL 20 MG 10 ML; ACCORD DOXORUBICIN VIAL 200 MG 100 ML; DOXORUBICIN COMP SOLN; DOXORUBICIN MYX VIAL 200 MG 100 ML; L-DOXORUBICIN SUN COMP SOLN; ACCORD DOXORUBICIN VIAL 10 MG 5 ML; ADRIAMYCIN SOLN VIAL 200 MG 100 ML; DOXORUBICIN EBEWE COMP SOLN; DOXORUBICIN SZ COMP SOLN; ADRIAMYCIN COMP SOLN
Durvalumab	IMFINZI COMP SOLN IMFINZI VIAL 120 MG 2.4 ML IMFINZI VIAL 500 MG 10 ML
Epirubicin	EPIRUBICIN ACTAVIS COMP SOLN; EPIRUBICIN ACT VIAL 50 MG 25 ML; EPIRUBICIN ACT VIAL 200 MG 100 ML; EPIRUBICIN ACTAVIS VIAL 100 MG 50 ML; EPIRUBICIN KABI COMP SOLN; EPIRUBICIN HCL INJECTION 50 MG 25 ML; DBL EPIRUBICIN VIAL 200 MG 100 ML; PHARMORUBICIN RD VIAL 50 MG; PHARMORUBICIN SOLUTION 50 MG 25 ML; DBL EPIRUBICIN COMP SOLN; EPIRUBICIN COMP SOLUTION; EPIRUBICIN HCL COMP SOLN; EPIRUBICIN ACT COMP SOLN; PHARMORUBICIN COMP SOLN; EPIRUBICIN SZ COMP SOLN; PHARMORUBICIN SOLUTION 200 MG 100 ML; EPIRUBICIN ACCORD COMP SOLN; EPIRUBE COMP SOLN; EPIRUBE VIAL 200 MG 100 ML; EPIRUBE VIAL 50 MG 25 ML; EPIRUBICIN ACCORD VIAL 200 MG 100 ML
Eribulin	HALAVEN VIAL 1 MG 2 ML; HALAVEN COMP SOLN

Drug	*Pack Types*
Etoposide / Etoposide Phosphate	ETOPOSIDE COMP SOLUTION; ETOPOSIDE EBEWE COMP SOLN; ETOPOSIDE EBEWE VIAL 100 MG 5 X 5 ML; ETOPOSIDE VIAL 100 MG 5 ML; ETOPOSIDE EBEWE VIAL 100 MG 5 ML; ETOPOSIDE COMP SOLN ETOPOPHOS COMP SOLN; ETOPOPHOS PDR VIAL 114 MG; ETOPOPHOS PDR VIAL 1136 MG
Fludarabine	FLUDARABINE ACTAV INJECTION 50 MG 5; FLUDARABINE ACT COMP SOLN; FARINE COMP SOLN; FLUDARABINE EBEWE INJECTION 50 MG 5 X 2 ML; FLUDARABINE ACTAV INJECTION 50 MG; FLUDARABINE EBEWE COMP SOLN; FLUDARABINE ACT VIAL 50 MG; FARINE INJECTION 50 MG; FLUDARABINE EBEWE INJECTION 50 MG 2 ML; FLUDARABINE COMP SOLUTION; FLUDARABINE AMNEAL COMP SOLN; FLUDARABINE AMNEAL VIAL 50 MG 2 ML; FLUDARABINE JUNO VIAL 50 MG 5 ML; FLUDARABINE JUNO COMP SOLN
Fluorouracil	FLUOROURACIL VIAL 2500 MG 50 ML; FLUOROURACIL COMP SOLN; FLUOROURACIL VIAL (OLD) 500 MG 5 X 10 ML; FLUOROURACIL EBEWE VIAL 5000 MG 100 ML; FLUOROURACIL VIAL 2500 MG 100 ML; FLUOROURACIL VIAL 1000 MG 5 X 20 ML; FLUOROURACIL EBEWE COMP SOLN; APO-APOC-5FU CREAM 5 % 20 G; FLUOROURACIL ACCORD COMP SOLN; FLUOROURACIL ACCORD INJECTION VIAL 1000 MG 20 ML; FLUOROURACIL ACCORD INJECTION VIAL 2500 MG 50 ML; FLUOROURACIL ACCORD INJECTION VIAL 5000 MG 100 ML; FLUOROURACIL-PC CREAM 5 % 20 G
Fotemustine	MUPHORAN VIAL 208 MG; MUPHORAN COMP SOLN; FOTEMUSTINE SOLUTION
Gemcitabine	GEMACCORD VIAL 200 MG; DBL GEMCITABINE VIAL 2 G 52.6 ML; GEMCITABINE ACTAV VIAL 1 G; DBL GEMCITABINE VIAL 200 MG 5.3 ML; DBL GEMCITABINE VIAL 1 G 26.3 ML; DBL GEMCITABINE COMP SOLN; GEMACCORD VIAL 1 G; GEMCITABINE ACTAV VIAL 2 G; DBL GEMCITABINE VIAL 1 G; DBL GEMCITABINE VIAL 2 G; DBL GEMCITABINE VIAL 200 MG; GEMCITABINE KABI COMP SOLN; GEMCITABINE ACTAV COMP SOLN; AS-GEMCITABINE COMP SOLN; GEMACCORD COMP SOLN; GEMCITABINE EBEWE COMP SOLN; GEMCITABINE SUN COMP SOLN
Idarubicin	IDARUBICIN EBEWE COMP SOLN; ZAVEDOS SOLN VIAL 5 MG 5 ML; ZAVEDOS SOLN VIAL 10 MG 10 ML; ZAVEDOS COMP SOLN; IDARUBICIN EBEWE VIAL 10 MG 10 ML; ZAVEDOS VIAL 10 MG; IDARUBICIN EBEWE VIAL 5 MG 5 ML; IDARUBICIN COMP SOLUTION
Ifosfamide	HOLOXAN VIAL 1 G; HOLOXAN COMP SOLN; HOLOXAN VIAL 2 G; IFOSFAMIDE COMP SOLUTION
Inotuzumab Ozogamicin	BESPONSA VIAL 1 MG 20 ML
Ipilimumab	YERVOY COMP SOLN; YERVOY VIAL 200 MG 40 ML; YERVOY VIAL 50 MG 10 ML; IPILIMUMAB SOLUTION
Irinotecan	IRINOTECAN MYX COMP SOLN; IRINOTECAN VIAL 100 MG 5 ML; IRINOCCORD VIAL 100 MG 5 ML; IRINOTECAN VIAL 500 MG 25 ML; IRINOTECAN ALPHAPHARM VIAL 100 MG 5 ML; IRINOTECAN ALPHAPHARM VIAL 500 MG 25 ML; IRINOTECAN MYX VIAL 100 MG 5 ML; CAMPTOSAR VIAL 300 MG 15 ML; IRINOTECAN VIAL 40 MG 2 ML; IRINOTECAN COMP SOLN; TECAN VIAL 100 MG 5 ML; IRINOCCORD VIAL 40 MG 2 ML; IRINOTECAN ACTAVIS VIAL 500 MG 25 ML; IRINOTECAN ACTAVIS VIAL 100 MG 5 ML; IRINOTECAN COMP SOLUTION; IRINOTECAN ACTAVIS COMP SOLN; IRINOTECAN EBEWE COMP SOLN; IRINOTECAN ALPHAPHARM COMP SOLN; IRINOCCORD COMP SOLN; IRINOTECAN KABI COMP SOLN; IRINOTECAN MEDITAB VIAL 100 MG 5 ML; IRINOTECAN MEDITAB COMP SOLN; IRINOTECAN ACCORD COMP SOLN; IRINOTECAN ACCORD VIAL 100 MG 5 ML; OMEGAPHRM IRINOTEC COMP SOLN; ONIVYDE VIAL 43 MG 10 ML ONIVYDE COMP SOLN
Methotrexate	METHACCORD VIAL 50 MG 2 ML; METHOTREXATE EBEWE INFUSION 5000 MG 50 ML; DBL METHOTREXATE VIAL 5 MG 5 X 2 ML; METHOTREXATE VIAL 50 MG 5 X 2 ML; DBL METHOTREXATE VIAL 50 MG 5 X 2 ML; METHACCORD VIAL 1000 MG 10 ML; METHACCORD COMP SOLN; DBL METHOTREXATE COMP SOLN; METHOTREXATE VIAL 1000 MG 10 ML; DBL METHOTREXATE VIAL 500 MG 20 ML; METHOTREXATE MYX INJ VIAL 50 MG /2ML 2 ML; DBL METHOTREXATE VIAL 1000 MG 10 ML; METHOTREXATE MYX COMP SOLN; METHOTREXATE MYX INJ VIAL 1000 MG /10M 10 ML; METHOTREXATE COMP SOLN; TREXJECT PREFILL SYR 10 MG 0.2 ML; METHOTREXATE EBEWE COMP SOLN; TREXJECT PREFILL SYR 25 MG 0.5 ML; TREXJECT PREFILL SYR 15 MG 0.3 ML; TREXJECT

Drug	*Pack Types*
	PREFILL SYR 20 MG 0.4 ML; TREXJECT PREFILL SYR 7.5 MG 0.15 ML; METHOTREXATE ACCORD VIAL 1 G 10 ML; DBL METHOTREXATE TABLETS 2.5 MG 30; METHOTREXATE ACCORD VIAL 50 MG 2 ML; METHOBLASTIN PFS 7.5 MG 4 X 0.3 ML; METHOBLASTIN PFS 25 MG 4 X 1 ML; METHOBLASTIN PFS 25 MG 1 ML; METHOBLASTIN PFS 10 MG 4 X 0.4 ML; METHOBLASTIN PFS 20 MG 4 X 0.8 ML; METHOBLASTIN PFS 15 MG 4 X 0.6 ML; METHOBLASTIN PFS 20 MG 0.8 ML; METHOBLASTIN PFS 10 MG 0.4 ML
Nivolumab	OPDIVO IV VIAL 40 MG 4 ML; OPDIVO IV VIAL 100 MG 10 ML; OPDIVO COMP SOLN
Obinutuzumab	GAZYVA VIAL 1 G 40 ML; GAZYVA COMP SOLN
Oxaliplatin	OXALIPLATIN SUN I V SOLUTION 100 MG 20 ML; DBL OXALIPLATIN COMP SOLN; OXALIPLATIN SZ COMP SOLN; OXALIPLATIN SUN I V SOLUTION 50 MG 10 ML; OXALIPLATIN MYX COMP SOLN; OXALICCORD COMP SOLN; DBL OXALIPLATIN I V SOLUTION 100 MG 20 ML; OXALICCORD VIAL 100 MG 20 ML; DBL OXALIPLATIN I V SOLUTION 50 MG 10 ML; OXALIPLATIN SZ VIAL 100 MG 20 ML; OXALIPLATIN EBEWE COMP SOLN; ELOXATIN SOLUTION 100 MG 20 ML; OXALIPLATIN SUN I V SOLUTION 200 MG 40 ML; OXALICCORD VIAL 50 MG 10 ML; OXALIPLATIN PDR VIAL 100 MG; OXALIPLATIN PDR VIAL 50 MG; ELOXATIN SOLUTION 200 MG 40 ML; OXALIPLATIN KABI COMP SOLN; OXALIPLATIN SUN COMP SOLN; OXALIPLAN COMP SOLN; ELOXATIN COMP SOLN; OXALIPLATIN ACCORD COMP SOLN; OXALIPLATIN ACCORD VIAL 100 MG 20 ML; OXALIPLATIN LINK COMP SOLN; OXALATIN COMP SOLN
Paclitaxel	ABRAXANE VIAL 100 MG; ANZATAX COMP SOLN; PACLITAXEL ACTAVIS VIAL 150 MG 25 ML; ANZATAX VIAL 150 MG 25 ML; ABRAXANE COMP SOLN; PLAXEL VIAL 100 MG 16.7 ML; PACLITAXEL ACTAVIS VIAL 300 MG 50 ML; ANZATAX VIAL 30 MG 5 ML; ANZATAX VIAL 300 MG 50 ML; PACLITAXEL ACTAVIS VIAL 30 MG 5 ML; PLAXEL VIAL 30 MG 5 ML; PACLITAXEL ACTAVIS VIAL 100 MG 16.7 ML; PACLITAXEL EBEWE VIAL 300 MG 50 ML; PACLITAXEL ACTAVIS COMP SOLN; PACLITAXEL EBEWE COMP SOLN; PACLITAXEL KABI COMP SOLN; PACLITAXEL ACCORD COMP SOLN; PACLITAXIN VIAL 30 MG 5 ML; PACLITAXIN VIAL 100 MG 16.7 ML; PACLITAXIN VIAL 300 MG 50 ML; PACLITAXEL ACCORD VIAL 300 MG 50 ML; PACLITAXIN VIAL 150 MG 25 ML; PACLITAXEL ACCORD VIAL 100 MG 16.7 ML
Panitumumab	VECTIBIX COMP SOLN; VECTIBIX VIAL 400 MG 20 ML; VECTIBIX VIAL 100 MG /5ML 5 ML; KEYTRUDA INJ VIAL 50 MG; KEYTRUDA COMP SOLN; KEYTRUDA VIAL 100 MG 4 ML
Pemetrexed	PEMETREXED MYX COMP SOLN; ALIMTA VIAL 100 MG; ALIMTA VIAL 500 MG; PEMETREXED MYX DRY VIAL 500 MG; PEMETREXED SANDOZ PDR VIAL 500 MG; PEMETREXED MYX DRY VIAL 100 MG; PEMETREXED JUNO VIALS 500 MG; DBL PEMETREXED COMP SOLN; ALIMTA COMP SOLN; APO-PEMETREXED VIAL 500 MG; PEMETREXED JUNO VIALS 100 MG; APO-PEMETREXED VIAL 100 MG; PEMETREXED SOLUTION; DBL PEMETREXED VIALS 1000 MG; DBL PEMETREXED VIALS 100 MG; DBL PEMETREXED VIALS 500 MG; RELADDIN INJECTION 100 MG; RELADDIN INJECTION 500 MG; PEMETREXED ACCORD COMP SOLN; APO-PEMETREXED COMP SOLN; PEMETREXED JUNO COMP SOLN; PEMETREXED DRLA COMP SOLN; PEMETREXED MYX DRY VIAL 1000 MG; PEMETREXED SANDOZ COMP SOLN; PEMETREXED DRLA DRY VIAL 500 MG; PEMETREXED DRLA DRY VIAL 100 MG; TEVATREXED COMP SOLN; PEMETREXED ACCORD VIAL 500 MG; PEMETREXED ACCORD VIAL 1 G; PEMETREXED ACCORD VIAL 100 MG; TEVATREXED VIAL 500 MG; PEMETREXED SUN VIAL 100 MG; PEMETREXED SUN VIAL 500 MG; PEMETREXED SUN COMP SOLN; PEMETREXED SUN VIAL 1 G
Pertuzumab	PERJETA COMP SOLN; PERJETA VIAL 420 MG 14 ML
Pralatrexate	FOLOTYN VIAL 20 MG 1 ML; FOLOTYN COMP SOLN
Raltitrexed	TOMUDEX COMP SOLN; TOMUDEX VIAL 2 MG
Rituximab	MABTHERA VIAL 500 MG 50 ML; MABTHERA VIAL 100 MG 2 X 10 ML; MABTHERA COMP SOLN; MABTHERA SC INJECTION 1400 MG 11.7 ML; RIXIMYO VIAL 500 MG 50 ML; RIXIMYO COMP SOLN; RIXIMYO VIAL 100 MG 2 X 10 ML; TRUXIMA VIALS 500 MG 50 ML; TRUXIMA VIALS 100 MG 2 X 10 ML; TRUXIMA COMP SOLN
Topotecan	HYCAMTIN COMP SOLN; HYCAMTIN IV INFUS PDR 4 MG 5; TOPOTECAN-KABI COMP SOLN; TOPOTECAN AGILA COMP SOLN; TOPOTECAN ACCORD VIAL 4 MG 5 X 4 ML
Trastuzumab	HERCEPTIN VIAL 60 MG; HERCEPTIN COMP SOLN; HERCEPTIN VIAL 150 MG; HERCEPTIN SC INJECTION 600 MG 5 ML; OGIVRI LYT VIAL 150 MG; OGIVRI COMP SOLN; HERZUMA

Drug	*Pack Types*
	POWDER FOR INJECTION VIAL 150 MG; HERZUMA COMP SOLN; ONTRUZANT COMP SOLN; KANJINTI VIAL 420 MG; KANJINTI VIAL 150 MG; KANJINTI COMP SOLN; TRAZIMERA VIAL 150 MG 15 ML; TRAZIMERA VIAL 60 MG 8 ML; ONTRUZANT VIAL 150 MG
Trastuzumab Emtansine	KADCYLA VIAL 100 MG 5 ML; KADCYLA VIAL 160 MG 8 ML; KADCYLA COMP SOLN
Vinblastine	VINBLASTINE DBL COMP SOLN; VINBLASTIN VIAL 10 MG 5 X 10 ML; VINBLASTINE TEVA COMP SOLN
Vincristine	VINCRISTINE SULP VIAL 2 MG 5 X 2 ML; VINCRISTINE SULP COMP SOLN; VINCRISTINE COMP SOLN; VINCRISTINE VIAL 2 MG /2ML 5 X 2 ML; VINCRISTINE VIAL 1 MG /1ML 5 X 1 ML
Vinorelbine	VINORELBINE EBEWE VIAL 10 MG 1 ML; VINORELBINE TART VIAL 10 MG 1 ML; VINORELBINE EBEWE VIAL 50 MG 5 ML; VINORELBINE EBEWE COMP SOLN; NAVELBINE VIAL 50 MG 5 ML; VINORELBINE KABI COMP SOLN; VINORELBINE TART VIAL 50 MG 5 ML; NAVELBINE VIAL 10 MG 1 ML; VINORELBINE TART COMP SOLN; VINORELBINE COMP SOLUTION; NAVELBINE COMP SOLN

Note: Table only includes molecules for which Australian in-market data were available.

IQVIA sales data reflects the totality of sales for cancer medicines (noting that sales through HPS may be underrepresented), as it contains sales data for medicines accessed via the EFC program, private prescriptions, clinical trials, and compassionate use programs. In comparison, PBS prescription data do not include private prescriptions or samples provided by the industry. Therefore, the sales data are broader than the corresponding PBS prescription data.

To minimise potential disparities between the sales data and PBS claims information, sales transactions for medicines provided to hospitals and pharmacies at no cost for clinical trials or compassionate use programs were removed from the analysis. These transactions accounted for approximately less than 0.01% of all sales (see sales analysis appendix). However, it was not possible to remove sales transactions that reflected purchases for self-funded use. This introduces a further point of difference between the sales data and PBS claims.

The comparison of PBS claims information and in-market sales was restricted to those medicines listed in Table A16. For those medicines for which in-market sales were not available, information was not requested as sales could not clearly be differentiated as pertaining to likely PBS use. As the data sets contained periods that mismatched by six months on either end (in-market sales information available from January 2016 to December 2020, PBS claims from July 2016 to June 2021), the analysis was restricted to January 2017 to December 2020

Table A16. EFC items included/excluded for comparison by data criteria

Criteria
Include as data was available in both the PBS and IQVIA datasets: arsenic; atezolizumab; avelumab; bendamustine; bevacizumab; bleomycin; blinatumomab; bortezomib; brentuximab vedotin; cabazitaxel; carboplatin; carfilzomib; cetuximab; cisplatin; cladribine;

cyclophosphamide; cytarabine; docetaxel; doxorubicin; durvalumab; epirubicin; eribulin; etoposide; fludarabine; fotemustine; gemcitabine; idarubicin; ifosfamide; inotuzumab ozogamicin; ipilimumab; irinotecan; methotrexate; nivolumab; obinutuzumab; oxaliplatin; paclitaxel; panitumumab; pembrolizumab; pemetrexed; pertuzumab; pralatrexate; raltitrexed; rituximab; topotecan; trastuzumab; trastuzumab emtansine; vinblastine; vincristine; vinorelbine

Exclude as data was only available in the PBS dataset:

doxorubicin hydrochloride; fluorouracil; mitozantrone; nanoparticle albumin-bound paclitaxel; ofatumumab

Exclude as data was only available in the IQVIA dataset:

etoposide phosphate

Further, it was not possible to compare the packs or vials dispensed between the PBS and sales datasets for all EFC medicines. For many of the EFC-medicines, there are multiple strengths available on the PBS under each PBS item code (see Table A17). However, in the PBS data provided, for any given PBS item only the first strength available is listed in the database. This means the strength as shown in the PBS data may not reflect the basis upon which the most efficient combination of vials was estimated. Therefore, it was only possible to estimate the number of vials dispensed to patients when only one vial size (i.e. strength) was available, limiting the analysis for which in-market sales and PBS claims could be compared on a per vial basis to those medicines supplied in only one strength.

Table A17. Product pack and/or vial sizes by EFC item and information source

Drug	*Information in PBS dataset on packs or vials dispensed*	*Pack or vial sizes available on the Australian market*
Arsenic	Injection concentrate containing arsenic trioxide 10 mg in 10 mL	10 mg/10 mL injection
Atezolizumab	Solution concentrate for I.V. infusion 1200 mg in 20 mL; Solution concentrate for I.V. infusion 840 mg in 14 mL	1.2 g/20 mL injection, 20 mL vial 840 mg/14 mL injection, 14 mL vial
Avelumab	Solution concentrate for I.V. infusion 200 mg in 10 mL	200 mg/10 mL injection, 10 mL vial
Bendamustine	Powder for injection containing bendamustine hydrochloride 100 mg	100 mg injection, 1 vial 25 mg injection, 1 vial
Bevacizumab	Solution for I.V. infusion 100 mg in 4 mL	400 mg/16 mL injection, 16 mL vial 100 mg/4 mL injection, 4 mL vial
Bleomycin	Powder for injection containing bleomycin sulfate 15,000 I.U.; Powder for injection containing bleomycin sulfate 15,000 I.U. in 1 vial	15 000 international units injection, 1 vial
Blinatumomab	Powder for I.V. infusion 38.5 micrograms	38.5 microgram injection [1 vial] (&) inert substance solution [10 mL vial], 1 pack
Bortezomib	Powder for injection 1 mg; Powder for injection 3.5 mg	1 mg injection, 1 vial 3 mg injection, 1 vial 3.5 mg injection, 1 vial
Brentuximab Vedotin	Powder for I.V. infusion 50 mg	50 mg injection, 1 vial
Cabazitaxel	Concentrated injection 60 mg (as acetone solvate) in 1.5 mL, with diluent	60 mg/1.5 mL injection [1.5 mL vial] (&) inert substance diluent [4.5 mL vial
Carboplatin	Solution for I.V. injection 450 mg in 45 mL	150 mg/15 mL injection, 15 mL vial 450 mg/45 mL injection, 45 mL vial

Drug	*Information in PBS dataset on packs or vials dispensed*	*Pack or vial sizes available on the Australian market*
Carfilzomib	Powder for injection 30 mg	10 mg injection, 1 vial 30 mg injection, 1 vial 60 mg injection, 1 vial
Cetuximab	Solution for I.V. infusion 500 mg in 100 mL	500 mg/100 mL injection, 100 mL vial 100 mg/20 mL injection, 20 mL vial
Cisplatin	I.V. injection 50 mg in 50 mL	50 mg/50 mL injection, 50 mL vial 100 mg/100 mL injection, 100 mL vial
Cladribine	Injection 10 mg in 5 mL	10 mg tablet 10 mg/10 mL injection, 10 mL vial 10 mg/5 mL injection, 5 mL vial
Cyclophosphamide	Powder for injection 1 g (anhydrous)	50 mg tablet, 50 500 mg injection, 1 vial 1 g injection, 1 vial 2 g injection, 1 vial
Cytarabine	Injection 100 mg in 5 mL vial	100 mg/5 mL injection, 5 x 5 mL vials
Daratumumab	Solution concentrate for I.V. infusion 160 mg in 16 mL	1.8 g/15 mL injection, 15 mL vial 100 mg/5 mL injection, 5 mL vial 400 mg/20 mL injection, 20 mL vial
Docetaxel	Solution for I.V. injection or intravesical administration containing doxorubicin hydrochloride 10 mg in 5 mL single-dose vial	160 mg/16 mL injection, 16 mL vial 80 mg/4 mL injection, 4 mL vial 80 mg/8 mL injection, 8 mL vial 160 mg/8 mL injection, 8 mL vial
Doxorubicin	Solution concentrate for I.V. infusion 120 mg in 2.4 mL	200 mg/100 mL injection, 100 mL vial 50 mg/25 mL injection, 25 mL vial
Durvalumab	Injection concentrate containing arsenic trioxide 10 mg in 10 mL	500 mg/10 mL injection, 10 mL vial 120 mg/2.4 mL injection, 2.4 mL vial
Epirubicin	Solution for injection containing epirubicin hydrochloride 200 mg in 100 mL	200 mg/100 mL injection, 100 mL vial 100 mg/50 mL injection, 50 mL vial 50 mg/25 mL injection, 25 mL vial
Eribulin	Solution for I.V. injection containing eribulin mesilate 1 mg in 2 mL	1 mg/2 mL injection, 2 mL vial
Etoposide / Etoposide Phosphate	Powder for I.V. infusion 100 mg (as phosphate)	50 mg capsule, 20 00 mg capsule, 10 100 mg/5 mL injection, 5 x 5 mL vials 100 mg/5 mL injection, 5 mL vial
Fludarabine	Solution for I.V. injection 50 mg fludarabine phosphate in 2 mL	10 mg tablet, 20 50 mg/2 mL injection, 5 x 2 mL vials 50 mg injection, 1 vial
Fluorouracil	Injection 5000 mg in 100 mL	5% cream, 20 g 5 g/100 mL injection, 100 mL vial 2.5 g/50 mL injection, 50 mL vial 1 g/20 mL injection, 20 mL vial 500 mg/10 mL injection, 10 mL vial
Fotemustine	Powder for injection 208 mg with solvent	208 mg injection [1 vial] (&) inert substance diluent [4 mL ampoule], 1 pack
Gemcitabine	Solution concentrate for I.V. infusion 500 mg (as hydrochloride) in 50 mL	1 g/26.3 mL injection, 26.3 mL vial 2 g/52.6 mL injection, 52.6 mL vial
Idarubicin	Solution for I.V. injection containing idarubicin hydrochloride 5 mg in 5 mL	5 mg/5 mL injection, 5 mL vial
Ifosfamide	Powder for I.V. injection 1 g	1 mg injection, 1 vial
Inotuzumab Ozogamicin	Powder for I.V. infusion 1 mg	·1 mg injection, 1 vial
Ipilimumab	Injection concentrate for I.V. infusion 200 mg in 40 mL; Injection concentrate for I.V. infusion 50 mg in 10 mL	·200 mg/40 mL injection, 40 mL vial ·50 mg/10 mL injection, 10 mL vial

Drug	*Information in PBS dataset on packs or vials dispensed*	*Pack or vial sizes available on the Australian market*
Irinotecan	I.V. injection containing irinotecan hydrochloride trihydrate 100 mg in 5 mL	·500 mg/25 mL injection, 25 mL vial ·100 mg/5 mL injection, 5 mL vial ·40 mg/2 mL injection, 2 mL vial
Methotrexate	Solution concentrate for I.V. infusion 5000 mg in 50 mL vial	·10 mg tablet ·50 mg/2 mL injection, 2 mL vial ·7.5 mg/0.3 mL injection, 4 x 0.3 mL syringes ·15 mg/0.6 mL injection, 4 x 0.6 mL syringes ·20 mg/0.8 mL injection, 4 x 0.8 mL syringes ·10 mg/0.4 mL injection, 4 x 0.4 mL syringes ·7.5 mg/0.15 mL injection, 0.15 mL syringe ·5 mg/2 mL injection, 5 x 2 mL vials ·25 mg/0.5 mL injection, 0.5 mL syringe ·2.5 mg tablet, 30 ·20 mg/0.4 mL injection, 0.4 mL syringe ·50 mg/2 mL injection, 5 x 2 mL vials ·10 mg/0.2 mL injection, 0.2 mL syringe ·15 mg/0.3 mL injection, 0.3 mL syringe ·25 mg/mL injection, 4 x 1 mL syringes ·1 g/10 mL injection, 10 mL vial ·500 mg/20 mL injection, 20 mL vial ·5 g/50 mL injection, 50 mL via
Nivolumab	Injection concentrate for I.V. infusion 100 mg in 10 mL	40 mg/4 mL injection, 4 mL vial 40 mg/4 mL injection, 4 mL vial
Obinutuzumab	Solution for I.V. infusion 1000 mg in 40 mL	1 g/40 mL injection, 40 mL vial
Ofatumumab	Solution concentrate for I.V. infusion 50 mg in 10 mL	20 mg/0.4 mL injection, 0.4 mL pen device
Oxaliplatin	Solution concentrate for I.V. infusion 150 mg in 25 mL	·100 mg/20 mL injection, 20 mL vial ·200 mg/40 mL injection, 40 mL vial
Paclitaxel	Solution concentrate for I.V. infusion 100 mg in 5 mL	·300 mg/50 mL injection, 50 mL vial ·30 mg/5 mL injection, 5 mL vial ·150 mg/25 mL injection, 25 mL vial ·100 mg/16.7 mL injection, 16.7 mL vial
Panitumumab	Injection concentrate for I.V. infusion 100 mg in 10 mL	·100 mg/5 mL injection, 5 mL vial ·400 mg/20 mL injection, 20 mL vial
Pembrolizumab	Powder for injection 50 mg Solution concentrate for I.V. infusion 100 mg in 4 mL	·100 mg/4 mL injection, 4 mL vial
Pemetrexed	Powder for I.V. infusion 100 mg (as disodium)	·500 mg injection, 1 vial ·100 mg injection, 1 vial ·1 g injection, 1 vial
Pralatrexate	Solution for I.V. infusion 420 mg in 14 mL	·20 mg/mL injection, 1 mL vial
Raltitrexed	Powder for I.V. infusion 2 mg in a single-use vial	·2 mg injection, 1 vial
Rituximab	Solution for I.V. infusion 500 mg in 50 mL	·1.4 g/11.7 mL injection, 11.7 mL vial ·100 mg/10 mL injection, 2 x 10 mL vials ·500 mg/50 mL injection, 50 mL vial
Topotecan	Powder for I.V. infusion 4 mg (as hydrochloride)	4 mg injection, 5 vials ·4 mg/4 mL injection, 5 x 4 mL vials
Trastuzumab	Powder for I.V. infusion 60 mg	·600 mg/5 mL injection, 5 mL vial ·150 mg injection, 1 vial ·60 mg injection, 1 vial 420 mg injection, 1 vial

Drug	*Information in PBS dataset on packs or vials dispensed*	*Pack or vial sizes available on the Australian market*
Trastuzumab-Emtansine	Powder for I.V. infusion 100 mg	·160 mg injection, 1 vial ·100 mg injection, 1 vial
Vinblastine	Solution for I.V. injection containing vinblastine sulfate 10 mg in 10 mL	·10 mg/10 mL injection, 5 x 10 mL vials
Vinorelbine	Solution for I.V. infusion 10 mg (as tartrate) in 1 mL	·20 mg capsule, 1 ·10 mg/mL injection, 1 mL vial ·50 mg/5 mL injection, 5 mL vial

Source: Prepared for this Review using PBS patient-level data.

Comparison of in-market sales (IQVIA) and PBS clains

The comparison of the total volume of cancer medicine dispensed by the pharmacist (expressed either as the number of packs or units dispensed) to the patient in the PBS dataset was compared to the amount of medicines purchased by pharmacies and hospitals in the IQVIA dataset is provided in Table A18.

Table A18. In-market sales volume (IQVIA) and PBS claims by EFC item (2017 - 2020)

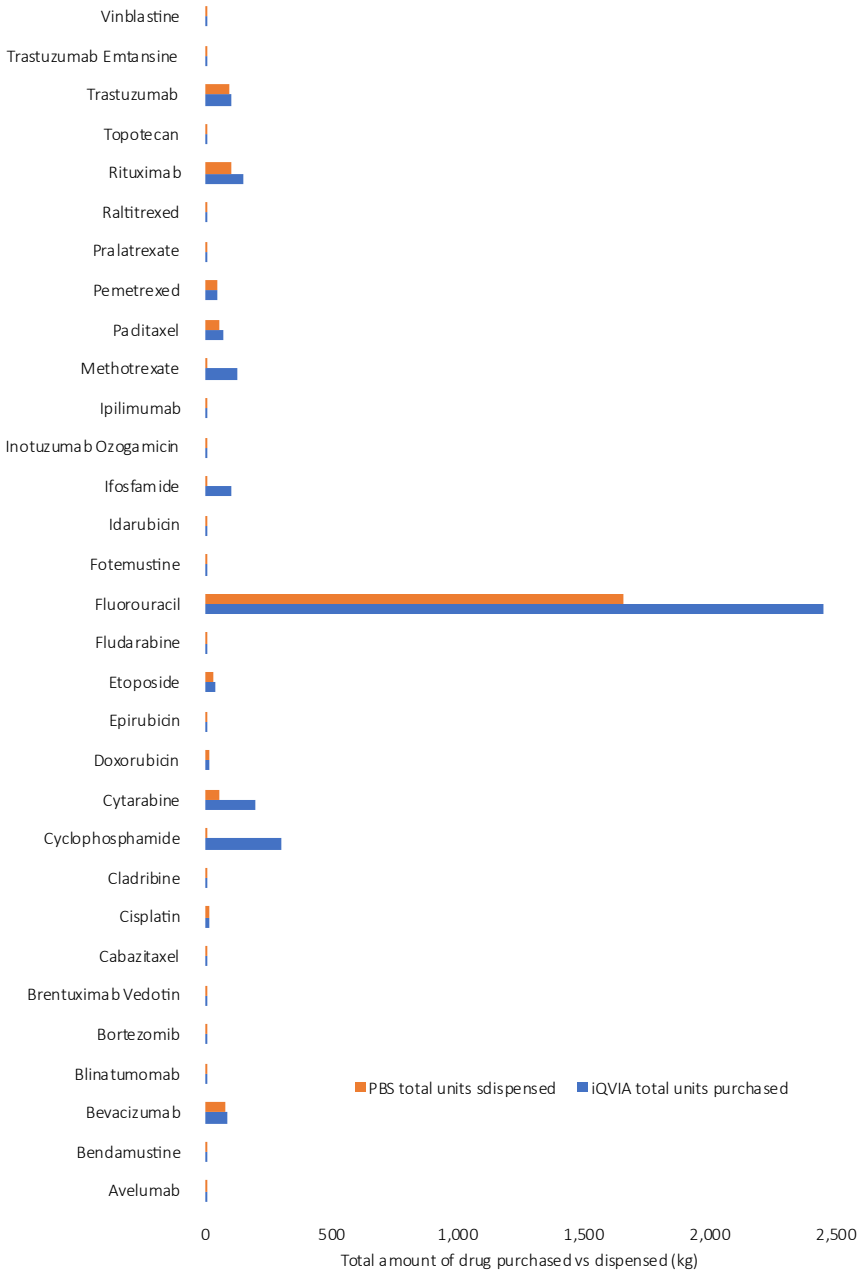
Drug Name	*Total purchased (mg) (IQVIA)*	*Total dispensed (mg) (PBS)*	*Difference*
Arsenic	192,934	262,874	-69,940
Atezolizumab	23,706,800	23,755,920	-49,120
Avelumab	4,224,718	4,071,269	153,449
Bendamustine	8,113,800	7,653,418	460,382
Bevacizumab	81,539,032	81,210,322	328,710
Bleomycin	3,631,288,064	553,712	3,630,734,352
Blinatumomab	316,043	244,600	71,443
Bortezomib	423,743	404,091	19,652
Brentuximab Vedotin	447,139	366,735	80,404
Cabazitaxel	771,857	732,189	39,668
Carboplatin	105,664,504	106,423,936	-759,432
Carfilzomib	6,139,928	6,663,684	-523,756
Cetuximab	40,008,796	41,630,963	-1,622,167
Cisplatin	11,033,151	10,464,249	568,902
Cladribine	33,069	24,217	8,852
Cyclophosphamide	296,297,504	243,640	296,053,864
Cytarabine	194,803,360	51,915,139	142,888,221
Docetaxel	13,745,911	14,212,613	-466,702
Doxorubicin	16,881,216	14,488,418	2,392,798
Durvalumab	6,582,718	7,199,418	-616,700
Epirubicin	1,974,820	1,956,989	17,831
Eribulin	53,109	68,748	-15,639
Etoposide	37,203,332	28,449,390	8,753,942
Fludarabine	1,247,097	617,010	630,087
Fotemustine	2,452,928,256	1,652,997,600	799,930,656
Gemcitabine	58,895	40,585	18,310
Idarubicin	373,290,848	400,737,696	-27,446,848
Ifosfamide	212,533	33,415	179,118
Inotuzumab Ozogamicin (mcg)	97,552,552	48,420	97,504,132

Drug Name	*Total purchased (mg) (IQVIA)*	*Total dispensed (mg) (PBS)*	*Difference*
Ipilimumab	618,000	316,663	301,337
Irinotecan	2,636,977	2,581,542	55,435
Methotrexate	42,759,464	45,401,601	-2,642,137
Nivolumab	122,988,792	2,959,345	120,029,447
Obinutuzumab	47,350,228	47,905,374	-555,146
Oxaliplatin	18,091,208	18,881,804	-790,596
Paclitaxel	31,287,560	32,960,396	-1,672,836
Panitumumab	65,617,936	55,384,634	10,233,302
Pembrolizumab	9,232,200	9,821,022	-588,822
Pemetrexed	20,530,638	21,248,171	-717,533
Pertuzumab	44,597,936	43,939,991	657,945
Pralatrexate	26,159,056	26,418,010	-258,954
Raltitrexed	119,457	106,507	12,950
Rituximab	8,484	6,723	1,761
Topotecan	147,753,632	104,594,440	43,159,192
Trastuzumab	23,100	21,512	1,588
Trastuzumab Emtansine	104,398,152	93,169,826	11,228,326
Vinblastine	4,519,444	4,492,010	27,434
Vincristine	256,331	230,381	25,950
Vinorelbine	216,431	170,867	45,564

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

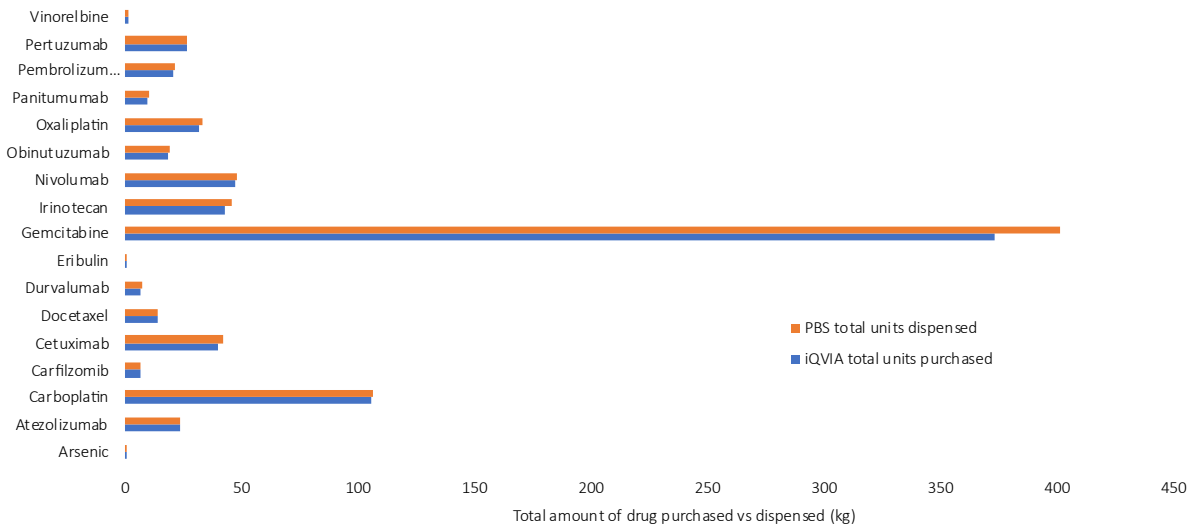
Cancer medicines for which the total amount dispensed to patients (PBS) was less than the amount purchased by hospitals and pharmacies are summarised in Figure A28. The corresponding figure for those medicines in which the volume dispensed via the PBS exceeded what was sold is summarised in Figure A29.

Figure A28. Volume purchased (IQVIA) exceeds volume dispensed (PBS) by EFC item



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A29. Volume dispensed (PBS) exceeds volume purchased (IQVIA) by EFC item



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

The comparison of the volume of each medicine as purchased in the in-market sales dataset (IQVIA) and claimed via the PBS per year is provided in Table A19.

Table A19. In-market sales (IQVIA) and PBS claims by EFC item (2017 - 2020)

Total mg purchased (IQVIA)	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*
	2017			*2018*			*2019*			*2020*	
Arsenic											
26,585	49,694	-23,109	43,112	56,439	-13,327	62,796	72,098	-9,302	60,441	84,643	-24,202
Atezolizumab											
-	-	-	2,412,000	2,438,520	-26,520	6,532,640	6,566,400	-33,760	14,762,160	14,751,000	11,160
Avelumab											
-	-	-	-	-	-	1,551,575	1,494,037	57,538	2,673,143	2,577,232	95,911
Bendamustine											
1,951,536	1,808,943	142,593	2,013,245	1,872,470	140,775	2,099,249	1,997,652	101,597	2,049,770	1,974,353	75,417
Bevacizumab											
19,000,000	18,200,000	788,612	18,600,000	18,000,000	566,638	18,500,000	19,100,000	-601,068	25,500,000	26,100,000	-601,068
Bleomycin (g)											
837,908	138	37,770	1,005,570	142	1,005,428	937,113	137	136,975	850,696	135	850,560
Blinatumomab											
40,136	40,957	-821	92,353	68,688	23,665	65,274	47,551	30,877	118,281	87,404	30,877
Bortezomib											
102,775	95,561	7,214	99,006	92,508	6,498	106,307	103,245	2,297	115,655	113,358	2,297
Brentuximab Vedotin											
97,892	67,967	29,925	110,597	91,966	18,631	114,288	92,159	9,719	124,362	114,643	9,719
Cabazitaxel											
172,563	161,089	11,474	168,209	167,624	585	208,490	192,979	11,200	222,595	211,395	11,200
Carboplatin											
24,300,000	25,100,000	-879,668	26,100,000	26,200,000	-35,702	26,800,000	26,800,000	-90,994	28,500,000	28,600,000	-90,994
Carfilzomib											
6,660	-	6,660	1,790,185	1,971,166	-180,981	2,098,129	2,263,548	-165,419	2,244,954	2,428,970	-184,016
Cetuximab											
10,025,835	10,631,798	-605,963	9,969,663	10,496,111	-526,448	9,975,076	10,245,104	-270,028	10,038,222	10,257,950	-219,728
Cisplatin											
2,791,651	2,566,941	224,710	2,737,523	2,619,992	117,531	2,785,639	2,694,796	110,721	2,718,338	2,607,617	110,721
Cladribine											
8,171	5,146	3,025	6,459	5,617	842	10,463	6,839	1,196	7,976	6,780	1,196
Cyclophosphamide											

Total mg purchased (IQVIA)	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*
	2017			*2018*			*2019*			*2020*	
72,489,312	59,327	72,429,985	75,746,848	61,231	75,685,617	75,804,064	61,977	75,742,087	72,257,296	61,105	72,196,191
Cytarabine											
47,510,528	12,991,932	34,518,596	47,665,944	13,740,930	33,925,014	49,472,136	12,125,867	37,346,269	50,154,764	13,056,410	37,098,354
Docetaxel											
3,404,601	3,481,843	-77,242	3,523,486	3,669,931	-146,445	3,543,462	3,653,476	-110,014	3,274,362	3,407,363	-133,001
Doxorubicin											
3,931,824	3,398,325	533,499	4,169,085	3,585,694	583,391	4,408,734	3,722,659	686,075	4,371,574	3,781,740	589,834
Durvalumab											
-	-	-	-	-	-	3,703	-	3,703	6,579,015	7,199,418	-620,403
Epirubicin											
814,310	801,083	13,227	529,246	546,397	-17,151	364,348	369,418	-5,070	266,916	240,091	26,825
Eribulin											
11,664	15,199	-3,535	13,964	17,573	-3,609	13,877	18,245	-4,368	13,604	17,731	-4,127
Etoposide											
8,912,313	6,685,889	2,226,424	9,658,387	7,328,731	2,329,656	9,360,720	7,253,983	2,106,737	9,271,913	7,265,622	2,006,291
Fludarabine											
308,727	167,038	141,689	334,369	172,851	161,518	334,734	157,645	177,089	269,267	119,476	149,791
Fotemustine											
	380,543,360	-380,543,360		397,871,168	-397,871,168		426,266,016			448,317,056	-448,317,056
Gemcitabine											
97,900,000	105,000,000	- 7,595,112	95,400,000	105,000,000	-9,743,704	90,300,000	96,500,000	- 4,820,112	89,700,000	94,500,000	- 4,820,112
Idarubicin											
56,134	11,194	44,940	60,688	9,238	51,450	50,342	6,795	43,547	45,369	6,188	39,181
Ifosfamide											
25,090,588	13,417	25,077,171	25,066,268	10,927	25,055,341	24,505,048	11,966	24,493,082	22,890,650	12,110	22,878,540
Inotuzumab Ozogamicin (mcg)											
-	-	-	-	-	-	278,000	105,927	172,073	340,000	210,736	129,264
Ipilimumab											
503,571	493,045	10,526	571,818	561,077	10,741	745,469	724,982	20,487	816,119	802,438	13,681
Irinotecan											
8,950,757	9,748,331	-797,574	9,993,416	10,855,185	-861,769	11,216,394	11,981,262	-764,868	12,598,898	12,816,823	-217,925
Methotrexate											
28,602,414	781,580	27,820,834	29,096,492	825,490	28,271,002	31,937,682	695,766	31,241,916	33,352,202	656,509	32,695,693
Nivolumab											
4,429,477	4,394,062	35,415	11,136,846	11,464,051	-327,205	13,417,550	13,427,401	-9,851	18,366,354	18,619,860	-253,506
Obinutuzumab											

Total mg purchased (IQVIA)	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*	*Total mg purchased (IQVIA)*	*Total mg dispensed (PBS)*	*Difference*
	2017			*2018*			*2019*			*2020*	
1,684,550	1,593,010	91,540	2,085,000	2,060,817	24,183	5,508,797	6,045,782	-536,985	8,812,860	9,182,195	-369,335
Oxaliplatin											
7,077,273	7,697,800	-620,527	7,719,421	8,004,916	-285,495	7,938,512	8,354,948	-416,436	8,552,353	8,902,732	-350,379
Paclitaxel											
15,032,129	12,902,303	2,129,826	16,113,533	13,447,748	2,665,785	16,750,441	14,245,389	2,505,052	17,721,836	14,789,194	2,932,642
Panitumumab											
2,237,729	2,407,290	-169,561	2,183,360	2,373,546	-190,186	2,326,871	2,478,472	-151,601	2,484,240	2,561,714	-77,474
Pembrolizumab											
2,700,413	2,769,709	-69,296	3,170,106	3,281,993	-111,887	5,626,895	5,833,150	-206,255	9,033,224	9,363,319	-330,095
Pemetrexed											
8,104,368	7,957,572	146,796	8,867,194	8,343,836	523,358	10,743,737	10,546,371	197,366	16,882,636	17,092,212	-209,576
Pertuzumab											
5,333,644	5,213,249	120,395	6,105,880	6,162,932	-57,052	6,825,135	7,026,391	-201,256	7,894,396	8,015,438	-121,042
Pralatrexate											
-	-	-	25,339	21,180	4,159	44,270	36,883	7,387	49,848	48,444	1,404
Raltitrexed											
2,363	2,058	305	1,915	1,641	274	2,266	1,480	786	1,940	1,544	396
Rituximab											
38,365,912	28,244,856	10,121,056	37,344,592	26,816,448	10,528,144	35,675,944	25,189,260	10,486,684	36,367,184	24,343,876	12,023,308
Topotecan											
5,877	5,066	811	5,475	4,843	632	5,933	5,776	-33	5,815	5,848	-33
Trastuzumab											
24,455,908	21,886,792	2,569,116	25,319,884	22,560,136	2,759,748	26,807,128	23,876,744	2,930,384	27,815,236	24,846,154	2,969,082
Trastuzumab-Emtansine											
1,058,373	1,008,262	50,111	960,689	975,737	-15,048	905,844	938,644	-32,800	1,594,538	1,569,367	25,171
Vinblastine											
63,077	61,286	1,791	57,171	54,221	2,950	65,501	56,950	8,551	70,582	57,924	12,658
Vincristine											
53,371	41,785	11,586	53,951	42,881	11,070	52,841	41,855	10,986	56,268	44,346	11,922
Vinorelbine											
327,462	332,725	-5,263	344,782	350,303	-5,521	311,168	307,525	3,643	259,530	269,253	-9,723

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Reconciling PBS claims using in-market sales data

As discussed previously, the PBS dataset provides information on the dose required by patients but not the number of optimal vials required to achieve this dose. Therefore, to estimate the number of vials required by patients in the PBS dataset, two scenarios were used: (1) perfect vial sharing in which there is no wastage of medicines; and (2) no vial sharing, which results in wastage. For example, cabazitaxel is supplied in 60 mg vials. For a patient requiring 55 mg per dose, under the first scenario, this would register as use of 0.92 of a 60 mg vial 90.92 x 60 = 55). Under the second scenario, this would register as exactly one 60 mg vial to achieve the 55 mg dose.

Utilising these two scenarios, a comparison of vials claimed (PBS) with vials sold (IQVIA) was conducted for those medicines available on the PBS in only one strength.

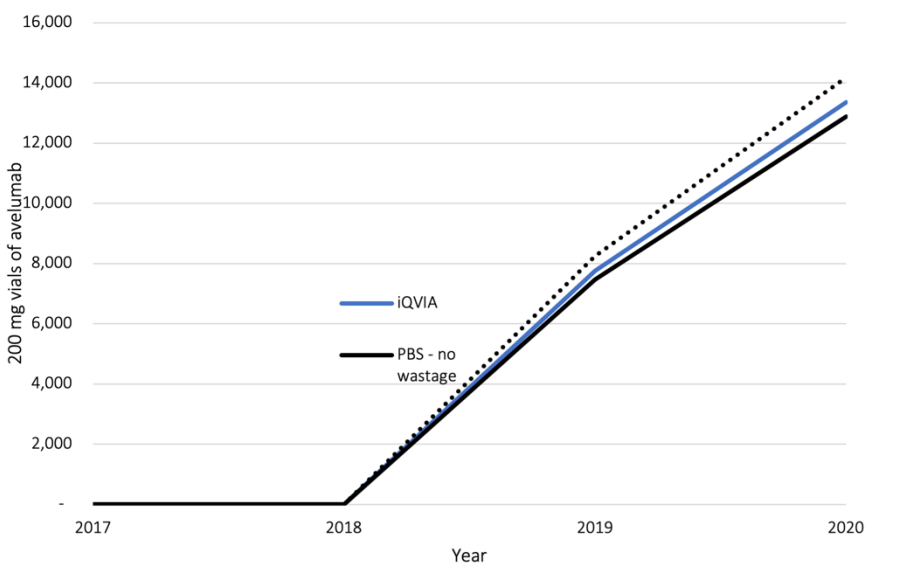
Avelumab - 200 mg vial: The number of 200 mg vials of avelumab that would have been dispensed via the PBS to patients under the assumption of no wastage was 20,356 and 22,423 with wastage (Table A20 and Figure A30). Reported sales of 21,124 200 mg vials of avelumab result in an excess of 767 vials (i.e., reported in-market sales exceeded PBS claims) under the assumption of no wastage and a deficit of 1,299 vials with wastage.

Table A20. In-market sales (IQVIA) and PBS claims of avelumab (200 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of avelumab purchased (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	-	-	1,551,575	2,673,143	4,224,718
PBS	-	-	1,494,037	2,577,232	4,071,269
Difference	-	-	57,538	95,911	153,449
Total number of 200 mg vials of avelumab purchased (IQVIA) vs. dispensed to patients (PBS) – assuming no wastage					
IQVIA	-	-	7,758	13,366	21,124
PBS	-	-	7,470	12,886	20,356
Difference	-	-	288	480	767
Total number of 200 mg vials of avelumab purchased (IQVIA) vs. dispensed to patients (PBS) – assuming wastage					
IQVIA	-	-	7,758	13,366	21,124
PBS	-	-	8,243	14,180	22,423
Difference	-	-	-485	-814	-1,299

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A30. In-market sales (IQVIA) and PBS claims of avelumab (200 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

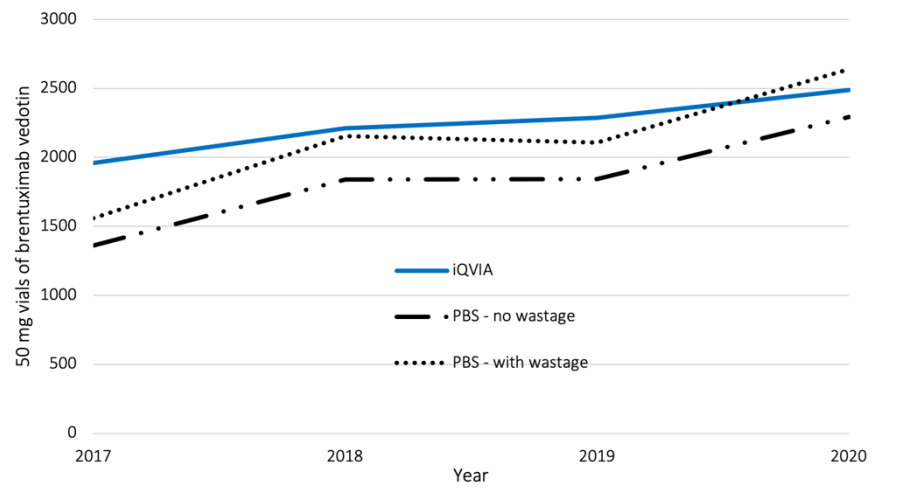
Brentuximab Vedotin - 50 mg vial: The number of 50 mg vials of brentuximab vedotin that would have been dispensed via the PBS to patients under the assumption of no wastage was 7,335 and 8,460 with wastage (Table A21 and Figure A31). Reported sales of 8,943 50 mg vials of brentuximab vedotin result in an excess of 1,608 vials under the assumption of no wastage and 483 with wastage.

Table A21. In-market sales (IQVIA) and PBS claims of brentuximab vedotin (50 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of brentuximab vedotin purchased (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	97,892	11,0597	114,288	124,362	447,139
PBS	67,967	91,966	92,159	114,643	366,735
Difference	29,925	18,631	22,129	9,719	80,404
Total number of 50 mg vials of brentuximab vedotin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	1,958	2,212	2,286	2,487	8,943
PBS	1,359	1,839	1,843	2,293	7,335
Difference	599	373	443	194	1,608
Total number of 50 mg vials of brentuximab vedotin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	1,958	2,212	2,286	2,487	8,943
PBS	1,560	2,153	2,107	2,640	8,460
Difference	398	59	179	-153	483

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A31. In-market sales (IQVIA) and PBS claims of brentuximab vedotin (50 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

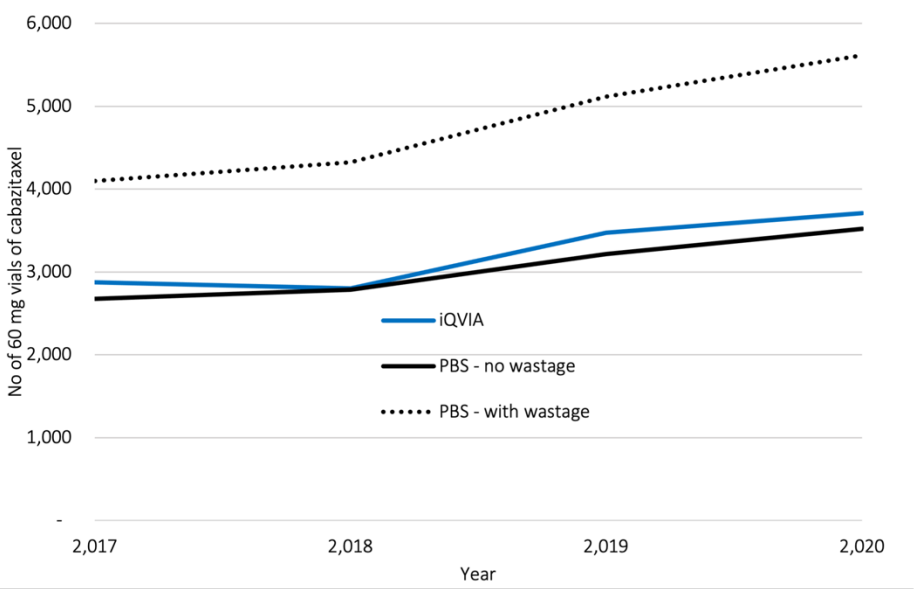
Cabazitaxel - 60 mg vial: The number of 60 mg vials of cabazitaxel that would have been dispensed via the PBS to patients under the assumption of no wastage was 12,203 and 19,154 with wastage during the period (see Table A22 and Figure A32). Sales of 12,864 vials of 60 mg of cabazitaxel resulted in an excess of 661 vials under the assumption of no wastage and deficit of 6,290 with wastage.

Table A22. In-market sales (IQVIA) and PBS claims of cabazitaxel (60 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of cabazitaxel purchased (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	172,563	168,209	208,490	222,595	771,857
PBS	160,714	167,324	192,935	211,216	732,189
Difference	11,849	885	15,555	11,379	39,668
Total number of 60 mg vials of cabazitaxel purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	2,876	2,803	3,475	3,710	12,864
PBS	2,679	2,789	3,216	3,520	12,203
Difference	197	15	259	190	661
Total number of 60 mg vials of cabazitaxel purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	2,876	2,803	3,475	3,710	12,864
PBS	4,096	4,325	5,115	5,618	19,154
Difference	-1,220	-1,522	-1,640	-1,908	-6,290

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A32. In-market sales (IQVIA) and PBS claims of cabazitaxel (60 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

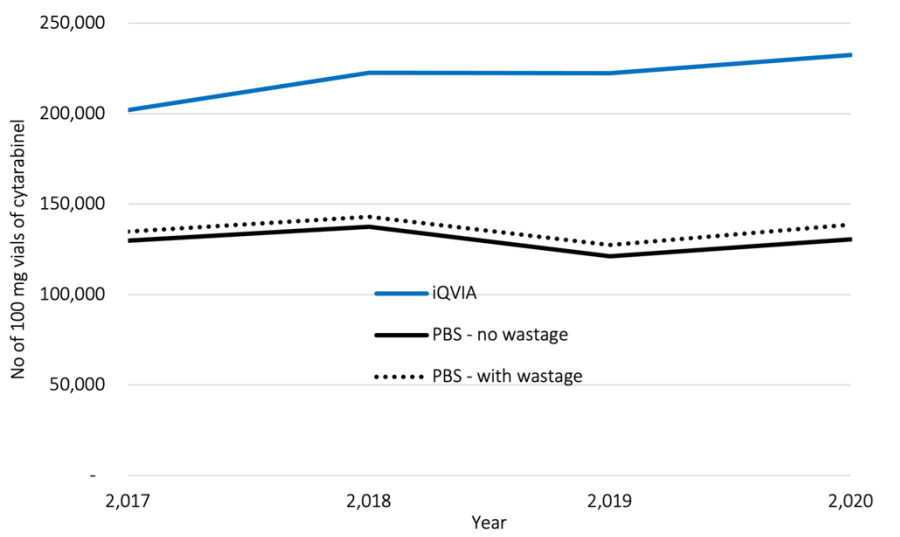
Cytarabine - 100 mg vial: The number of 100 mg vials of cytarabine that would have been dispensed via the PBS to patients under the assumption of no wastage was 519,151 and 544,005 with wastage during the period (Table A23 and Figure A33). Sales of 879,368 vials of 100 mg of cytarabine resulted in an excess of 360,217 vials under the assumption of no wastage and 335,363 vials with wastage.

Table A23. In-market sales (IQVIA) and PBS claims of cytarabine (100 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of cytarabine purchased (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	47,510,526	47,665,943	49,472,134	50,154,764	194,803,367
PBS	12,991,932	13,740,930	12,125,867	13,056,410	51,915,139
Difference	34,518,594	33,925,013	37,346,267	37,098,354	142,888,228
Total number of 100 mg vials of cytarabine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	201,918	222,565	222,439	232,446	879,368
PBS	129,919	137,409	121,259	130,564	519,151
Difference	71,999	85,156	101,180	101,882	360,217
Total number of 100 mg vials of cytarabine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	201,918	222,565	222,439	232,446	879,368
PBS	134,851	142,936	127,530	138,688	544,005
Difference	67,067	79,629	94,909	93,758	335,363

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A33. In-market sales (IQVIA) and PBS claims of cytarabine (100 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales

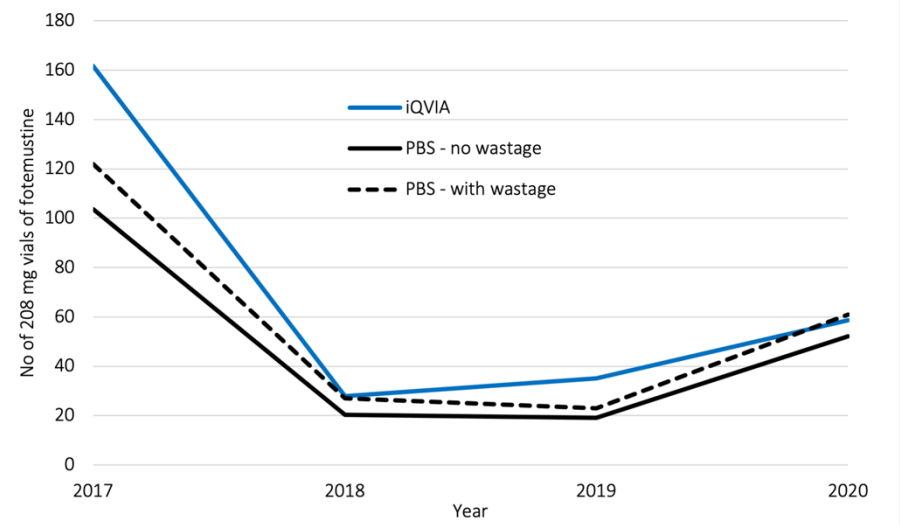
Fotemustine - 208 mg vial: The number of 208 mg vials of fotemustine that would have been dispensed to patients via the PBS under the assumption of no wastage was 195 and 233 with wastage during the period (Table A24 and Figure A34). Sales of 283 vials of 208 mg of fotemustine resulted in an excess of 88 vials under the assumption of no wastage and 50 with wastage.

Table A24. In-market sales (IQVIA) and PBS claims of fotemustine (208 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of fotemustine (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	33,620	5,788	7,304	12,183	58,895
PBS	21,568	4,206	3,975	10,836	40,585
Difference	12,052	1,582	3,329	1,347	18,310
Total number of 208 mg vials of fotemustine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	162	28	35	59	283
PBS	104	20	19	52	195
Difference	58	8	16	6	88
Total number of 208 mg vials of fotemustine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	162	28	35	59	283
PBS	122	27	23	61	233
Difference	40	1	12	-2	50

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A34. In-market sales (IQVIA) and PBS claims of fotemustine (208 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

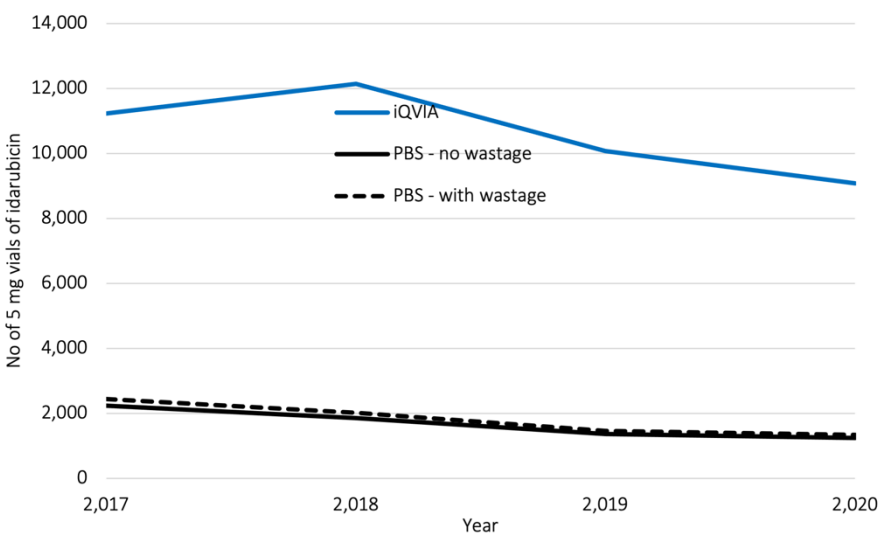
Idarubicin - 5 mg vial: The number of 5 mg vials of idarubicin that would have been dispensed to patients via the PBS under the assumption of no wastage was 6,683 and 7,246 with wastage (Table Ref and Figure Ref). Sales of 42,507 5 mg vials of idarubicin resulted in an excess of 35,824 vials under the assumption of no wastage and 35,261 with wastage.

Table A25. In-market sales (IQVIA) and claims (PBS) of idarubicin (5 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of idarubicin purchased (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	56,134	60,688	50,342	45,369	212,533
PBS	11,194	9,238	6,795	6,188	33,415
Difference	44,940	51,450	43,547	39,181	33,457
Total number of 5 mg vials of idarubicin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	11,227	12,138	10,068	9,074	42,507
PBS	2,239	1,848	1,359	1,238	6,683
Difference	8,988	10,290	8,709	7,836	35,824
Total number of 5 mg vials of idarubicin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	11,227	12,138	10,068	9,074	42,507
PBS	2,443	2,010	1,460	1,333	7,246
Difference	8,784	10,128	8,608	7,741	35,261

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A35. Sales (IQVIA) and claims (PBS) of idarubicin (5 mg vials) (2017 - 2020)



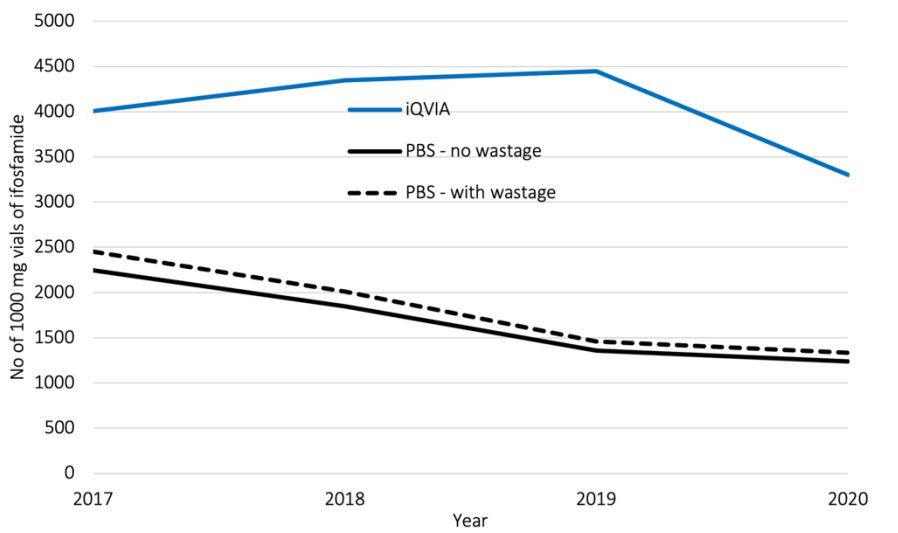
Ifosfamide - 1,000 mg vial: The number of 1,000 mg vials of ifosfamide that would have been dispensed to patients via the PBS under the assumption of no wastage was 48,527 and 55,086 with wastage (Table A26 and Figure A36). Sales of 97,553 vials of 1,000 mg of ifosfamide resulted in an excess of 49,026 vials under the assumption of no wastage and 42,467 with wastage.

Table A26. In-market sales (IQVIA) and claims (PBS) of ifosfamide (1,000 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of ifosfamide (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	25,090,587	25,066,267	24,505,048	22,890,650	97,552,552
PBS	13,417,397	10,993,446	12,001,232	12,114,666	48,526,741
Difference	11,673,190	14,072,821	12,503,816	10,775,984	33,457
Total number of 1000 mg vials of ifosfamide purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	25,091	25,066	24,505	22,891	97,553
PBS	13,417	10,993	12,001	12,115	48,527
Difference	11,673	14,073	12,504	10,776	49,026
Total number of 1000 mg vials of ifosfamide purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	25,091	25,066	24,505	22,891	97,553
PBS	15,208	12,499	13,653	13,726	55,086
Difference	9,883	12,567	10,852	9,165	42,467

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A36. In-market sales (IQVIA) and claims (PBS) of ifosfamide (1,000 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

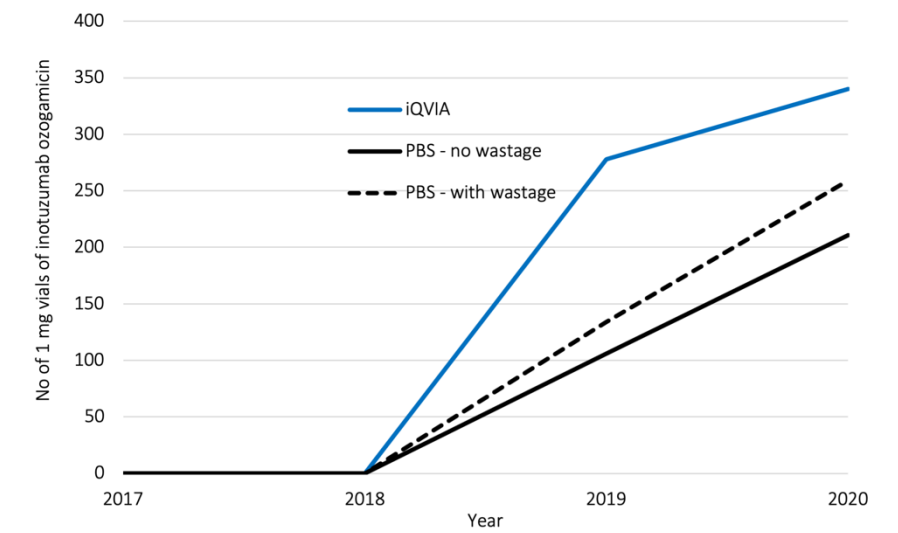
Inotuzumab ozogamicin - 1 mg vial: The number of 1 mg vials of inotuzumab ozogamicin that would have been dispensed to patients via the PBS under the assumption of no wastage was 317 and 393 vials with wastage (see Table A27 and Figure A37). Sales of 618 vials of 1 mg of inotuzumab ozogamicin resulted in an excess of 301 vials under the assumption of no wastage and 225 with wastage.

Table A27. In-market sales (IQVIA) and claims (PBS) of inotuzumab ozogamicin (1 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of inotuzumab ozogamicin (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	-	-	278	340	618
PBS	-	-	106	211	317
Difference	-	-	172	129	301
Total number of 1 mg vials of inotuzumab ozogamicin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	-	-	278	340	618
PBS	-	-	106	211	317
Difference	-	-	172	129	301
Total number of 1 mg vials of inotuzumab ozogamicin purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	-	-	278	340	618
PBS	-	-	134	259	393
Difference	-	-	144	81	225

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A37. In-market sales (IQVIA) and claims (PBS) of inotuzumab ozogamicin (1 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

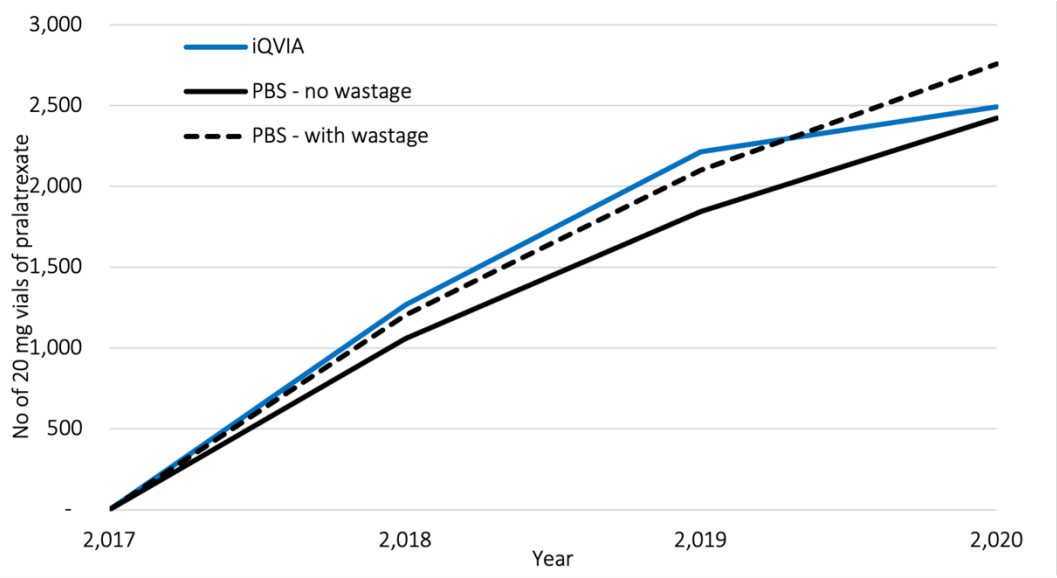
Pralatrexate - 20 mg/mL injection, 1 mL vial: The number of 20 mg vials of pralatrexate that would have been dispensed to patients via the PBS under the assumption of no wastage was 5,325 and 6,062 vials with wastage (Table A28 and Figure A38). Sales of 5,973 vials of 20 mg pralatrexate resulted in an excess of 648 vials under the assumption of no wastage and a deficit of 89 with wastage.

Table A28. In-market sales (IQVIA) and claims (PBS) of pralatrexate (20 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of pralatraxate (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	0	25,339	44,270	49,848	119,457
PBS	0	21,180	36,883	48,444	106,507
Difference	0	4,159	7,387	1,404	12,950
Total number of 20 mg vials of pralatrexate purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	0	1,267	2,214	2,492	5,973
PBS	0	1,059	1,844	2,422	5,325
Difference	0	208	369	70	648
Total number of 20 mg vials of pralatrexate purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	0	1,267	2,214	2,492	5,973
PBS	0	1,203	2,101	2,758	6,062
Difference	0	64	113	-266	-89

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A38. In-market sales (IQVIA) and claims (PBS) of pralatrexate (20 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

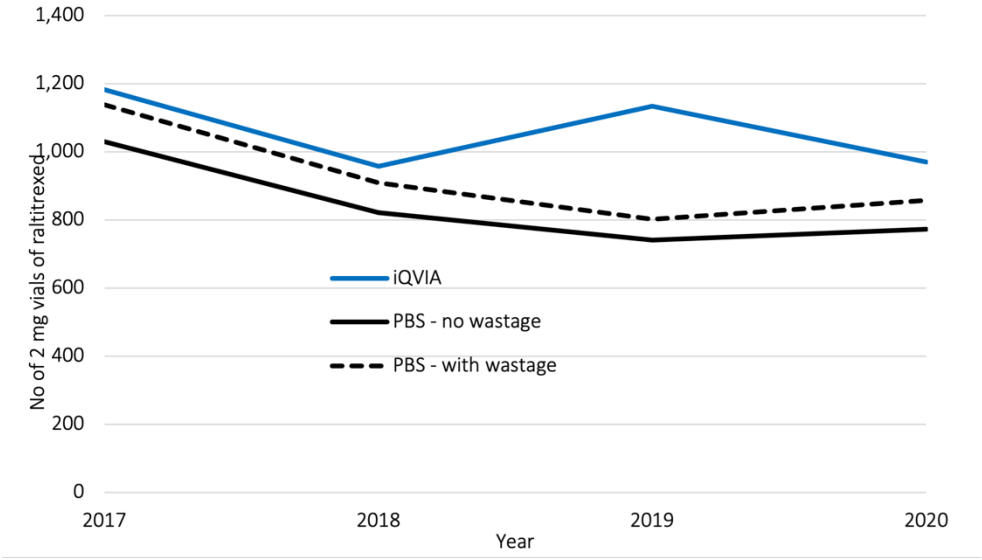
Raltitrexed - 2 mg vial: The number of 2 mg vials of raltitrexed that would have been dispensed to patients via the PBS under the assumption of no wastage was 3,362 and 3,703 with wastage (Table A29 and Figure A39.). Sales of 4,242 2 mg vials of raltitrexed resulted in an excess of 881 vials under the assumption of no wastage and 539 with wastage.

Table A29. In-market sales (IQVIA) and claims (PBS) of raltitrexed (2 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of raltitrexed (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	2,363	1,915	2,266	1,940	8,484
PBS	2,058	1,641	1,480	1,544	6,723
Difference	305	274	786	396	1,761
Total number of 2 mg vials of raltitrexed purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	1,182	958	1,133	970	4,242
PBS	1,029	821	740	772	3,362
Difference	153	137	393	198	881
Total number of 2 mg vials of raltitrexed purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	1,182	958	1,133	970	4,242
PBS	1,137	908	801	857	3,703
Difference	45	50	332	113	539

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A39. In-market sales (IQVIA) and claims (PBS) of raltitrexed (2 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

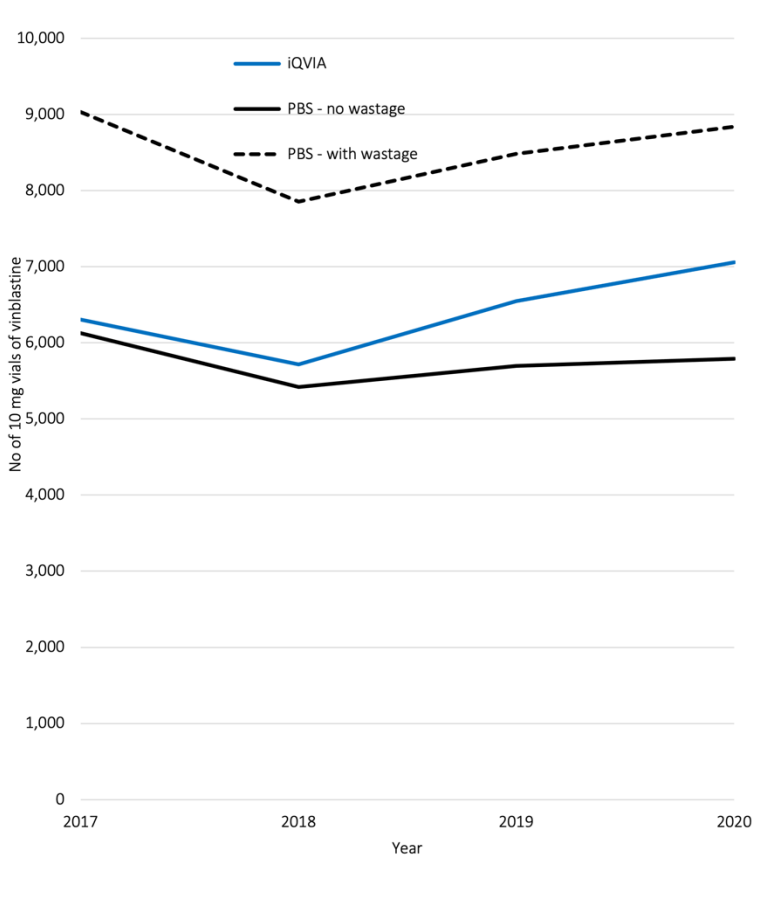
Vinblastine - 10 mg vial: The number of 10 mg vials of vinblastine that would have been dispensed to patients via the PBS under the assumption of no wastage was 23,038 and 34,209 with wastage (Table A30 and Figure A40.). Sales of 25,633 10 mg vials of vinblastine resulted in an excess of 2,595 vials under the assumption of no wastage and a deficit of 8,576 with wastage.

Table A30. In-market sales (IQVIA) and claims (PBS) of vinblastine (10 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of vinblastine (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	63,077	57,171	65,501	70,582	256,331
PBS	61,286	54,221	56,950	57,924	230,381
Difference	1,791	2,950	8,551	12,658	25,950
Total number of 10 mg vials of vinblastine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	6,308	5,717	6,550	7,058	25,633
PBS	6,129	5,422	5,695	5,792	23,038
Difference	179	295	855	1,266	2,595
Total number of 10 mg vials of vinblastine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	6,308	5,717	6,550	7,058	25,633
PBS	9,033	7,857	8,482	8,837	34,209
Difference	-2,725	-2,140	-1,932	-1,779	-8,576

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A40. In-market sales (IQVIA) and claims (PBS) of vinblastine (10 mg vials) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

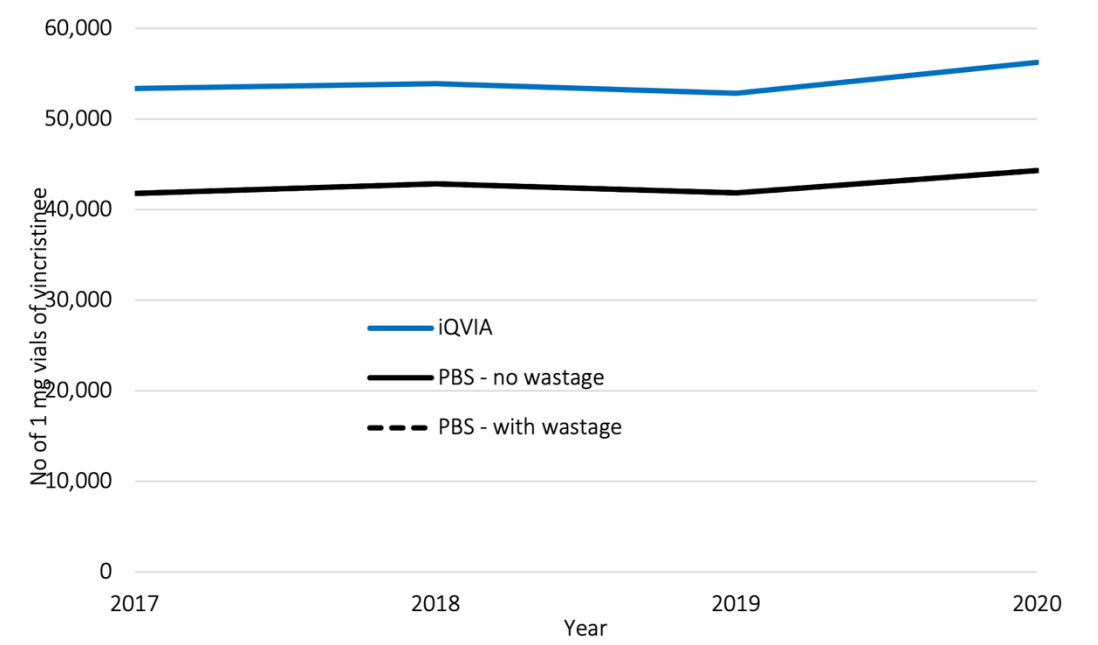
Vincristine - 1 mg vial: The number of 1 mg vials of vincristine that would have been dispensed to patients via the PBS was 170,867 under both wastage scenarios. Sales of 216,431 vials of 1 mg vincristine resulted in an excess of 45,564 vials.

Table A31. In-market sales (IQVIA) and claims (PBS) of vincristine (1 mg vials) (2017 - 2020)

	2017	*2018*	*2019*	*2020*	*2017-2020*
Amount of vincristine (IQVIA) vs. dispensed to patients (PBS) - mg					
IQVIA	53,371	53,951	52,841	56,268	216,431
PBS	41,785	42,881	41,855	44,346	170,867
Difference	11,586	11,070	10,986	11,922	45,564
Total number of 1 mg vials of vincristine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming no wastage					
IQVIA	53,371	53,951	52,841	56,268	216,431
PBS	41,785	42,881	41,855	44,346	170,867
Difference	11,586	11,070	10,986	11,922	45,564
Total number of 1 mg vials of vincristine purchased (IQVIA) vs. dispensed to patients (PBS) - assuming wastage					
IQVIA	53,371	53,951	52,841	56,268	216,431
PBS	41,785	42,881	41,855	44,346	170,867
Difference	11,586	11,070	10,986	11,922	45,564

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Figure A41. In-market sales (IQVIA) and claims (PBS) of vincristine (1 mg vials) (2017 - 2020)



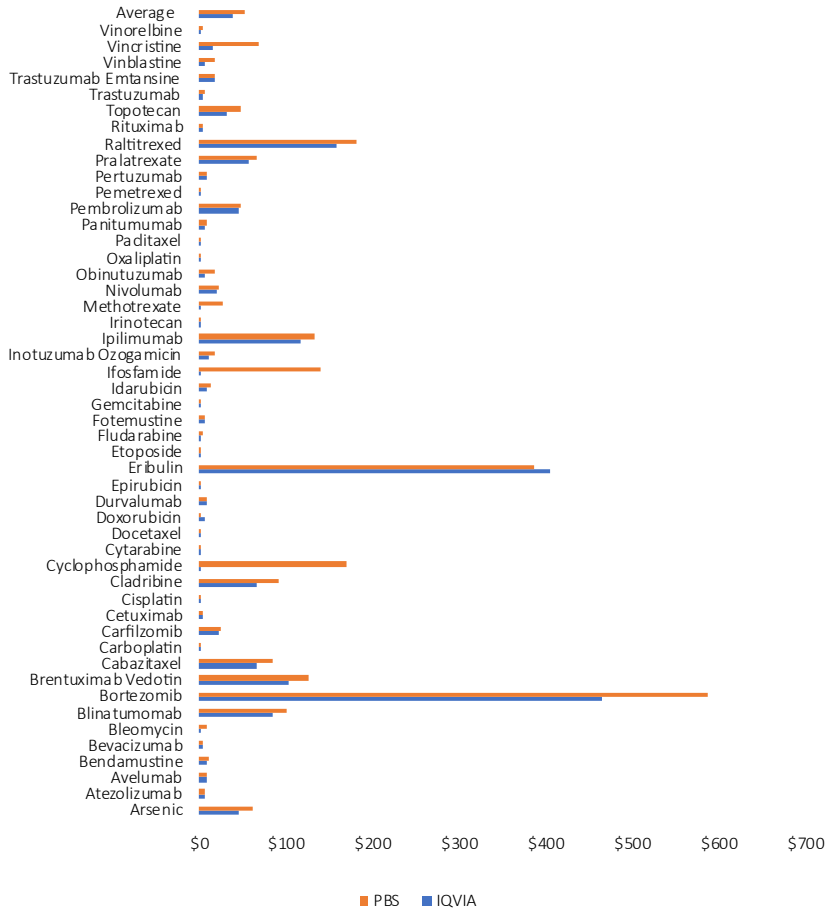
Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Comparison of price per unit (mg or international units)

The price paid per unit (mg or international units) for cancer medicines for in-market sales was compared to that associated with PBS claims. The resulting comparison is summarised, as an average price per medicine, in Table A32 and Figure A42. On average, in-market sales reveal a price per unit that was 72% of the PBS price per unit (an average price differential of $15.53 per unit).

An annual price per mg is provided in Table A33. As discussed previously, the PBS dataset provides the dose required by patients but not the number of vials or strength dispensed to patients to achieve that dose. Therefore, the price per unit in the PBS dataset was calculated by dividing the benefit paid by Government by the dose required by the patient. However, this method does not allow for wastage and likely overestimates the price per unit paid by the PBS.

Figure A42. Price per unit—PBS claims and in-market sales (IQVIA) (2017 - 2020)



Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Table A32. Price per unit—PBS claims and in-market sales (IQVIA) (2017 - 2020)

Drug	*IQVIA*	*PBS*	*Δ $/mg*	*IQVIA/PBS $/mg*
Arsenic	$44.42	$60.12	$15.70	74%
Atezolizumab	$6.14	$6.22	$0.08	99%
Avelumab	$7.41	$8.91	$1.49	83%
Bendamustine	$8.39	$9.55	$1.16	88%
Bevacizumab	$4.42	$4.42	$0.00	100%
Bleomycin	$0.92	$8.25	$7.33	11%
Blinatumomab	$85.17	$100.84	$15.67	84%
Bortezomib	$463.43	$585.58	$122.15	79%
Brentuximab Vedotin	$103.75	$125.60	$21.85	83%
Cabazitaxel	$66.63	$83.31	$16.69	80%
Carboplatin	$0.09	$0.51	$0.41	18%
Carfilzomib	$21.51	$24.09	$2.58	89%
Cetuximab	$3.14	$3.45	$0.31	91%
Cisplatin	$0.31	$1.96	$1.65	16%
Cladribine	$65.78	$90.16	$24.38	73%
Cyclophosphamide	$0.04	$169.87	$169.83	0%
Cytarabine	$0.09	$2.21	$2.13	4%
Docetaxel	$0.35	$1.32	$0.97	26%
Doxorubicin	$5.87	$2.07	$3.80	35%

Drug	*IQVIA*	*PBS*	*Δ $/mg*	*IQVIA/PBS $/mg*
Durvalumab	$8.07	$8.50	$0.43	95%
Epirubicin	$1.13	$1.95	$0.82	58%
Eribulin	$403.82	$387.08	$16.75	96%
Etoposide	$0.23	$1.18	$0.95	20%
Fludarabine	$1.11	$3.21	$2.11	34%
Fotemustine	$5.65	$6.46	$0.81	87%
Gemcitabine	$0.03	$0.11	$0.08	26%
Idarubicin	$8.41	$11.97	$3.56	70%
Ifosfamide	$0.06	$140.23	$140.17	0%
Inotuzumab Ozogamicin	$11.61	$17.21	$5.60	67%
Ipilimumab	$117.52	$132.15	$14.63	89%
Irinotecan	$0.40	$0.55	$0.15	73%
Methotrexate	$0.85	$26.09	$25.24	3%
Nivolumab	$20.26	$22.51	$2.25	90%
Obinutuzumab	$5.34	$17.81	$12.47	30%
Oxaliplatin	$0.24	$1.04	$0.80	23%
Paclitaxel	$1.21	$0.96	$0.25	79%
Panitumumab	$6.38	$7.26	$0.88	88%
Pembrolizumab	$45.01	$47.89	$2.88	94%
Pemetrexed	$0.23	$0.43	$0.20	53%
Pertuzumab	$7.39	$8.90	$1.52	83%
Pralatrexate	$57.15	$66.42	$9.27	86%
Raltitrexed	$157.07	$179.86	$22.79	87%
Rituximab	$2.67	$3.45	$0.78	77%
Topotecan	$30.59	$48.05	$17.45	64%
Trastuzumab	$4.45	$5.65	$1.21	79%
Trastuzumab Emtansine	$16.95	$18.52	$1.57	92%
Vinblastine	$5.31	$17.52	$12.21	30%
Vincristine	$14.96	$67.50	$52.54	22%
Vinorelbine	$1.18	$3.71	$2.52	32%
Average	*$37.21*	*$51.89*	*$15.53*	*72%*

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales.

Table A33. Comparison of the Price per Unit for PBS Claims and In-Market Sales – Annual Basis

	2017		2018		2019		2020		2017-2020	
Drug	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*
Arsenic	$51.24	$60.40	$44.94	$65.88	$44.31	$60.32	$39.38	$55.74	$44.42	$60.12
Atezolizumab	-	-	$6.27	$6.38	$6.26	$6.36	$6.00	$6.14	$6.14	$6.22
Avelumab	-	-	-	-	$7.99	$10.87	$7.05	$7.72	$7.41	$8.91
Bendamustine	$8.44	$9.41	$8.38	$9.87	$8.34	$9.44	$8.39	$9.47	$8.39	$9.55
Bevacizumab	$4.63	$4.89	$4.79	$4.86	$4.51	$4.41	$3.79	$3.66	$4.42	$4.42
Bleomycin	$0.94	$9.82	$0.99	$7.95	$0.61	$6.85	$1.19	$8.26	$0.92	$8.25
Blinatumomab	$88.28	$77.05	$86.11	$105.14	$84.00	$105.24	$84.05	$105.76	$85.17	$100.84
Bortezomib	$506.44	$625.37	$464.82	$589.58	$441.76	$563.64	$441.10	$568.90	$463.43	$585.58
Brentuximab Vedotin	$96.82	$123.57	$109.49	$154.64	$105.46	$115.96	$102.56	$111.14	$103.75	$125.60
Cabazitaxel	$68.90	$82.66	$64.25	$81.61	$68.05	$82.55	$65.25	$85.80	$66.63	$83.31
Carboplatin	$0.10	$0.50	$0.09	$0.54	$0.09	$0.49	$0.09	$0.49	$0.09	$0.51
Carfilzomib	-	-	$21.77	$25.47	$21.43	$23.52	$21.38	$23.50	$21.51	$24.09
Cetuximab	$3.40	$3.67	$3.15	$3.47	$2.99	$3.31	$3.00	$3.31	$3.14	$3.45
Cisplatin	$0.28	$1.93	$0.27	$1.91	$0.31	$1.97	$0.35	$2.01	$0.31	$1.96
Cladribine	$71.02	$97.35	$66.56	$86.47	$62.70	$90.39	$63.34	$87.10	$65.78	$90.16
Cyclophosphamide	$0.04	$175.02	$0.03	$179.96	$0.04	$167.98	$0.04	$156.16	$0.04	$169.87
Cytarabine	$0.07	$1.77	$0.06	$2.15	$0.08	$2.32	$0.14	$2.49	$0.09	$2.21
Docetaxel	$0.38	$1.22	$0.34	$1.29	$0.33	$1.41	$0.34	$1.35	$0.35	$1.32
Doxorubicin	$6.79	$2.00	$5.52	$2.22	$5.54	$2.04	$5.43	$2.01	$5.87	$2.07
Durvalumab	-	-	-	-	-	-	$8.07	$8.50	$8.07	$8.50
Epirubicin	$1.32	$2.06	$1.18	$2.00	$0.84	$1.79	$1.14	$1.73	$1.13	$1.95
Eribulin	$536.74	$501.83	$490.23	$500.39	$294.13	$287.77	$274.34	$279.42	$403.82	$387.08
Etoposide	$0.22	$1.20	$0.23	$1.22	$0.25	$1.17	$0.24	$1.15	$0.23	$1.18
Fludarabine	$1.18	$3.28	$0.97	$3.24	$1.13	$3.10	$1.14	$3.23	$1.11	$3.21
Fotemustine	$5.66	$6.67	$5.87	$7.08	$5.08	$6.44	$5.92	$5.77	$5.65	$6.46
Gemcitabine	$0.03	$0.12	$0.03	$0.10	$0.03	$0.10	$0.03	$0.11	$0.03	$0.11
Idarubicin	$11.79	$13.03	$9.37	$12.77	$6.64	$10.41	$5.34	$10.48	$8.41	$11.97
Ifosfamide	$0.07	$108.14	$0.06	$99.71	$0.06	$92.47	$0.06	$260.22	$0.06	$140.23
Inotuzumab Ozogamicin	-	-	-	-	$10.97	$16.86	$12.26	$17.40	$11.61	$17.21
Ipilimumab	$120.94	$131.05	$121.19	$130.50	$115.29	$134.42	$113.74	$131.59	$117.52	$132.15
Irinotecan	$0.25	$0.64	$0.18	$0.56	$0.49	$0.50	$0.75	$0.50	$0.40	$0.55
Methotrexate	$0.73	$19.86	$0.76	$23.74	$0.91	$28.05	$0.93	$34.87	$0.85	$26.09

	2017		*2018*		*2019*		*2020*		*2017-2020*	
Drug	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*	*IQVIA*	*PBS*
Nivolumab	$20.15	$22.16	$20.60	$22.10	$20.28	$22.97	$20.01	$22.56	$20.26	$22.51
Obinutuzumab	$5.36	$38.96	$5.35	$49.42	$5.32	$18.87	$5.33	$6.33	$5.34	$17.81
Oxaliplatin	$0.29	$1.03	$0.21	$1.06	$0.22	$1.01	$0.23	$1.08	$0.24	$1.04
Paclitaxel	$1.20	$0.94	$1.08	$0.96	$1.24	$0.96	$1.36	$1.00	$1.21	$0.96
Panitumumab	$7.54	$9.06	$7.51	$8.34	$5.54	$6.26	$4.93	$5.59	$6.38	$7.26
Pembrolizumab	$46.51	$51.65	$45.64	$51.26	$45.16	$49.33	$42.35	$44.13	$45.01	$47.89
Pemetrexed	$0.53	$1.38	$0.15	$0.27	$0.10	$0.21	$0.09	$0.21	$0.23	$0.43
Pertuzumab	$7.41	$8.44	$7.37	$7.87	$7.38	$9.80	$7.38	$9.21	$7.39	$8.90
Pralatrexate	-	-	$58.57	$65.60	$55.57	$67.22	$57.67	$66.13	$57.15	$66.42
Raltitrexed	$178.25	$195.67	$158.42	$182.19	$144.18	$165.65	$144.07	$169.70	$157.07	$179.86
Rituximab	$3.75	$4.10	$3.32	$3.69	$2.69	$3.27	$1.60	$2.62	$2.67	$3.45
Topotecan	$34.44	$44.75	$30.41	$46.13	$28.50	$48.34	$28.82	$51.97	$30.59	$48.05
Trastuzumab	$6.14	$7.03	$5.70	$6.62	$4.38	$5.32	$2.58	$3.82	$4.45	$5.65
Trastuzumab Emtansine	$16.85	$18.47	$16.96	$18.54	$16.94	$18.62	$17.05	$18.47	$16.95	$18.52
Vinblastine	$4.93	$17.84	$5.72	$17.80	$5.48	$16.98	$5.11	$17.47	$5.31	$17.52
Vincristine	$12.71	$65.58	$13.13	$68.18	$16.41	$67.42	$17.56	$68.70	$14.96	$67.50
Vinorelbine	$1.18	$3.70	$1.13	$3.70	$1.18	$3.66	$1.25	$3.77	$1.18	$3.71
Average	*$44.98*	*$53.23*	*$41.29*	*$55.51*	*$34.61*	*$47.92*	*$33.35*	*$50.79*	*$37.21*	*$51.89*

Source: Prepared for this Review using PBS patient-level data and IQVIA in-market sales

Appendix 7. Analysis of IQVIA Sales Data

The purpose of this analysis was to examine and describe the purchasing behaviours of hospitals and pharmacies in regards to cancer medicines listed on the EFC. In particular, this analysis sought to understand the impact factors such as the channel of purchasing the drug (i.e. hospital or pharmacy), the compounding status of the drug (non-compounded vs. compounded), and the location of purchase (state the pharmacy or hospital was from) had on the price paid per unit, total units purchased and total purchases.

IQVIA sales data

Sales data for cancer medicines listed on the EFC were requested from IQVIA for the period January 2016 to December 2021, based on the month and year of sale. The data were extracted in June 2021. The supplied data comprised 86,108 unique sales transactions to pharmacies and hospitals pertaining to 51 EFC-listed medicines (see Table A34).

The IQVIA sales data provided information regarding the amount of the drug purchased in a single transaction unit per-molecule basis, the manufacturer's name, pack or vial named purchased, the number of packs purchased, the price paid in a single transaction, the channel purchasing the drug (i.e. hospital or pharmacy), the compounding status of the drug (non-compounded vs. compounded), the state the pharmacy or hospital was from, and the month and date of sale.

Table A34. Pack types purchased by EFC medicine

Drug	*Pack Types Purchased on the Australian Market*
Arsenic	PHENASEN COMP SOLN; PHENASEN IV INFUSION 10 MG 10 X 10 ML; ARSENIC TRIOXIDE JUNO VIAL 10 MG 10 X 10 ML
Atezolizumab	TECENTRIQ VIAL 1200 MG 20 ML; TECENTRIQ COMP SOLN; TECENTRIQ VIAL 840 MG 14 ML
Avelumab	BAVENCIO COMP SOLN; BAVENCIO VIAL 200 MG 10 ML
Bendamustine	RIBOMUSTIN COMP SOLN; RIBOMUSTIN VIAL 25 MG; RIBOMUSTIN VIAL 100 MG
Bevacizumab	AVASTIN COMP SOLN; AVASTIN VIAL 100 MG 4 ML; AVASTIN VIAL 400 MG 16 ML
Bleomycin	BLEOMYCIN SULPH VIAL 15 K; BLEO VIAL 15 K; BLEO COMP SOLN; BLEOMYCIN DBL COMP SOLN; WILLOW BLEOMYCIN COMP SOLN; BLEOMYCIN COMP SOLUTION; BLEOMYCIN CIPLA COMP SOLN; BLEOMYCIN CIPLA 15K VIAL; BLEOMYCIN FOR INJECTION USP COMP SOLN; BLEOMYCIN FOR INJECTION USP VIAL 15 U
Blinatumomab	BLINCYTO VIAL AND SOLUTION STABILISER 38.5 Y; BLINCYTO COMP SOLN
Bortezomib	VELCADE COMP SOLN; VELCADE PDR VIAL 3.5 MG; VELCADE PDR VIAL 1 MG; VELCADE PDR VIAL 3 MG
Brentuximab Vedotin	ADCETRIS VIAL 50 MG; ADCETRIS COMP SOLN
Cabazitaxel	JEVTANA VIAL 60 MG /1.5 1.83 ML; JEVTANA COMP SOLN
Carboplatin	DBL CARBOPLATIN VIAL 150 MG 15 ML; CARBOPLATIN KABI COMP SOLN; DBL CARBOPLATIN COMP SOLN; CARBACCORD VIAL 450 MG 45 ML; DBL CARBOPLATIN VIAL 450 MG 45 ML; DBL CARBOPLATIN VIAL 50 MG 5 ML; CARBACCORD VIAL 150 MG 15 ML; CARBOPLATIN EBEWE COMP SOLN; CARBOPLATIN VIAL 450 MG 45 ML; CARBOPLATIN

Drug	*Pack Types Purchased on the Australian Market*
	COMP SOLN; CARBACCORD COMP SOLN; CARBOPLATIN VIAL 50 MG 5 ML; CARBOPLATIN ACCORD COMP SOLN; CARBOPLATIN ACCORD VIAL 450 MG 45 ML
Carfilzomib	KYPROLIS VIAL 60 MG; KYPROLIS VIAL 30 MG; KYPROLIS COMP SOLN; KYPROLIS VIAL 10 MG
Cetuximab	ERBITUX COMP SOLN; ERBITUX VIAL 500 MG 100 ML; ERBITUX VIAL 100 MG 20 ML
Cisplatin	CISPLATIN EBEWE VIAL 100 MG 100 ML; CISPLATIN VIAL 50 MG 50 ML; CISPLATIN COMP SOLN; CISPLATIN VIAL 100 MG 100 ML; CISPLATIN EBEWE COMP SOLN; CISPLATIN ACCORD COMP SOLN; CISPLATIN ACCORD CONCENTRATED INJECTION VIAL 50 MG 50 ML; CISPLATIN ACCORD CONCENTRATED INJECTION VIAL 100 MG 100 ML
Cladribine	LITAK VIAL 10 MG 5 ML; LEUSTATIN VIAL 10 MG 10 ML LITAK COMP SOLN LEUSTATIN COMP SOLN
Cyclophosphamide	ENDOXAN VIAL 2 G; ENDOXAN VIAL 1 G; ENDOXAN VIAL 500 MG; ENDOXAN COMP SOLN; CYCLOBLASTIN TABLETS 50 MG 50
Cytarabine	CYTARABINE FOT VIAL 100 MG 5 X 5 ML; CYTARABINE FOT COMP SOLN; CYTARABINE FOT VIAL 1000 MG /10M 10 ML; CYTARABINE COMP SOLN; CYTARABINE VIAL 2000 MG 20 ML; CYTARABINE VIAL 1000 MG 10 ML; CYTARABINE FOT VIAL 2000 MG /20M 20 ML; CYTOSAR U VIAL 1 G
Docetaxel	ONCOTAXEL VIAL 80 MG 4 ML; ONCOTAXEL VIAL 140 MG 7 ML; DBL DOCETAXEL VIAL 20 MG 2 ML; DBL DOCETAXEL COMP SOLN; DBL DOCETAXEL VIAL 80 MG 8 ML; ONCOTAXEL VIAL 20 MG 1 ML; DBL DOCETAXEL VIAL 160 MG 16 ML; TAXOTERE COMP SOLN; ONCOTAXEL COMP SOLN; TAXOTERE VIAL 20 MG 1 ML; AS-DOCETAXEL COMP SOLN; DOCETAXEL SANDOZ COMP SOLN; DOCETAXEL SUN VIAL 80 MG; DOCETAXEL SUN COMP SOLN; DOCETAXEL ACCORD COMP SOLN; DOCETAXEL ACCORD VIAL 160 MG 8 ML; DOCETAXEL ACCORD VIAL 80 MG 4 ML; DOCETAXEL ACCORD VIAL 20 MG 1 ML
Doxorubicin	CAELYX VIAL 50 MG 25 ML; ACCORD DOXORUBICIN COMP SOLN; CAELYX COMP SOLN; ADRIAMYCIN SOLN VIAL 50 MG 25 ML; L-DOXORUBICIN SUN VIAL 20 MG 10 ML; DOXORUBICIN MYX COMP SOLN; DOXORUBICIN VIAL 10 MG 5 ML; DOXORUBICIN VIAL 50 MG 25 ML; L-DOXORUBICIN SUN VIAL 50 MG 25 ML; CAELYX VIAL 20 MG 10 ML; ACCORD DOXORUBICIN VIAL 200 MG 100 ML; DOXORUBICIN COMP SOLN; DOXORUBICIN MYX VIAL 200 MG 100 ML; L-DOXORUBICIN SUN COMP SOLN; ACCORD DOXORUBICIN VIAL 10 MG 5 ML; ADRIAMYCIN SOLN VIAL 200 MG 100 ML; DOXORUBICIN EBEWE COMP SOLN; DOXORUBICIN SZ COMP SOLN; ADRIAMYCIN COMP SOLN
Durvalumab	IMFINZI COMP SOLN IMFINZI VIAL 120 MG 2.4 ML IMFINZI VIAL 500 MG 10 ML
Epirubicin	EPIRUBICIN ACTAVIS COMP SOLN; EPIRUBICIN ACT VIAL 50 MG 25 ML; EPIRUBICIN ACT VIAL 200 MG 100 ML; EPIRUBICIN ACTAVIS VIAL 100 MG 50 ML; EPIRUBICIN KABI COMP SOLN; EPIRUBICIN HCL INJECTION 50 MG 25 ML; DBL EPIRUBICIN VIAL 200 MG 100 ML; PHARMORUBICIN RD VIAL 50 MG; PHARMORUBICIN SOLUTION 50 MG 25 ML; DBL EPIRUBICIN COMP SOLN; EPIRUBICIN COMP SOLUTION; EPIRUBICIN HCL COMP SOLN; EPIRUBICIN ACT COMP SOLN; PHARMORUBICIN COMP SOLN; EPIRUBICIN SZ COMP SOLN; PHARMORUBICIN SOLUTION 200 MG 100 ML; EPIRUBICIN ACCORD COMP SOLN; EPIRUBE COMP SOLN; EPIRUBE VIAL 200 MG 100 ML; EPIRUBE VIAL 50 MG 25 ML; EPIRUBICIN ACCORD VIAL 200 MG 100 ML
Eribulin	HALAVEN VIAL 1 MG 2 ML; HALAVEN COMP SOLN
Etoposide / Etoposide Phosphate	ETOPOSIDE COMP SOLUTION; ETOPOSIDE EBEWE COMP SOLN; ETOPOSIDE EBEWE VIAL 100 MG 5 X 5 ML; ETOPOSIDE VIAL 100 MG 5 ML; ETOPOSIDE EBEWE VIAL 100 MG 5 ML; ETOPOSIDE COMP SOLN ETOPOPHOS COMP SOLN; ETOPOPHOS PDR VIAL 114 MG; ETOPOPHOS PDR VIAL 1136 MG
Fludarabine	FLUDARABINE ACTAV INJECTION 50 MG 5; FLUDARABINE ACT COMP SOLN; FARINE COMP SOLN; FLUDARABINE EBEWE INJECTION 50 MG 5 X 2 ML; FLUDARABINE ACTAV INJECTION 50 MG; FLUDARABINE EBEWE COMP SOLN; FLUDARABINE ACT VIAL 50 MG; FARINE INJECTION 50 MG; FLUDARABINE EBEWE INJECTION 50 MG 2 ML; FLUDARABINE

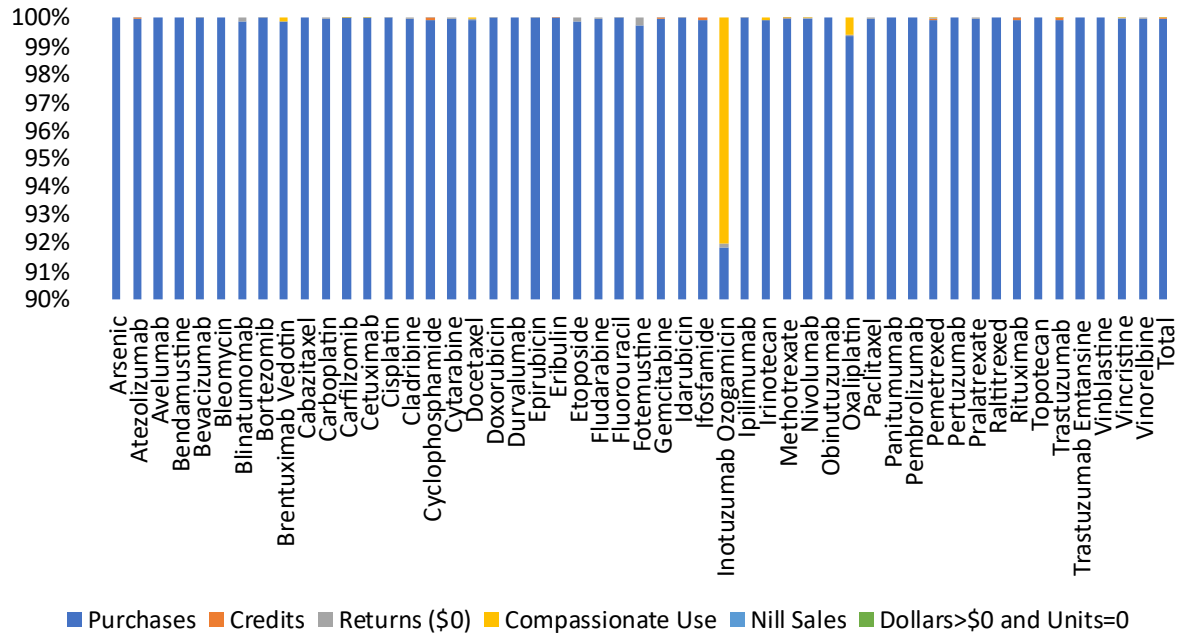
Drug	*Pack Types Purchased on the Australian Market*
	COMP SOLUTION; FLUDARABINE AMNEAL COMP SOLN; FLUDARABINE AMNEAL VIAL 50 MG 2 ML; FLUDARABINE JUNO VIAL 50 MG 5 ML; FLUDARABINE JUNO COMP SOLN
Fluorouracil	FLUOROURACIL VIAL 2500 MG 50 ML; FLUOROURACIL COMP SOLN; FLUOROURACIL VIAL (OLD) 500 MG 5 X 10 ML; FLUOROURACIL EBEWE VIAL 5000 MG 100 ML; FLUOROURACIL VIAL 2500 MG 100 ML; FLUOROURACIL VIAL 1000 MG 5 X 20 ML; FLUOROURACIL EBEWE COMP SOLN; APO-APOC-5FU CREAM 5 % 20 G; FLUOROURACIL ACCORD COMP SOLN; FLUOROURACIL ACCORD INJECTION VIAL 1000 MG 20 ML; FLUOROURACIL ACCORD INJECTION VIAL 2500 MG 50 ML; FLUOROURACIL ACCORD INJECTION VIAL 5000 MG 100 ML; FLUOROURACIL-PC CREAM 5 % 20 G
Fotemustine	MUPHORAN VIAL 208 MG; MUPHORAN COMP SOLN; FOTEMUSTINE SOLUTION
Gemcitabine	GEMACCORD VIAL 200 MG; DBL GEMCITABINE VIAL 2 G 52.6 ML; GEMCITABINE ACTAV VIAL 1 G; DBL GEMCITABINE VIAL 200 MG 5.3 ML; DBL GEMCITABINE VIAL 1 G 26.3 ML; DBL GEMCITABINE COMP SOLN; GEMACCORD VIAL 1 G; GEMCITABINE ACTAV VIAL 2 G; DBL GEMCITABINE VIAL 1 G; DBL GEMCITABINE VIAL 2 G; DBL GEMCITABINE VIAL 200 MG; GEMCITABINE KABI COMP SOLN; GEMCITABINE ACTAV COMP SOLN; AS-GEMCITABINE COMP SOLN; GEMACCORD COMP SOLN; GEMCITABINE EBEWE COMP SOLN; GEMCITABINE SUN COMP SOLN
Idarubicin	IDARUBICIN EBEWE COMP SOLN; ZAVEDOS SOLN VIAL 5 MG 5 ML; ZAVEDOS SOLN VIAL 10 MG 10 ML; ZAVEDOS COMP SOLN; IDARUBICIN EBEWE VIAL 10 MG 10 ML; ZAVEDOS VIAL 10 MG; IDARUBICIN EBEWE VIAL 5 MG 5 ML; IDARUBICIN COMP SOLUTION
Ifosfamide	HOLOXAN VIAL 1 G; HOLOXAN COMP SOLN; HOLOXAN VIAL 2 G; IFOSFAMIDE COMP SOLUTION
Inotuzumab Ozogamicin	BESPONSA VIAL 1 MG 20 ML
Ipilimumab	YERVOY COMP SOLN; YERVOY VIAL 200 MG 40 ML; YERVOY VIAL 50 MG 10 ML; IPILIMUMAB SOLUTION
Irinotecan	IRINOTECAN MYX COMP SOLN; IRINOTECAN VIAL 100 MG 5 ML; IRINOCCORD VIAL 100 MG 5 ML; IRINOTECAN VIAL 500 MG 25 ML; IRINOTECAN ALPHAPHARM VIAL 100 MG 5 ML; IRINOTECAN ALPHAPHARM VIAL 500 MG 25 ML; IRINOTECAN MYX VIAL 100 MG 5 ML; CAMPTOSAR VIAL 300 MG 15 ML; IRINOTECAN VIAL 40 MG 2 ML; IRINOTECAN COMP SOLN; TECAN VIAL 100 MG 5 ML; IRINOCCORD VIAL 40 MG 2 ML; IRINOTECAN ACTAVIS VIAL 500 MG 25 ML; IRINOTECAN ACTAVIS VIAL 100 MG 5 ML; IRINOTECAN COMP SOLUTION; IRINOTECAN ACTAVIS COMP SOLN; IRINOTECAN EBEWE COMP SOLN; IRINOTECAN ALPHAPHARM COMP SOLN; IRINOCCORD COMP SOLN; IRINOTECAN KABI COMP SOLN; IRINOTECAN MEDITAB VIAL 100 MG 5 ML; IRINOTECAN MEDITAB COMP SOLN; IRINOTECAN ACCORD COMP SOLN; IRINOTECAN ACCORD VIAL 100 MG 5 ML; OMEGAPHRM IRINOTEC COMP SOLN; ONIVYDE VIAL 43 MG 10 ML ONIVYDE COMP SOLN
Methotrexate	METHACCORD VIAL 50 MG 2 ML; METHOTREXATE EBEWE INFUSION 5000 MG 50 ML; DBL METHOTREXATE VIAL 5 MG 5 X 2 ML; METHOTREXATE VIAL 50 MG 5 X 2 ML; DBL METHOTREXATE VIAL 50 MG 5 X 2 ML; METHACCORD VIAL 1000 MG 10 ML; METHACCORD COMP SOLN; DBL METHOTREXATE COMP SOLN; METHOTREXATE VIAL 1000 MG 10 ML; DBL METHOTREXATE VIAL 500 MG 20 ML; METHOTREXATE MYX INJ VIAL 50 MG /2ML 2 ML; DBL METHOTREXATE VIAL 1000 MG 10 ML; METHOTREXATE MYX COMP SOLN; METHOTREXATE MYX INJ VIAL 1000 MG /10M 10 ML; METHOTREXATE COMP SOLN; TREXJECT PREFILL SYR 10 MG 0.2 ML; METHOTREXATE EBEWE COMP SOLN; TREXJECT PREFILL SYR 25 MG 0.5 ML; TREXJECT PREFILL SYR 15 MG 0.3 ML; TREXJECT PREFILL SYR 20 MG 0.4 ML; TREXJECT PREFILL SYR 7.5 MG 0.15 ML; METHOTREXATE ACCORD VIAL 1 G 10 ML; DBL METHOTREXATE TABLETS 2.5 MG 30; METHOTREXATE ACCORD VIAL 50 MG 2 ML; METHOBLASTIN PFS 7.5 MG 4 X 0.3 ML; METHOBLASTIN PFS 25 MG 4 X 1 ML; METHOBLASTIN PFS 25 MG 1 ML; METHOBLASTIN PFS 10 MG 4 X 0.4 ML; METHOBLASTIN PFS 20 MG 4 X 0.8 ML; METHOBLASTIN PFS 15 MG 4 X 0.6 ML; METHOBLASTIN PFS 20 MG 0.8 ML; METHOBLASTIN PFS 10 MG 0.4 ML
Nivolumab	OPDIVO IV VIAL 40 MG 4 ML; OPDIVO IV VIAL 100 MG 10 ML; OPDIVO COMP SOLN
Obinutuzumab	GAZYVA VIAL 1 G 40 ML; GAZYVA COMP SOLN

Drug	*Pack Types Purchased on the Australian Market*
Oxaliplatin	OXALIPLATIN SUN I V SOLUTION 100 MG 20 ML; DBL OXALIPLATIN COMP SOLN; OXALIPLATIN SZ COMP SOLN; OXALIPLATIN SUN I V SOLUTION 50 MG 10 ML; OXALIPLATIN MYX COMP SOLN; OXALICCORD COMP SOLN; DBL OXALIPLATIN I V SOLUTION 100 MG 20 ML; OXALICCORD VIAL 100 MG 20 ML; DBL OXALIPLATIN I V SOLUTION 50 MG 10 ML; OXALIPLATIN SZ VIAL 100 MG 20 ML; OXALIPLATIN EBEWE COMP SOLN; ELOXATIN SOLUTION 100 MG 20 ML; OXALIPLATIN SUN I V SOLUTION 200 MG 40 ML; OXALICCORD VIAL 50 MG 10 ML; OXALIPLATIN PDR VIAL 100 MG; OXALIPLATIN PDR VIAL 50 MG; ELOXATIN SOLUTION 200 MG 40 ML; OXALIPLATIN KABI COMP SOLN; OXALIPLATIN SUN COMP SOLN; OXALIPLAN COMP SOLN; ELOXATIN COMP SOLN; OXALIPLATIN ACCORD COMP SOLN; OXALIPLATIN ACCORD VIAL 100 MG 20 ML; OXALIPLATIN LINK COMP SOLN; OXALATIN COMP SOLN
Paclitaxel	ABRAXANE VIAL 100 MG; ANZATAX COMP SOLN; PACLITAXEL ACTAVIS VIAL 150 MG 25 ML; ANZATAX VIAL 150 MG 25 ML; ABRAXANE COMP SOLN; PLAXEL VIAL 100 MG 16.7 ML; PACLITAXEL ACTAVIS VIAL 300 MG 50 ML; ANZATAX VIAL 30 MG 5 ML; ANZATAX VIAL 300 MG 50 ML; PACLITAXEL ACTAVIS VIAL 30 MG 5 ML; PLAXEL VIAL 30 MG 5 ML; PACLITAXEL ACTAVIS VIAL 100 MG 16.7 ML; PACLITAXEL EBEWE VIAL 300 MG 50 ML; PACLITAXEL ACTAVIS COMP SOLN; PACLITAXEL EBEWE COMP SOLN; PACLITAXEL KABI COMP SOLN; PACLITAXEL ACCORD COMP SOLN; PACLITAXIN VIAL 30 MG 5 ML; PACLITAXIN VIAL 100 MG 16.7 ML; PACLITAXIN VIAL 300 MG 50 ML; PACLITAXEL ACCORD VIAL 300 MG 50 ML; PACLITAXIN VIAL 150 MG 25 ML; PACLITAXEL ACCORD VIAL 100 MG 16.7 ML
Panitumumab	VECTIBIX COMP SOLN; VECTIBIX VIAL 400 MG 20 ML; VECTIBIX VIAL 100 MG /5ML 5 ML; KEYTRUDA INJ VIAL 50 MG; KEYTRUDA COMP SOLN; KEYTRUDA VIAL 100 MG 4 ML
Pemetrexed	PEMETREXED MYX COMP SOLN; ALIMTA VIAL 100 MG; ALIMTA VIAL 500 MG; PEMETREXED MYX DRY VIAL 500 MG; PEMETREXED SANDOZ PDR VIAL 500 MG; PEMETREXED MYX DRY VIAL 100 MG; PEMETREXED JUNO VIALS 500 MG; DBL PEMETREXED COMP SOLN; ALIMTA COMP SOLN; APO-PEMETREXED VIAL 500 MG; PEMETREXED JUNO VIALS 100 MG; APO-PEMETREXED VIAL 100 MG; PEMETREXED SOLUTION; DBL PEMETREXED VIALS 1000 MG; DBL PEMETREXED VIALS 100 MG; DBL PEMETREXED VIALS 500 MG; RELADDIN INJECTION 100 MG; RELADDIN INJECTION 500 MG; PEMETREXED ACCORD COMP SOLN; APO-PEMETREXED COMP SOLN; PEMETREXED JUNO COMP SOLN; PEMETREXED DRLA COMP SOLN; PEMETREXED MYX DRY VIAL 1000 MG; PEMETREXED SANDOZ COMP SOLN; PEMETREXED DRLA DRY VIAL 500 MG; PEMETREXED DRLA DRY VIAL 100 MG; TEVATREXED COMP SOLN; PEMETREXED ACCORD VIAL 500 MG; PEMETREXED ACCORD VIAL 1 G; PEMETREXED ACCORD VIAL 100 MG; TEVATREXED VIAL 500 MG; PEMETREXED SUN VIAL 100 MG; PEMETREXED SUN VIAL 500 MG; PEMETREXED SUN COMP SOLN; PEMETREXED SUN VIAL 1 G
Pertuzumab	PERJETA COMP SOLN; PERJETA VIAL 420 MG 14 ML
Pralatrexate	FOLOTYN VIAL 20 MG 1 ML; FOLOTYN COMP SOLN
Raltitrexed	TOMUDEX COMP SOLN; TOMUDEX VIAL 2 MG
Rituximab	MABTHERA VIAL 500 MG 50 ML; MABTHERA VIAL 100 MG 2 X 10 ML; MABTHERA COMP SOLN; MABTHERA SC INJECTION 1400 MG 11.7 ML; RIXIMYO VIAL 500 MG 50 ML; RIXIMYO COMP SOLN; RIXIMYO VIAL 100 MG 2 X 10 ML; TRUXIMA VIALS 500 MG 50 ML; TRUXIMA VIALS 100 MG 2 X 10 ML; TRUXIMA COMP SOLN
Topotecan	HYCAMTIN COMP SOLN; HYCAMTIN IV INFUS PDR 4 MG 5; TOPOTECAN-KABI COMP SOLN; TOPOTECAN AGILA COMP SOLN; TOPOTECAN ACCORD VIAL 4 MG 5 X 4 ML
Trastuzumab	HERCEPTIN VIAL 60 MG; HERCEPTIN COMP SOLN; HERCEPTIN VIAL 150 MG; HERCEPTIN SC INJECTION 600 MG 5 ML; OGIVRI LYT VIAL 150 MG; OGIVRI COMP SOLN; HERZUMA POWDER FOR INJECTION VIAL 150 MG; HERZUMA COMP SOLN; ONTRUZANT COMP SOLN; KANJINTI VIAL 420 MG; KANJINTI VIAL 150 MG; KANJINTI COMP SOLN; TRAZIMERA VIAL 150 MG 15 ML; TRAZIMERA VIAL 60 MG 8 ML; ONTRUZANT VIAL 150 MG
Trastuzumab Emtansine	KADCYLA VIAL 100 MG 5 ML; KADCYLA VIAL 160 MG 8 ML; KADCYLA COMP SOLN
Vinblastine	VINBLASTINE DBL COMP SOLN; VINBLASTIN VIAL 10 MG 5 X 10 ML; VINBLASTINE TEVA COMP SOLN

Drug	*Pack Types Purchased on the Australian Market*
Vincristine	VINCRISTINE SULP VIAL 2 MG 5 X 2 ML; VINCRISTINE SULP COMP SOLN; VINCRISTINE COMP SOLN; VINCRISTINE VIAL 2 MG /2ML 5 X 2 ML; VINCRISTINE VIAL 1 MG /1ML 5 X 1 ML
Vinorelbine	VINORELBINE EBEWE VIAL 10 MG 1 ML; VINORELBINE TART VIAL 10 MG 1 ML; VINORELBINE EBEWE VIAL 50 MG 5 ML; VINORELBINE EBEWE COMP SOLN; NAVELBINE VIAL 50 MG 5 ML; VINORELBINE KABI COMP SOLN; VINORELBINE TART VIAL 50 MG 5 ML; NAVELBINE VIAL 10 MG 1 ML; VINORELBINE TART COMP SOLN; VINORELBINE COMP SOLUTION; NAVELBINE COMP SOLN

IQVIA in-market sales data reflect the totality of sales for cancer medicines, containing data for medicines accessed via the EFC program, private prescriptions, clinical trials and compassionate use programs (see Figure A43). To, as much as possible restrict those data to sales of medicines that were publicly funded, transactions which reflected medicines provided at no cost for clinical trials or compassionate use programs were removed from the analysis. These transactions accounted for approximately less than 0.01% of all sales (see Figure A43). However, it was not possible to remove transactions for medicines that were purchased for self-funded patients. Hence, the IQVIA data are still likely to be broader than the corresponding PBS prescription data (see the appendix comparing PBS claims data with IQVIA sales data). In addition, IQVIA sales do not include transactions provided by the HPS group of distributors, and therefore will understate transactions for some medicines.

Figure A43. Distribution of drugs purchased by sales type

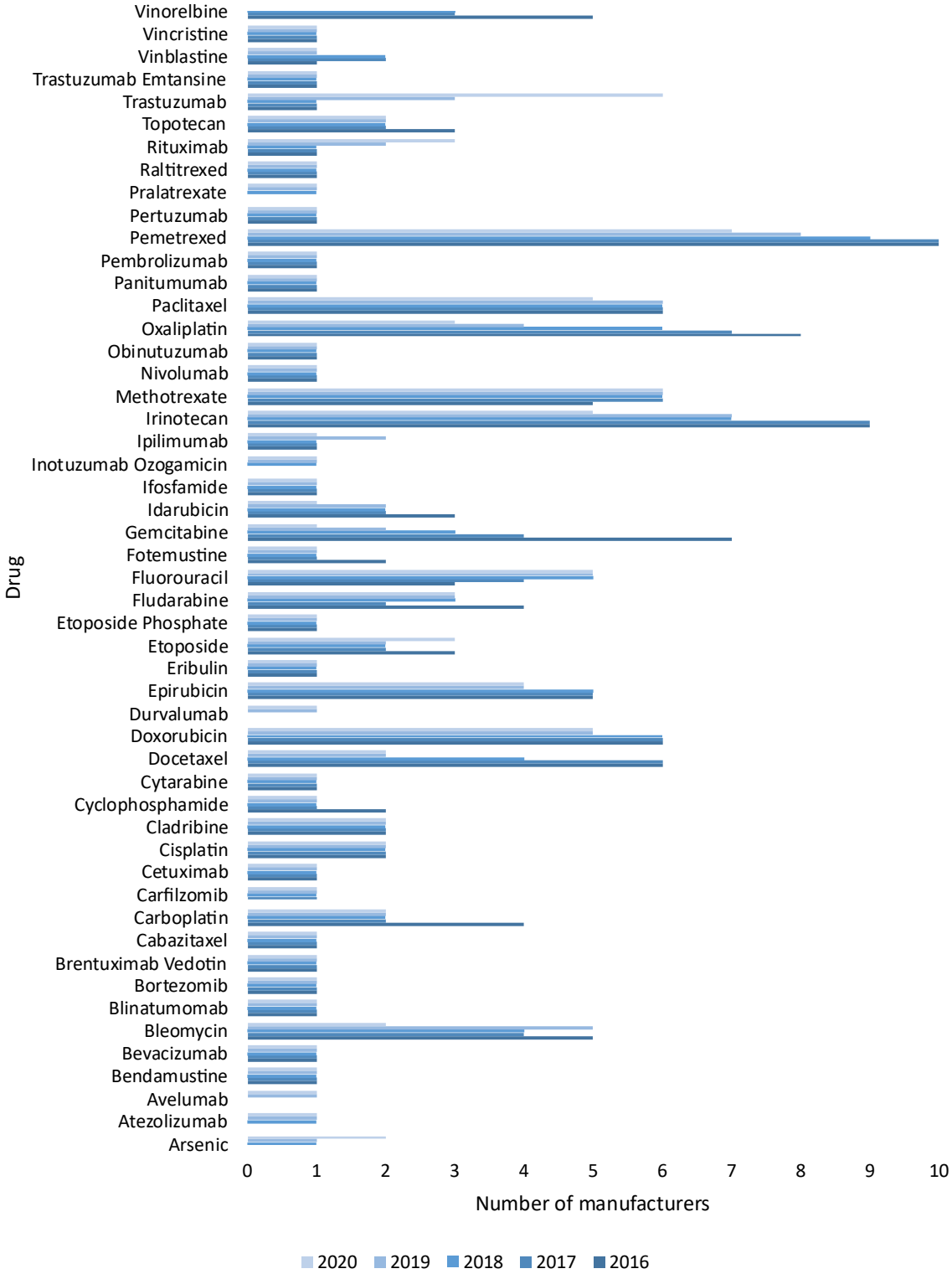


Source: Developed for this Review using in-market sales data (IQVIA).

Number of manufacturers of each drug

The number of manufacturers for drugs over the period, 2016-2020 is provided in Figure A44, with information on the name of manufacturer per medicine provided in Table A35.

Figure A44. Number of manufacturers of each EFC-listed drug (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

Table A35. Drug manufacturers by EFC-listed molecule (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
Arsenic	OPHTHALMIC LABS	OPHTHALMIC LABS	OPHTHALMIC LABS	OPHTHALMIC LABS	JUNO PTY LTD OPHTHALMIC LABS
Atezolizumab			ROCHE	ROCHE	ROCHE
Avelumab				MERCK SERONO AUST	MERCK SERONO AUST
Bendamustine	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG
Bevacizumab	ROCHE	ROCHE	ROCHE	ROCHE	ROCHE
Bleomycin	AMNEAL PHARMA AUST BAXTER HEALTHCARE CIPLA MEDIS PHARMA P/L PFIZER,	AMNEAL PHARMA AUST BAXTER HEALTHCARE CIPLA PFIZER	AMNEAL PHARMA AUST CIPLA MEDIS PHARMA P/L PFIZER	AMNEAL PHARMA AUST CIPLA MEDIS PHARMA P/L PFIZER PRO PHARMACEUTICALS GROUP	PFIZER PRO PHARMACEUTICALS GROUP
Blinatumomab	AMGEN	AMGEN	AMGEN	AMGEN	AMGEN
Bortezomib	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG
Brentuximab Vedotin	TAKEDA PHARMACEUT	TAKEDA PHARMACEUT	TAKEDA PHARMACEUT	TAKEDA PHARMACEUT	TAKEDA PHARMACEUT
Cabazitaxel	SANOFI-AVENTIS	SANOFI-AVENTIS	SANOFI-AVENTIS	SANOFI-AVENTIS	SANOFI-AVENTIS
Carboplatin	ACTAVIS AUST P/L FRESENIUS-KABI PFIZER SANDOZ	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER
Carfilzomib		AMGEN	AMGEN	AMGEN	AMGEN
Cetuximab	MERCK SERONO AUST	MERCK SERONO AUST	MERCK SERONO AUST	MERCK SERONO AUST	MERCK SERONO AUST
Cisplatin	PFIZER SANDOZ	PFIZER SANDOZ	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER
Cladribine	ASPEN PHARMA PL	ASPEN PHARMA PL	ASPEN PHARMA PL	ASPEN PHARMA PL	ASPEN PHARMA PL
Cladribine	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG	JANSSEN CILAG
Cyclophosph…	BAXTER HEALTHCARE PFIZER	BAXTER HEALTHCARE	BAXTER HEALTHCARE	BAXTER HEALTHCARE	BAXTER HEALTHCARE
Cytarabine	PFIZER	PFIZER	PFIZER	PFIZER	PFIZER
Docetaxel	AGILA AUSTRALASIA AMNEAL PHARMA AUST PFIZER SANDOZ SANOFI-AVENTIS SUN PHARMACEUT…	ACCORD HEALTHCARE AMNEAL PHARMA AUST PFIZER SANDOZ SANOFI-AVENTIS SUN PHARMACEUT…	ACCORD HEALTHCARE PFIZER SANDOZ SUN PHARMACEUT…	ACCORD HEALTHCARE PFIZER	ACCORD HEALTHCARE PFIZER
Doxorubicin	AMNEAL PHARMA AUST JANSSEN CILAG MAYNE PHARMA PFIZER SANDOZ SUN PHARMACEUT…	AMNEAL PHARMA AUST JANSSEN CILAG MAYNE PHARMA PFIZER SANDOZ SUN PHARMACEUT…	AMNEAL PHARMA AUST JANSSEN CILAG MAYNE PHARMA PFIZER SANDOZ SUN PHARMACEUT…	AMNEAL PHARMA AUST JANSSEN CILAG MAYNE PHARMA PFIZER SUN PHARMACEUT…	AMNEAL PHARMA AUST JANSSEN CILAG MAYNE PHARMA PFIZER SUN PHARMACEUT…

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
Durvalumab				ASTRAZENECA	ASTRAZENECA
Epirubicin	AMNEAL PHARMA AUST BAXTER HEALTHCARE FRESENIUS-KABI PFIZER SANDOZ	ACCORD HEALTHCARE AMNEAL PHARMA AUST PFIZER SANDOZ TEVA PHARMA AUST	ACCORD HEALTHCARE AMNEAL PHARMA AUST PFIZER SANDOZ TEVA PHARMA AUST	ACCORD HEALTHCARE AMNEAL PHARMA AUST PFIZER TEVA PHARMA AUST	ACCORD HEALTHCARE AMNEAL PHARMA AUST PFIZER TEVA PHARMA AUST
Eribulin	EISAI AUST P/L	EISAI AUST P/L	EISAI AUST P/L	EISAI AUST P/L	EISAI AUST P/L
Etoposide	BAXTER HEALTHCARE PFIZER SANDOZ LINK PHARMACEUTICS	PFIZER SANDOZ LINK PHARMACEUTICS	PFIZER SANDOZ LINK PHARMACEUTICS	SANDOZ LINK PHARMACEUTICS	BAXTER HEALTHCARE PFIZER SANDOZ LINK PHARMACEUTICS
Fludarabine	ACTAVIS AUST P/L AMNEAL PHARMA AUST BAXTER HEALTHCARE SANDOZ	AMNEAL PHARMA AUST SANDOZ	AMNEAL PHARMA AUST ARROW PHARMA SANDOZ	AMNEAL PHARMA AUST ARROW PHARMA SANDOZ	ARROW PHARMA JUNO PTY LTD SANDOZ
Fluorouracil	INOVA PFIZER SANDOZ	APOTEX INOVA PFIZER SANDOZ	ACCORD HEALTHCARE APOTEX INOVA PFIZER SANDOZ	ACCORD HEALTHCARE APOTEX INOVA PFIZER SANDOZ	ACCORD HEALTHCARE APOTEX INOVA PFIZER SANDOZ
Fotemustine	BAXTER HEALTHCARE SERVIER	SERVIER	SERVIER	SERVIER	SERVIER
Gemcitabine	ACTAVIS AUST P/L AGILA AUSTRALASIA AMNEAL PHARMA AUST FRESENIUS-KABI PFIZER SANDOZ SUN PHARMACEUT…	ACTAVIS AUST P/L AMNEAL PHARMA AUST PFIZER SANDOZ	AGILA AUSTRALASIA PFIZER SANDOZ	AGILA AUSTRALASIA PFIZER	PFIZER
Idarubicin	BAXTER HEALTHCARE PFIZER SANDOZ	PFIZER SANDOZ	PFIZER SANDOZ	PFIZER SANDOZ	PFIZER
Ifosfamide	BAXTER HEALTHCARE	BAXTER HEALTHCARE	BAXTER HEALTHCARE	BAXTER HEALTHCARE	BAXTER HEALTHCARE
Inotuzumab Ozogamicin			PFIZER	PFIZER	PFIZER
Ipilimumab	BRISTOLMYER SQUIBB	BRISTOLMYER SQUIBB	BRISTOLMYER SQUIBB	BAXTER HEALTHCARE BRISTOLMYER SQUIBB	BRISTOLMYER SQUIBB
Irinotecan	ACTAVIS AUST P/L AMNEAL PHARMA AUST BAXTER HEALTHCARE	ACCORD HEALTHCARE ACTAVIS AUST P/L AMNEAL PHARMA AUST CIPLA	ACCORD HEALTHCARE AMNEAL PHARMA AUST CIPLA MAYNE PHARMA	ACCORD HEALTHCARE AMNEAL PHARMA AUST CIPLA MYLAN AUSTRALIA	ACCORD HEALTHCARE AMNEAL PHARMA AUST CIPLA PFIZER SERVIER

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
	CIPLA	MAYNE PHARMA	MYLAN	OMEGAPHARM	
	FRESENIUS-KABI	MYLAN	AUSTRALIA	P/L	
	MAYNE PHARMA	AUSTRALIA	OMEGAPHARM	PFIZER	
	MYLAN	OMEGAPHARM	P/L	SERVIER	
	AUSTRALIA	P/L	PFIZER		
	PFIZER	PFIZER			
	SANDOZ	SANDOZ			
Methotrexate		ACCORD	ACCORD	ACCORD	ACCORD
	ACTAVIS AUST	HEALTHCARE	HEALTHCARE	HEALTHCARE	HEALTHCARE
	P/L	ACTAVIS AUST	ACTAVIS AUST	ACTAVIS AUST	ACTAVIS AUST
	LINK	P/L	P/L	P/L	P/L
	PHARMACEUTICS	LINK	LINK	LINK	LINK
	MAYNE PHARMA	PHARMACEUTICS	PHARMACEUTICS	PHARMACEUTICS	PHARMACEUTICS
	PFIZER	MAYNE PHARMA	MAYNE PHARMA	MAYNE PHARMA	MAYNE PHARMA
	SANDOZ	PFIZER	PFIZER	PFIZER	PFIZER
		SANDOZ	SANDOZ	SANDOZ	SANDOZ
Nivolumab	BRISTOLMYER	BRISTOLMYER	BRISTOLMYER	BRISTOLMYER	BRISTOLMYER
	SQUIBB	SQUIBB	SQUIBB	SQUIBB	SQUIBB
Obinutuzumab	ROCHE	ROCHE	ROCHE	ROCHE	ROCHE
Oxaliplatin		ACCORD	ACCORD	ACCORD	ACCORD
	ACTAVIS AUST	HEALTHCARE	HEALTHCARE	HEALTHCARE	HEALTHCARE
	P/L	AMNEAL	ACTAVIS AUST	ACTAVIS AUST	PFIZER
	AMNEAL	PHARMA AUST	P/L	P/L	
	PHARMA AUST	LINK	AMNEAL	PFIZER	
	FRESENIUS-KABI	PHARMACEUTICS	PHARMA AUST		
	MAYNE PHARMA	PFIZER	MEDIS PHARMA		
	PFIZER	SANDOZ	P/L		
	SANDOZ	SANOFI-AVENTIS	PFIZER		
	SANOFI-AVENTIS				
	SUN	SUN	SUN	SUN	SUN
	PHARMACEUT…	PHARMACEUT…	PHARMACEUT…	PHARMACEUT…	PHARMACEUT…
Paclitaxel		ACCORD	ACCORD	ACCORD	ACCORD
	ACTAVIS AUST	HEALTHCARE	HEALTHCARE	HEALTHCARE	HEALTHCARE
	P/L	AMNEAL	AMNEAL	AMNEAL	PFIZER
	AMNEAL	PHARMA AUST	PHARMA AUST	PHARMA AUST	SANDOZ
	PHARMA AUST	PFIZER	PFIZER	PFIZER	SPECIALISED
	FRESENIUS-KABI	SANDOZ	SANDOZ	SANDOZ	THERAP
	PFIZER	SPECIALISED	SPECIALISED	SPECIALISED	TEVA PHARMA
	SANDOZ	THERAP	THERAP	THERAP	AUST
	SPECIALISED	TEVA PHARMA	TEVA PHARMA	TEVA PHARMA	
	THERAP	AUST	AUST	AUST	
Panitumumab	AMGEN	AMGEN	AMGEN	AMGEN	AMGEN
Pembrolizumab	MSD	MSD	MSD	MSD	MSD
Pemetrexed	ACCORD	ACCORD	ACCORD	ACCORD	ACCORD
	HEALTHCARE	HEALTHCARE	HEALTHCARE	HEALTHCARE	HEALTHCARE
	APOTEX	APOTEX	APOTEX	APOTEX	APOTEX
	BAXTER	DR REDDYS LABS	JUNO PTY LTD	JUNO PTY LTD	JUNO PTY LTD
	HEALTHCARE	JUNO PTY LTD	LILLY	LILLY	LILLY
	DR REDDYS LABS	LILLY	MAYNE PHARMA	MAYNE PHARMA	MAYNE PHARMA
	JUNO PTY LTD	MAYNE PHARMA	MYLAN	PFIZER	SUN
	LILLY	MYLAN	AUSTRALIA	SUN	PHARMACEUT…
	MAYNE PHARMA	AUSTRALIA	PFIZER	PHARMACEUT…	TEVA PHARMA
	MYLAN	PFIZER	SANDOZ	TEVA PHARMA	AUST
	AUSTRALIA	SANDOZ	TEVA PHARMA	AUST	
	PFIZER	TEVA PHARMA	AUST		
	SANDOZ	AUST			
Epratuzumab	ROCHE	ROCHE	ROCHE	ROCHE	ROCHE
Pralatrexate			MUNDIPHARMA	MUNDIPHARMA	MUNDIPHARMA
Raltitrexed	PFIZER	PFIZER	PFIZER	PFIZER	PFIZER
Rituximab	ROCHE	ROCHE	ROCHE	ROCHE	CELLTRION
				SANDOZ	HEALTHCARE
					AUSTRALIA

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
Topotecan	AGILA AUSTRALASIA FRESENIUS-KABI SANDOZ	AGILA AUSTRALASIA SANDOZ	AGILA AUSTRALASIA SANDOZ	FRESENIUS-KABI SANDOZ	ROCHE SANDOZ ACCORD HEALTHCARE SANDOZ
Trastuzumab	ROCHE	ROCHE	ROCHE	CELLTRION HEALTHCARE AUSTRALIA MYLAN AUSTRALIA ROCHE	AMGEN CELLTRION HEALTHCARE AUSTRALIA MSD MYLAN AUSTRALIA PFIZER ROCHE
Trastuzumab Etamine	ROCHE	ROCHE	ROCHE	ROCHE	ROCHE
Vinblastine	PFIZER	MEDSURGE HLTHCARE PFIZER	MEDSURGE HLTHCARE PFIZER	PFIZER	PFIZER
Vincristine	PFIZER	PFIZER	PFIZER	PFIZER	PFIZER
Vinorelbine	BAXTER HEALTHCARE FRESENIUS-KABI PFIZER PIERRE FABRE SANDOZ	PFIZER PIERRE FABRE SANDOZ	PFIZER PIERRE FABRE SANDOZ	PFIZER PIERRE FABRE SANDOZ	PIERRE FABRE SANDOZ

Source: Developed for this Review using in-market sales data (IQVIA).

Total purchases by year

A summary of the total purchases made each year by hospital and pharmacies is provided in Table A36 and Figure A45 and Figure A46, and shows that the total amount spent on cancer drugs is increasing each year.

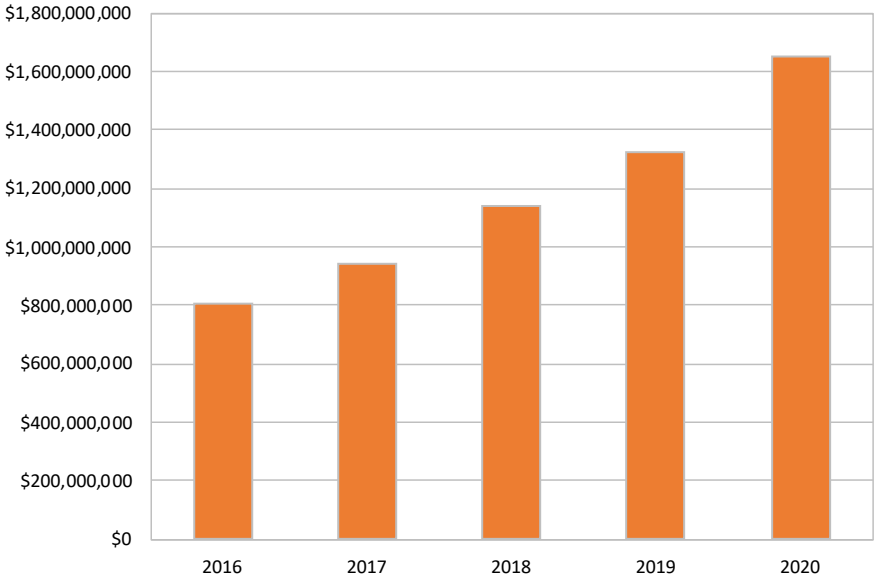
Table A36. Total purchases (hospital/pharmacy) by EFC-listed molecule (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic	$1,237,287	$1,318,501	$1,858,799	$2,614,061	$2,267,871	$9,296,519
Atezolizumab	-	-	$15,114,512	$40,873,841	$88,545,208	$144,533,561
Avelumab	-	-	-	$12,136,455	$18,892,073	$31,028,528
Bendamustine	$8,554,247	$16,576,607	$17,044,333	$17,779,098	$17,408,016	$77,362,300
Bevacizumab	$80,227,647	$80,128,772	$77,317,898	$71,180,468	$81,696,147	$390,550,931
Bleomycin	$962,555	$590,121	$336,725	$457,469	$478,898	$2,825,770
Blinatumomab	-	$3,312,224	$7,515,605	$5,194,457	$9,379,962	$25,402,247
Bortezomib	$57,147,883	$53,924,091	$46,914,214	$47,900,090	$51,907,339	$257,793,618
Brentuximab Vedotin	$4,340,389	$9,169,678	$11,790,640	$11,563,846	$12,463,495	$49,328,049
Cabazitaxel	$21,380,561	$11,605,227	$10,692,981	$13,076,497	$14,026,715	$70,781,980
Carboplatin	$2,312,936	$2,434,150	$2,427,736	$2,552,028	$2,698,320	$12,425,171
Carfilzomib	-	$143,392	$39,077,365	$45,157,344	$48,231,783	$132,609,883
Cetuximab	$39,257,621	$34,206,950	$31,424,565	$29,904,684	$30,165,430	$164,959,249
Cisplatin	$921,050	$889,251	$899,665	$963,616	$985,547	$4,659,130
Cladribine	$710,113	$584,395	$444,524	$665,576	$497,450	$2,902,058
Cyclophosph…	$3,553,851	$3,283,975	$3,331,477	$3,337,551	$3,113,627	$16,620,483
Cytarabine	$1,513,004	$2,050,952	$2,097,607	$3,207,250	$4,706,370	$13,575,183

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Docetaxel	$1,558,281	$1,378,879	$1,215,594	$1,273,221	$1,170,784	$6,596,758
Doxorubicin	$6,282,812	$5,355,152	$5,006,517	$5,056,486	$5,307,594	$27,008,561
Durvalumab	-	-	-	$31,445	$53,473,997	$53,505,442
Epirubicin	$1,115,133	$741,536	$425,002	$279,015	$206,440	$2,767,126
Eribulin	$5,089,293	$6,135,473	$6,948,202	$3,995,269	$3,648,993	$25,817,229
Etoposide	$516,854	$1,303,111	$411,555	$304,097	$277,353	$2,812,970
Etoposide Phosphate	$2,842,965	$725,422	$3,280,041	$3,434,370	$3,498,021	$13,780,820
Fludarabine	$435,785	$364,526	$334,127	$346,448	$275,942	$1,756,829
Fluorouracil	$15,220,499	$14,663,309	$14,942,492	$15,806,628	$18,164,488	$78,797,415
Fotemustine	$108,979	$193,560	$32,379	$35,578	$67,683	$438,178
Gemcitabine	$2,739,678	$3,046,381	$3,061,008	$2,855,336	$2,735,837	$14,438,239
Idarubicin	$871,091	$619,401	$557,379	$333,599	$246,942	$2,628,412
Ifosfamide	$1,933,119	$1,770,328	$1,557,796	$1,453,326	$1,333,214	$8,047,783
Inotuzumab Ozogamicin	-	-	-	$3,080,682	$4,116,302	$7,196,983
Ipilimumab	$27,209,751	$61,018,229	$69,424,710	$87,404,353	$95,331,444	$340,388,486
Irinotecan	$2,388,723	$2,366,503	$1,744,290	$1,647,462	$1,900,582	$10,047,559
Methotrexate	$2,213,579	$2,196,197	$3,322,572	$5,316,480	$6,835,505	$19,884,333
Nivolumab	$4,631,883	$90,776,566	$231,609,339	$277,123,820	$378,027,250	$982,168,857
Obinutuzumab	$5,529,755	$9,022,841	$11,144,532	$29,298,410	$46,898,273	$101,893,811
Oxaliplatin	$1,587,325	$1,999,401	$1,856,901	$1,894,228	$2,123,487	$9,461,342
Paclitaxel	$18,250,573	$19,180,220	$18,439,639	$18,565,635	$19,783,200	$94,219,267
Panitumumab	$12,192,213	$17,247,900	$16,727,621	$13,102,995	$12,560,580	$71,831,310
Pembrolizumab	$108,004,022	$125,711,142	$145,708,479	$254,677,967	$381,435,498	$1,015,537,108
Pemetrexed	$13,935,819	$4,889,411	$1,354,454	$1,023,627	$1,594,777	$22,798,087
Pertuzumab	$31,118,244	$39,491,831	$45,033,408	$50,370,985	$58,227,403	$224,241,869
Pralatrexate	-	-	$1,434,936	$2,471,220	$2,888,409	$6,794,565
Raltitrexed	$422,521	$417,612	$303,945	$330,495	$287,306	$1,761,879
Rituximab	$151,018,715	$143,725,732	$122,709,551	$99,221,277	$57,992,656	$574,667,930
Topotecan	$232,959	$184,455	$131,757	$120,881	$125,891	$795,943
Trastuzumab	$153,515,539	$157,735,426	$151,336,346	$124,805,592	$77,801,025	$665,193,928
Trastuzumab Emtansine	$17,983,780	$17,986,049	$16,527,548	$15,573,718	$27,418,690	$95,489,785
Vinblastine	$352,961	$313,513	$324,293	$345,144	$369,240	$1,705,150
Vincristine	$676,188	$756,682	$911,146	$981,898	$1,058,086	$4,384,000
Vinorelbine	$464,652	$429,396	$432,760	$386,336	$332,631	$2,045,774
Total	*$812,562,832*	*$951,964,468*	*$1,146,538,964*	*$1,331,512,351*	*$1,654,979,771*	*$5,897,558,386*

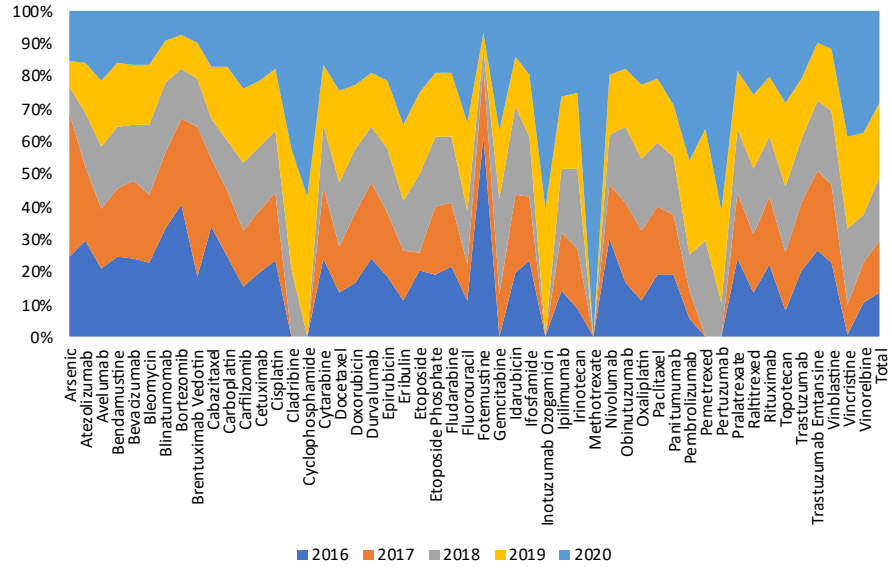
Source: Developed for this Review using in-market sales data (IQVIA).

Figure A45. Total purchases of EFC-listed drugs by year (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

Figure A46. Distribution of purchases by EFC-listed drug and year (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

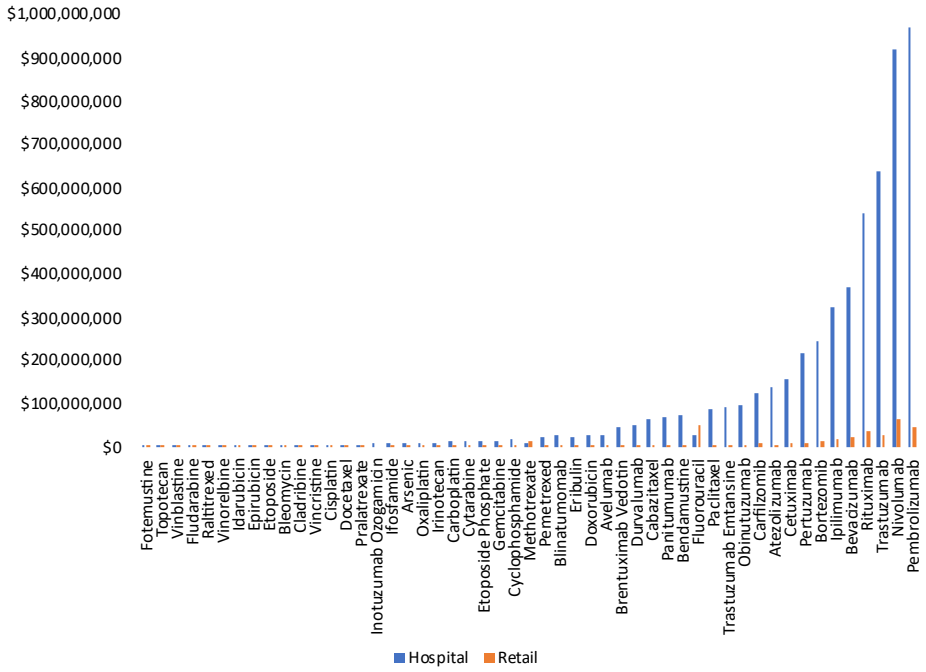
Total sales by purchasing channel (hospitals and retail pharmacies) are provided in Figure A47 and Table A37. Retail pharmacies accounted for approximately 6% of all purchases made between 2016-2020, whilst hospitals accounted for the remaining 94% (Figure A48). Inotuzumab ozogamicin and docetaxel had the highest proportion of retail pharmacy sales (36% and 58%, respectively).

Table A37. Total sales by setting (hospital, retail pharmacy) (2016 - 2021)

Drug	*Hospital*	*Retail Pharmacy*
Arsenic	$9,256,192	$40,327
Atezolizumab	$139,774,224	$4,759,342
Avelumab	$29,265,460	$1,763,067
Bendamustine	$72,942,664	$4,419,637
Bevacizumab	$370,039,680	$20,511,252
Bleomycin	$2,701,766	$124,004
Blinatumomab	$24,954,912	$447,335
Bortezomib	$242,712,832	$15,080,786
Brentuximab Vedotin	$47,803,160	$1,524,891
Cabazitaxel	$64,582,240	$6,199,741
Carboplatin	$11,813,935	$611,236
Carfilzomib	$125,773,720	$6,836,161
Cetuximab	$156,098,992	$8,860,259
Cisplatin	$4,459,488	$199,642
Cladribine	$2,745,999	$156,059
Cyclophosphamide	$16,021,890	$598,593
Cytarabine	$13,438,548	$136,635
Docetaxel	$6,189,480	$407,278
Doxorubicin	$25,462,708	$1,545,853
Durvalumab	$52,388,140	$1,117,305
Epirubicin	$2,632,632	$134,494
Eribulin	$24,162,140	$1,655,089
Etoposide	$2,680,811	$132,159
Etoposide Phosphate	$13,382,052	$398,767
Fludarabine	$1,719,554	$37,275
Fluorouracil	$26,382,610	$14,967,874
Fotemustine	$397,070	$41,108
Gemcitabine	$13,654,811	$783,429
Idarubicin	$2,605,680	$22,732
Ifosfamide	$7,870,654	$177,129
Inotuzumab Ozogamicin	$7,196,983	-
Ipilimumab	$324,673,376	$15,715,108
Irinotecan	$9,485,081	$562,478
Methotrexate	$8,347,717	$11,536,617
Nivolumab	$917,364,672	$64,804,176
Obinutuzumab	$96,102,320	$5,791,490
Oxaliplatin	$9,021,854	$439,488
Paclitaxel	$88,694,120	$5,525,145
Panitumumab	$68,016,256	$3,815,055
Pembrolizumab	$968,315,904	$47,221,180
Pemetrexed	$21,733,376	$1,064,711
Pertuzumab	$215,502,032	$8,739,833
Pralatrexate	$6,005,128	$789,437
Raltitrexed	$1,622,590	$139,290
Rituximab	$538,543,424	$36,124,500
Topotecan	$748,003	$47,940
Trastuzumab	$635,884,032	$29,309,928
Trastuzumab Emtansine	$91,338,600	$4,151,185
Vinblastine	$1,637,413	$67,738
Vincristine	$4,275,847	$108,153
Vinorelbine	$1,936,991	$108,783

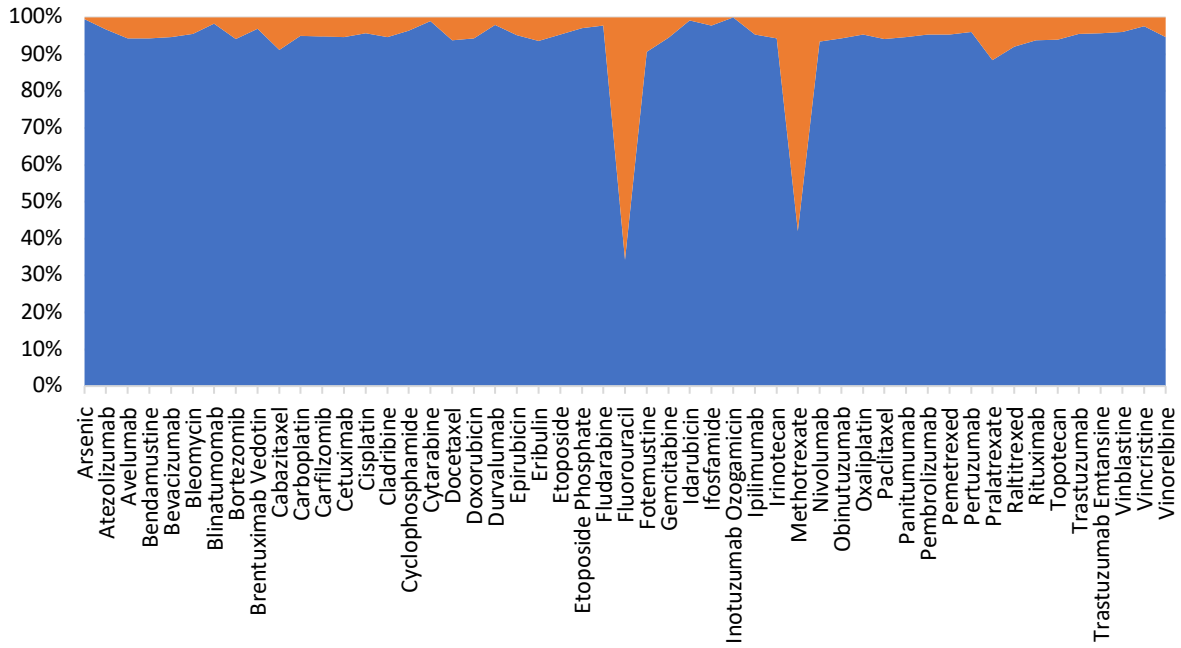
Source: Developed for this Review using in-market sales data (IQVIA).

Figure A47. Purchase value by EFC-listed drug and setting (2016 - 2021)



Source: Developed for this Review using in-market sales data (IQVIA).

Figure A48. Distribution of purchases by EFC-listed drug and setting (hospital, retail pharmacy) (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).
Notes: Blue denotes Hospital sales, orange denotes retail sales.

A summary of total purchases by drug, year and compounding status is provided in Table A38.

Table A38. Total purchases by EFC-listed drug and compounding status (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic						
Comp. Pack	$868,612	$974,923	$1,141,143	$1,255,427	$1,275,903	$5,516,008
Not Comp	$368,675	$343,577	$717,656	$1,358,634	$991,969	$3,780,511
Total	$1,237,287	$1,318,501	$1,858,799	$2,614,061	$2,267,871	$9,296,519
Atezolizumab						
Comp. Pack	-	-	$5,049,853	$19,593,596	$50,571,204	$75,214,653
Not Comp	-	-	$10,064,658	$21,280,244	$37,974,004	$69,318,906
Total	-	-	$15,114,511	$40,873,840	$88,545,208	$144,533,559
Avelumab						
Comp. Pack	-	-	-	$6,438,144	$10,155,631	$16,593,775
Not Comp	-	-	-	$5,698,311	$8,736,442	$14,434,753
Total	-	-	-	$12,136,455	$18,892,073	$31,028,528
Bendamustine						
Comp. Pack	$4,120,581	$9,560,612	$10,813,177	$11,549,825	$11,734,935	$47,779,130
Not Comp	$4,433,666	$7,015,995	$6,231,156	$6,229,272	$5,673,083	$29,583,171
Total	$8,554,247	$16,576,607	$17,044,333	$17,779,097	$17,408,018	$77,362,300
Bevacizumab						
Comp. Pack	$43,340,244	$43,382,280	$43,347,180	$44,525,504	$52,158,076	$226,753,284
Not Comp	$36,887,408	$36,746,496	$33,970,712	$26,654,964	$29,538,072	$163,797,652
Total	$80,227,652	$80,128,776	$77,317,892	$71,180,468	$81,696,148	$390,550,936
Bleomycin						
Comp. Pack	$692,405	$463,873	$239,213	$368,539	$325,324	$2,089,353
Not Comp	$270,151	$126,249	$97,512	$88,931	$153,574	$736,417
Total	$962,555	$590,122	$336,725	$457,470	$478,898	$2,825,770
Blinatumomab						
Comp. Pack	-	$1,092,980	$2,263,781	$1,975,770	$2,832,611	$8,165,141
Not Comp	-	$2,219,244	$5,251,824	$3,218,687	$6,547,352	$17,237,106
Total	-	$3,312,224	$7,515,605	$5,194,457	$9,379,962	$25,402,247
Bortezomib						
Comp. Pack	$30,879,116	$32,107,246	$28,656,794	$30,360,732	$34,298,912	$156,302,800
Not Comp	$26,268,768	$21,816,846	$18,257,422	$17,539,360	$17,608,428	$101,490,824
Total	$57,147,884	$53,924,092	$46,914,216	$47,900,092	$51,907,340	$257,793,624
Brentuximab Vedotin						
Comp. Pack	$1,086,878	$1,712,596	$3,398,244	$3,808,666	$5,332,310	$15,338,694
Not Comp	$3,253,511	$7,457,083	$8,392,396	$7,755,180	$7,131,186	$33,989,355
Total	$4,340,389	$9,169,678	$11,790,640	$11,563,846	$12,463,496	$49,328,049
Cabazitaxel						
Comp. Pack	$15,000,911	$8,305,686	$7,983,968	$9,483,643	$10,932,885	$51,707,092
Not Comp	$6,379,651	$3,299,541	$2,709,013	$3,592,853	$3,093,830	$19,074,888
Total	$21,380,562	$11,605,227	$10,692,981	$13,076,496	$14,026,715	$70,781,980
Carboplatin						
Comp. Pack	$1,762,256	$1,790,559	$1,765,061	$1,925,079	$2,101,651	$9,344,605
Not Comp	$550,680	$643,592	$662,676	$626,949	$596,669	$3,080,566
Total	$2,312,936	$2,434,151	$2,427,736	$2,552,028	$2,698,320	$12,425,171
Carfilzomib						
Comp. Pack	-	-	$25,215,668	$32,152,826	$33,652,216	$91,020,710
Not Comp	-	$143,392	$13,861,697	$13,004,519	$14,579,565	$41,589,173
Total	-	$143,392	$39,077,365	$45,157,345	$48,231,781	$132,609,883
Cetuximab						
Comp. Pack	$23,006,272	$21,104,348	$20,707,422	$19,838,192	$21,366,838	$106,023,072
Not Comp	$16,251,348	$13,102,602	$10,717,142	$10,066,492	$8,798,591	$58,936,175
Total	$39,257,620	$34,206,950	$31,424,564	$29,904,684	$30,165,429	$164,959,247
Cisplatin						
Comp. Pack	$745,639	$699,576	$728,707	$814,018	$831,538	$3,819,477
Not Comp	$175,410	$189,676	$170,959	$149,599	$154,009	$839,653
Total	$921,050	$889,251	$899,665	$963,616	$985,547	$4,659,130
Cladribine						

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Comp. Pack	$379,920	$315,804	$312,500	$402,849	$326,747	$1,737,820
Not Comp	$330,193	$268,591	$132,024	$262,728	$170,704	$1,164,239
Total	$710,113	$584,395	$444,524	$665,576	$497,450	$2,902,058
Cyclophosphamide						
Comp. Pack	$3,112,187	$2,912,864	$2,958,441	$2,981,533	$2,807,107	$14,772,131
Not Comp	$441,664	$371,112	$373,036	$356,019	$306,521	$1,848,352
Total	$3,553,851	$3,283,976	$3,331,477	$3,337,551	$3,113,627	$16,620,483
Cytarabine						
Comp. Pack	$906,953	$1,035,683	$1,117,231	$1,618,923	$2,428,833	$7,107,622
Not Comp	$606,051	$1,015,270	$980,376	$1,588,327	$2,277,537	$6,467,561
Total	$1,513,004	$2,050,952	$2,097,607	$3,207,250	$4,706,370	$13,575,183
Docetaxel						
Comp. Pack	$1,330,853	$1,110,558	$933,944	$1,018,474	$987,177	$5,381,005
Not Comp	$227,428	$268,322	$281,650	$254,747	$183,607	$1,215,753
Total	$1,558,281	$1,378,879	$1,215,594	$1,273,221	$1,170,784	$6,596,758
Doxorubicin						
Comp. Pack	$3,861,683	$3,584,378	$3,289,646	$3,448,295	$3,754,335	$17,938,336
Not Comp	$2,421,129	$1,770,774	$1,716,871	$1,608,192	$1,553,260	$9,070,225
Total	$6,282,812	$5,355,152	$5,006,517	$5,056,486	$5,307,594	$27,008,561
Durvalumab						
Comp. Pack	-	-	-	$10,277	$27,996,030	$28,006,307
Not Comp	-	-	-	$21,168	$25,477,968	$25,499,136
Total	-	-	-	$31,445	$53,473,998	$53,505,443
Epirubicin						
Comp. Pack	$840,282	$499,257	$267,523	$171,468	$113,751	$1,892,282
Not Comp	$274,850	$242,278	$157,479	$107,547	$92,689	$874,845
Total	$1,115,133	$741,536	$425,002	$279,015	$206,440	$2,767,126
Eribulin						
Comp. Pack	$2,838,639	$4,024,615	$4,827,624	$2,884,577	$2,533,301	$17,108,755
Not Comp	$2,250,654	$2,110,857	$2,120,578	$1,110,692	$1,115,692	$8,708,474
Total	$5,089,293	$6,135,472	$6,948,202	$3,995,269	$3,648,993	$25,817,229
Etoposide						
Comp. Pack	$226,085	$856,422	$297,992	$234,101	$204,077	$1,818,676
Not Comp	$290,769	$446,689	$113,563	$69,996	$73,276	$994,293
Total	$516,854	$1,303,110	$411,555	$304,097	$277,353	$2,812,970
Etoposide Phosphate						
Comp. Pack	$1,756,410	$263,617	$1,904,635	$2,188,180	$2,239,188	$8,352,030
Not Comp	$1,086,555	$461,805	$1,375,406	$1,246,190	$1,258,833	$5,428,789
Total	$2,842,965	$725,422	$3,280,041	$3,434,370	$3,498,021	$13,780,819
Fludarabine						
Comp. Pack	$330,394	$273,881	$232,929	$239,248	$195,093	$1,271,546
Not Comp	$105,391	$90,645	$101,198	$107,200	$80,849	$485,283
Total	$435,785	$364,526	$334,127	$346,448	$275,942	$1,756,829
Fluorouracil						
Comp. Pack	$5,278,644	$4,822,401	$4,612,704	$4,694,441	$5,465,833	$24,874,023
Not Comp	$587,277	$2,520,992	$3,482,973	$4,521,443	$5,363,776	$16,476,460
Total	$5,865,921	$7,343,393	$8,095,677	$9,215,884	$10,829,608	$41,350,483
Fotemustine						
Comp. Pack	$47,506	$100,155	$14,982	$11,069	$44,896	$218,608
Not Comp	$61,473	$93,405	$17,397	$24,509	$22,787	$219,570
Total	$108,979	$193,560	$32,379	$35,578	$67,683	$438,178
Gemcitabine						
Comp. Pack	$2,323,477	$2,531,601	$2,573,197	$2,427,296	$2,297,465	$12,153,036
Not Comp	$416,200	$514,780	$487,811	$428,040	$438,372	$2,285,204
Total	$2,739,678	$3,046,381	$3,061,008	$2,855,336	$2,735,837	$14,438,239
Idarubicin						
Comp. Pack	$515,408	$357,216	$298,119	$163,159	$115,750	$1,449,652
Not Comp	$355,683	$262,185	$259,260	$170,440	$131,193	$1,178,761
Total	$871,091	$619,401	$557,379	$333,599	$246,942	$2,628,412
Ifosfamide						
Comp. Pack	$1,136,479	$1,114,147	$929,587	$908,514	$870,555	$4,959,281
Not Comp	$796,640	$656,182	$628,209	$544,812	$462,660	$3,088,502

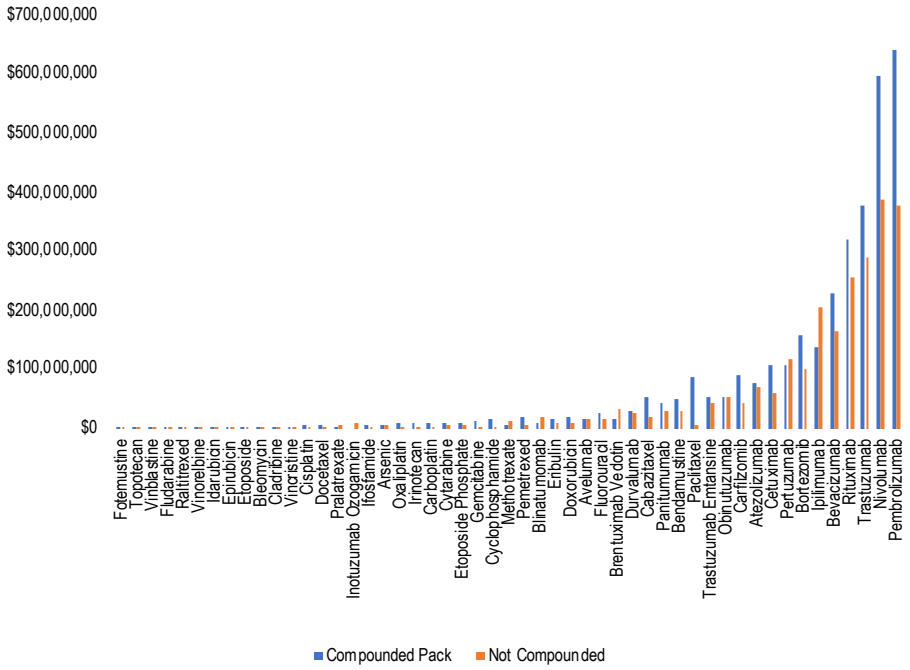
Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Total	$1,933,119	$1,770,328	$1,557,796	$1,453,326	$1,333,214	$8,047,783
Inotuzumab Ozogamicin						
Comp. Pack	-	-	-	-	-	-
Not Comp	-	-	-	$3,080,682	$4,116,302	$7,196,983
Total	-	-	-	$3,080,682	$4,116,302	$7,196,983
Ipilimumab						
Comp. Pack	$6,843,910	$17,047,040	$23,162,366	$38,541,924	$49,881,584	$135,476,824
Not Comp	$20,365,840	$43,971,192	$46,262,344	$48,862,432	$45,449,860	$204,911,668
Total	$27,209,750	$61,018,232	$69,424,710	$87,404,356	$95,331,444	$340,388,492
Irinotecan						
Comp. Pack	$1,917,455	$2,040,851	$1,463,439	$1,322,434	$1,521,618	$8,265,796
Not Comp	$471,268	$325,652	$280,852	$325,028	$378,964	$1,781,764
Total	$2,388,723	$2,366,502	$1,744,290	$1,647,462	$1,900,582	$10,047,560
Methotrexate						
Comp. Pack	$1,126,832	$1,438,645	$1,384,034	$1,274,060	$1,230,680	$6,454,251
Not Comp	$1,086,747	$757,552	$1,938,538	$4,042,421	$5,604,825	$13,430,082
Total	$2,213,579	$2,196,197	$3,322,572	$5,316,481	$6,835,505	$19,884,333
Nivolumab						
Comp. Pack	$1,637,906	$39,861,028	$132,859,264	$173,971,280	$247,327,344	$595,656,822
Not Comp	$2,993,977	$50,915,540	$98,750,080	$103,152,536	$130,699,920	$386,512,053
Total	$4,631,883	$90,776,568	$231,609,344	$277,123,816	$378,027,264	$982,168,875
Obinutuzumab						
Comp. Pack	$1,804,093	$3,901,690	$4,179,769	$15,061,506	$25,978,274	$50,925,332
Not Comp	$3,725,661	$5,121,152	$6,964,764	$14,236,904	$20,919,998	$50,968,479
Total	$5,529,754	$9,022,842	$11,144,533	$29,298,410	$46,898,272	$101,893,811
Oxaliplatin						
Comp. Pack	$1,383,602	$1,710,814	$1,537,457	$1,598,613	$1,791,466	$8,021,951
Not Comp	$203,723	$288,587	$319,445	$295,615	$332,020	$1,439,391
Total	$1,587,325	$1,999,401	$1,856,901	$1,894,228	$2,123,486	$9,461,342
Paclitaxel						
Comp. Pack	$16,926,008	$17,992,348	$17,152,504	$17,392,344	$18,414,348	$87,877,552
Not Comp	$1,324,564	$1,187,872	$1,287,134	$1,173,292	$1,368,851	$6,341,713
Total	$18,250,572	$19,180,220	$18,439,638	$18,565,636	$19,783,199	$94,219,265
Panitumumab						
Comp. Pack	$6,323,532	$9,695,312	$10,361,821	$8,217,548	$8,514,384	$43,112,596
Not Comp	$5,868,683	$7,552,589	$6,365,801	$4,885,447	$4,046,196	$28,718,715
Total	$12,192,214	$17,247,901	$16,727,622	$13,102,995	$12,560,580	$71,831,311
Pembrolizumab						
Comp. Pack	$41,599,396	$55,163,968	$84,837,200	$178,880,768	$278,750,720	$639,232,052
Not Comp	$66,404,624	$70,547,168	$60,871,284	$75,797,192	$102,684,752	$376,305,020
Total	$108,004,020	$125,711,136	$145,708,484	$254,677,960	$381,435,472	$1,015,537,072
Pemetrexed						
Comp. Pack	$10,818,414	$4,274,139	$977,605	$763,595	$1,271,477	$18,105,229
Not Comp	$3,117,405	$615,273	$376,849	$260,032	$323,300	$4,692,858
Total	$13,935,819	$4,889,411	$1,354,454	$1,023,627	$1,594,777	$22,798,088
Pertuzumab						
Comp. Pack	$11,421,680	$16,738,799	$20,961,988	$25,755,284	$31,215,694	$106,093,445
Not Comp	$19,696,564	$22,753,032	$24,071,418	$24,615,700	$27,011,708	$118,148,422
Total	$31,118,244	$39,491,831	$45,033,406	$50,370,984	$58,227,402	$224,241,867
Pralatrexate						
Comp. Pack	-	-	$508,889	$1,081,078	$1,465,283	$3,055,250
Not Comp	-	-	$926,048	$1,390,141	$1,423,126	$3,739,315
Total	-	-	$1,434,936	$2,471,220	$2,888,409	$6,794,565
Raltitrexed						
Comp. Pack	$320,586	$246,912	$190,166	$200,088	$213,776	$1,171,528
Not Comp	$101,934	$170,701	$113,779	$130,407	$73,531	$590,351
Total	$422,521	$417,612	$303,945	$330,495	$287,306	$1,761,879
Rituximab						
Comp. Pack	$79,310,024	$80,020,288	$68,948,848	$55,923,808	$36,710,252	$320,913,220
Not Comp	$71,708,696	$63,705,436	$53,760,696	$43,297,468	$21,282,404	$253,754,700
Total	$151,018,720	$143,725,724	$122,709,544	$99,221,276	$57,992,656	$574,667,920
Topotecan						

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Comp. Pack	$180,955	$153,329	$108,962	$91,873	$100,879	$635,999
Not Comp	$52,004	$31,126	$22,795	$29,007	$25,012	$159,943
Total	$232,959	$184,455	$131,757	$120,881	$125,891	$795,943
Trastuzumab						
Comp. Pack	$82,258,112	$84,698,632	$84,851,216	$74,674,560	$49,381,304	$375,863,824
Not Comp	$71,257,424	$73,036,800	$66,485,128	$50,131,028	$28,419,726	$289,330,106
Total	$153,515,536	$157,735,432	$151,336,344	$124,805,588	$77,801,030	$665,193,930
Trastuzumab Emtansine						
Comp. Pack	$9,387,579	$10,162,914	$8,900,315	$8,722,954	$16,297,095	$53,470,857
Not Comp	$8,596,201	$7,823,136	$7,627,233	$6,850,764	$11,121,596	$42,018,930
Total	$17,983,780	$17,986,050	$16,527,548	$15,573,718	$27,418,691	$95,489,787
Vinblastine						
Comp. Pack	$223,023	$188,475	$188,527	$245,983	$252,783	$1,098,790
Not Comp	$129,938	$125,039	$135,766	$99,161	$116,457	$606,360
Total	$352,961	$313,513	$324,293	$345,144	$369,240	$1,705,150
Vincristine						
Comp. Pack	$558,140	$541,366	$688,236	$715,911	$718,128	$3,221,781
Not Comp	$118,048	$215,316	$222,910	$265,988	$339,958	$1,162,219
Total	$676,188	$756,682	$911,146	$981,898	$1,058,086	$4,384,000
Vinorelbine						
Comp. Pack	$359,954	$311,791	$320,644	$286,587	$264,218	$1,543,193
Not Comp	$104,698	$117,605	$112,116	$99,749	$68,413	$502,581
Total	$464,652	$429,396	$432,760	$386,336	$332,631	$2,045,774
All molecules						
Comp. Pack	$420,789,024	$491,185,600	$639,464,512	$812,214,592	$1,061,251,456	$3,424,905,184
Not Comp	$382,419,232	$453,458,944	$500,227,648	$512,707,040	$586,393,408	$2,435,206,272
Total	*$803,208,256*	*$944,644,544*	*$1,139,692,160*	*$1,324,921,632*	*$1,647,644,864*	*$5,860,111,456*

Source: Developed for this Review using in-market sales data (IQVIA).

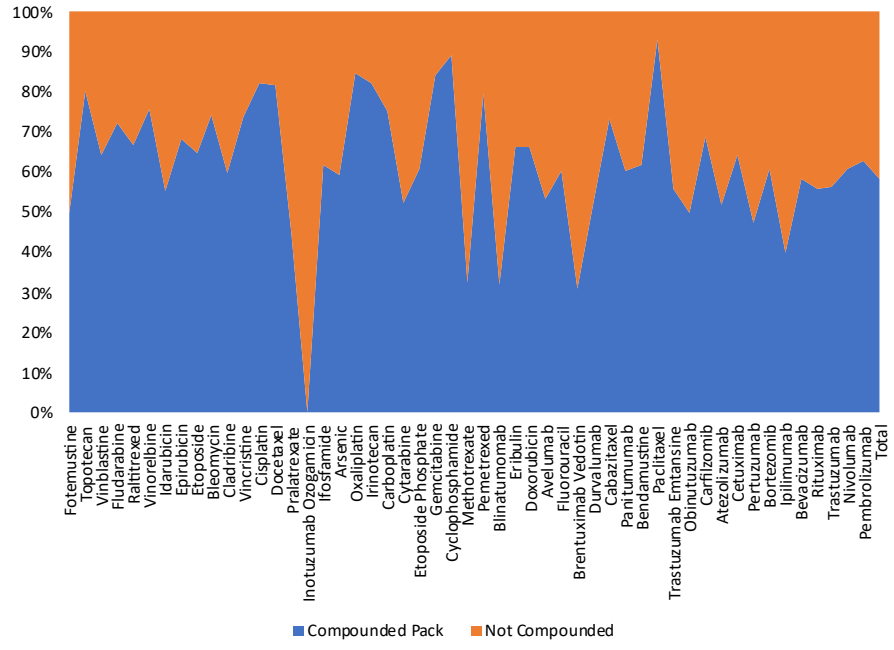
The total purchases by drug and compounding status are summarised in Figure A49. Overall, approximately 58% of purchases were for compounded products and 42% were for not compounded packs. The distribution of sales by compounding status is reported in Figure A50. Overall, the proportion of sales accounted for by compounded solutions was highest for paclitaxel and cyclophosphamide (93% and 89% respectively), while brentuximab vedotin and inotuzumab ozogamicin were mostly purchased in non-compounded solutions (60% and 100 %, respectively).

Figure A49. Total purchases by EFC-listed drug and compounding status (2016 - 2021)



Source: Developed for this Review using in-market sales data (IQVIA).

Figure A50. Distribution of total purchases by EFC-listed drug and compounding status (2016 - 2020)

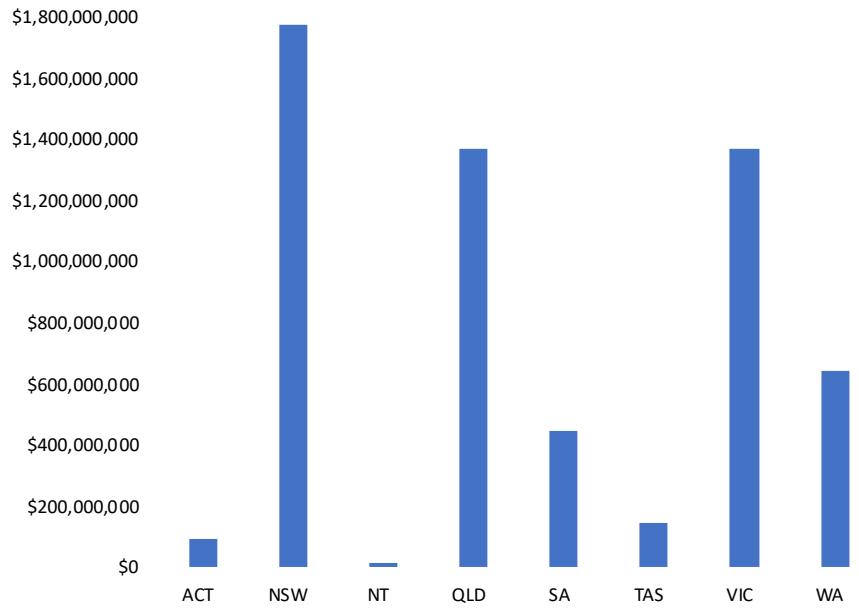


Source: Developed for this Review using in-market sales data (IQVIA).

A summary of total purchases made by each state is provided in Figure A51. Overall, the amount spent on cancer medicines by each state is proportional to the size of the population (see Figure A52

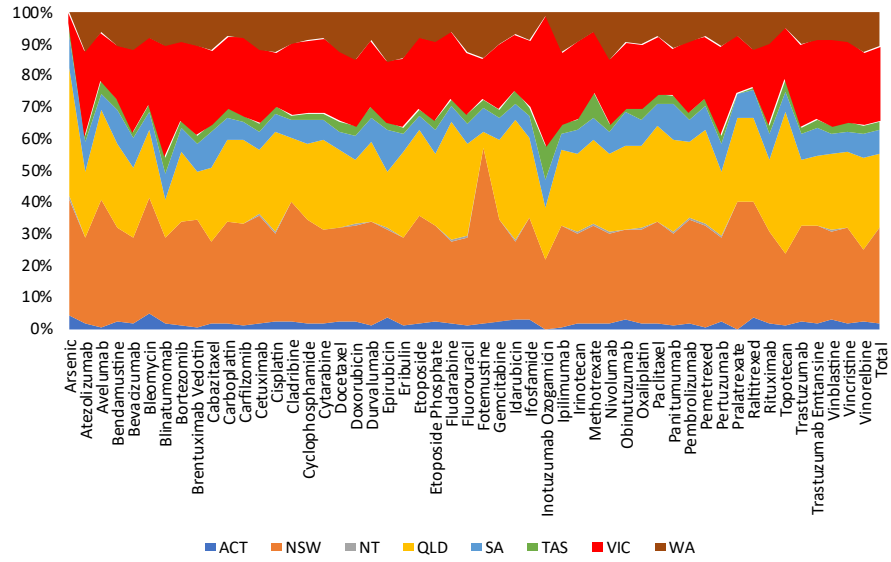
for the distribution across states). However, there were differences in the total expenditure by each state with regard to the types of medicines purchased. For example, Western Australia did not purchase arsenic, whilst New South Wales accounted for an higher proportion of fotemustine expenditure and Queensland a higher proportion of rituximab expenditure than would be anticipated based on their relative population size.

Figure A51. Total purchases of EFC-listed drugs by State and Territory (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

Figure A52. Distribution of purchases by EFC-listed drug and State and Territory (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

A summary of total purchases by drug and state is provided in Table A39.

Table A39. Total purchases of EFC-listed drugs by State and Territory (2016 - 2020)

Drug	*ACT*	*NSW*	*NT*	*QLD*	*SA*	*TAS*	*VIC*	*WA*	*Australia*
Arsenic	$402,222	$3,369,973	$128,691	$3,767,994	$942,609	$361,671	$323,359	-	$9,296,519
Atezolizumab	$2,284,654	$39,228,368	-	$30,261,818	$13,540,014	$2,695,508	$38,360,280	$18,162,914	$144,533,556
Avelumab	$107,442	$12,456,126	$81,923	$8,779,282	$1,667,462	$1,240,383	$4,712,912	$1,982,999	$31,028,529
Bendamustine	$1,901,367	$22,760,048	$142,888	$20,146,416	$8,289,305	$2,888,116	$13,129,038	$8,105,122	$77,362,300
Bevacizumab	$6,360,591	$105,763,104	$1,244,666	$84,801,600	$36,154,692	$8,427,199	$101,515,496	$46,283,592	$390,550,940
Bleomycin	$129,361	$1,032,422	$4,809	$600,129	$169,185	$70,559	$592,992	$226,313	$2,825,770
Blinatumomab	$441,134	$6,942,826	-	$2,925,457	$2,136,192	$1,336,447	$8,910,180	$2,710,012	$25,402,248
Bortezomib	$2,990,331	$83,643,440	$373,129	$57,533,356	$19,557,922	$5,831,629	$63,713,220	$24,150,588	$257,793,615
Brentuximab Vedotin	$261,665	$16,708,837	-	$7,428,773	$4,304,952	$1,398,144	$13,958,042	$5,267,638	$49,328,051
Cabazitaxel	$1,130,131	$18,402,408	$93,077	$16,560,403	$7,786,723	$1,780,982	$16,432,257	$8,595,999	$70,781,980
Carboplatin	$233,885	$3,963,256	$31,303	$3,212,759	$833,610	$353,020	$2,844,650	$952,687	$12,425,170
Carfilzomib	$1,571,426	$42,236,132	-	$34,916,852	$8,203,420	$2,040,275	$33,180,154	$10,461,625	$132,609,884
Cetuximab	$2,711,791	$55,999,704	$938,850	$33,596,792	$9,456,607	$4,439,082	$38,440,796	$19,375,624	$164,959,246
Cisplatin	$94,596	$1,318,322	$20,639	$1,463,248	$269,694	$105,591	$790,554	$596,486	$4,659,130
Cladribine	$63,872	$1,093,239	$5,114	$584,479	$161,423	$45,978	$658,818	$289,136	$2,902,059
Cyclophosphamide	$317,162	$5,410,406	$29,536	$3,924,738	$1,242,877	$395,828	$3,828,136	$1,471,801	$16,620,484
Cytarabine	$226,500	$4,028,534	$25,041	$3,850,980	$786,089	$318,360	$3,186,067	$1,153,613	$13,575,184
Docetaxel	$154,443	$1,941,701	$27,274	$1,598,043	$386,734	$212,229	$1,460,247	$816,087	$6,596,758
Doxorubicin	$549,075	$8,278,231	$53,484	$5,477,688	$2,093,911	$774,627	$5,760,344	$4,021,201	$27,008,561
Durvalumab	$571,147	$17,421,502	$79,500	$13,660,129	$4,019,170	$1,744,600	$11,242,620	$4,766,778	$53,505,446
Epirubicin	$95,770	$763,218	$22,642	$494,912	$357,966	$66,826	$531,055	$434,737	$2,767,126
Eribulin	$298,007	$7,173,218	$16,387	$6,909,365	$1,538,047	$445,741	$5,612,573	$3,823,892	$25,817,230
Etoposide	$48,592	$953,583	$7,152	$751,981	$128,772	$55,626	$637,357	$229,907	$2,812,970
Etoposide Phosphate	$283,633	$4,186,727	$27,160	$3,149,957	$966,101	$433,964	$3,430,956	$1,302,322	$13,780,820
Fludarabine	$29,499	$457,629	$6,044	$655,411	$82,447	$40,707	$377,405	$107,688	$1,756,830
Fluorouracil	$551,048	$11,357,978	$192,557	$12,151,317	$2,490,627	$1,241,302	$8,113,279	$5,252,376	$41,350,484
Fotemustine	$6,619	$242,845	-	$23,795	$32,272	$11,359	$56,781	$64,508	$438,179
Gemcitabine	$363,158	$4,603,327	$32,181	$3,590,813	$1,065,592	$356,600	$2,957,428	$1,469,141	$14,438,240
Idarubicin	$82,030	$646,572	$19,439	$985,495	$136,820	$104,865	$470,089	$183,103	$2,628,413
Ifosfamide	$239,098	$2,563,187	$17,683	$2,046,502	$561,997	$184,870	$1,712,370	$722,075	$8,047,782
Inotuzumab Ozogamicin	-	$1,586,593	-	$1,166,805	$645,599	$745,113	$2,975,857	$77,017	$7,196,984
Ipilimumab	$2,119,408	$108,362,136	$1,084,030	$81,578,200	$16,954,634	$9,455,280	$77,429,736	$43,405,068	$340,388,492
Irinotecan	$163,736	$2,842,872	$61,408	$2,466,929	$782,210	$328,860	$2,468,925	$932,620	$10,047,560
Methotrexate	$394,367	$6,099,919	$106,228	$5,294,379	$1,344,057	$1,580,828	$3,826,443	$1,238,113	$19,884,334
Nivolumab	$15,396,799	$281,248,224	$2,049,909	$243,217,216	$67,339,792	$23,247,056	$202,009,376	$147,660,496	$982,168,868
Obinutuzumab	$3,017,771	$29,121,306	$32,442	$26,529,836	$11,308,073	$813,478	$21,272,524	$9,798,384	$101,893,814

Drug	*ACT*	*NSW*	*NT*	*QLD*	*SA*	*TAS*	*VIC*	*WA*	*Australia*
Oxaliplatin	$149,737	$2,818,452	$56,685	$2,447,662	$766,836	$341,936	$1,912,941	$967,094	$9,461,343
Paclitaxel	$1,768,283	$29,856,226	$262,594	$28,216,724	$6,579,926	$3,129,800	$17,161,152	$7,244,560	$94,219,265
Panitumumab	$626,044	$20,947,828	$248,572	$21,154,446	$7,833,435	$2,136,225	$10,617,044	$8,267,717	$71,831,311
Pembrolizumab	$14,528,793	$336,508,576	$3,788,821	$242,584,576	$73,607,352	$24,282,534	$227,025,056	$93,211,376	$1,015,537,084
Pemetrexed	$157,476	$7,284,892	$60,212	$6,812,397	$1,690,351	$563,283	$4,452,769	$1,776,709	$22,798,089
Pertuzumab	$5,249,191	$59,620,052	$922,184	$44,697,292	$20,510,838	$5,807,024	$63,145,156	$24,290,132	$224,241,869
Pralatrexate	$3,247	$2,733,038	-	$1,771,482	$518,980	$33,093	$1,239,916	$494,810	$6,794,566
Raltitrexed	$64,589	$639,635	$5,498	$461,793	$156,250	$17,055	$211,537	$205,520	$1,761,877
Rituximab	$10,092,577	$166,229,808	$1,068,464	$130,291,520	$44,672,272	$17,091,986	$148,453,232	$56,768,064	$574,667,923
Topotecan	$6,827	$182,596	$870	$355,906	$47,153	$33,306	$129,671	$39,612	$795,941
Trastuzumab	$13,953,759	$201,060,880	$2,244,493	$139,102,176	$51,531,400	$15,097,221	$174,917,600	$67,286,408	$665,193,937
Trastuzumab Emtansine	$1,316,526	$29,711,902	$157,382	$21,016,706	$8,379,762	$2,562,431	$23,943,572	$8,401,506	$95,489,787
Vinblastine	$50,956	$476,244	$2,981	$408,106	$106,144	$46,471	$464,721	$149,529	$1,705,152
Vincristine	$73,326	$1,322,737	$5,127	$1,046,441	$267,617	$140,352	$1,124,641	$403,759	$4,384,000
Vinorelbine	$49,826	$460,296	$3,286	$588,172	$157,939	$54,790	$471,159	$260,305	$2,045,773
Total	*$93,683,487*	*$1,774,061,075*	*$15,782,355*	*$1,367,059,248*	*$444,563,852*	*$146,910,210*	*$1,372,192,483*	*$645,858,763*	*$5,860,111,473*

Total units purchased by pharmacy setting (hospital/retail)

A summary of the total units purchased by drug and channel status is provided in Table A40,Figure A53 and Figure A54. Overall, approximately 95% of medicine sales were to hospitals, the remaining 5% being to retail pharmacies.

Table A40. Total units purchased (mg) by EFC-listed drug and pharmacy setting (2016 - 2020)

Setting	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic						
Hospital	25,820	26,413	42,812	62,796	60,441	218,282
Retail	370	172	300	-	-	842
Total	26,190	26,585	43,112	62,796	60,441	219,124
Atezolizumab						
Hospital	-	-	2,370,000	6,374,240	14,200,000	22,944,240
Retail			42,000	158,400	583,200	783,600
Total	-	-	2,412,000	6,532,640	14,783,200	23,727,840
Avelumab						
Hospital	-	-	-	1,483,075	2,492,303	3,975,378
Retail				68,500	180,840	249,340
Total	-	-	-	1,551,575	2,673,143	4,224,718
Bendamustine						
Hospital	945,270	1,813,069	1,931,799	1,975,732	1,957,061	8,622,931
Retail	82,305	138,467	81,446	123,517	92,709	518,444
Total	1,027,575	1,951,536	2,013,245	2,099,249	2,049,770	9,141,375
Bevacizumab						
Hospital	17,300,000	18,000,000	18,000,000	17,700,000	24,200,000	95,200,000
Retail	1,407,812	961,356	594,444	809,626	1,259,801	5,033,039
Total	18,707,812	18,961,356	18,594,444	18,509,626	25,459,801	100,233,039
Bleomycin						
Hospital	753,000,000	792,000,000	996,000,000	925,000,000	847,000,000	4,313,000,000
Retail	70,400,000	45,500,000	9,838,905	11,700,000	3,833,640	141,272,545
Total	823,400,000	837,500,000	1,005,838,905	936,700,000	850,833,640	4,454,272,545
Blinatumomab						
Hospital	-	39,534	90,274	65,274	115,124	310,205
Retail	-	602	2,079	-	3,157	5,838
Total	-	40,136	92,353	65,274	118,281	316,043
Bortezomib						
Hospital	98,533	98,236	94,636	100,516	108,654	500,573
Retail	9,266	4,539	4,371	5,791	7,002	30,968
Total	107,798	102,775	99,006	106,307	115,655	531,541
Brentuximab Vedotin						
Hospital	48732	95,442	104,859	112,430	122,346	483,809
Retail	2350	2,450	5,738	1,858	2,016	14,412
Total	97,892	110,597	114,288	124,362	498,221	498,221
Cabazitaxel						
Hospital	153,196	158,144	160,281	195,196	207,651	874,468
Retail	22,545	14,419	7,928	13,294	14,944	73,130
Total	175,741	172,563	168,209	208,490	222,595	947,598
Carboplatin						
Hospital	21,900,000	23,000,000	25,100,000	25,900,000	27,400,000	123,300,000
Retail	2,293,474	1,257,243	984,841	902,849	1,123,690	6,562,097
Total	24,193,474	24,257,243	26,084,841	26,802,849	28,523,690	129,862,097
Carfilzomib						

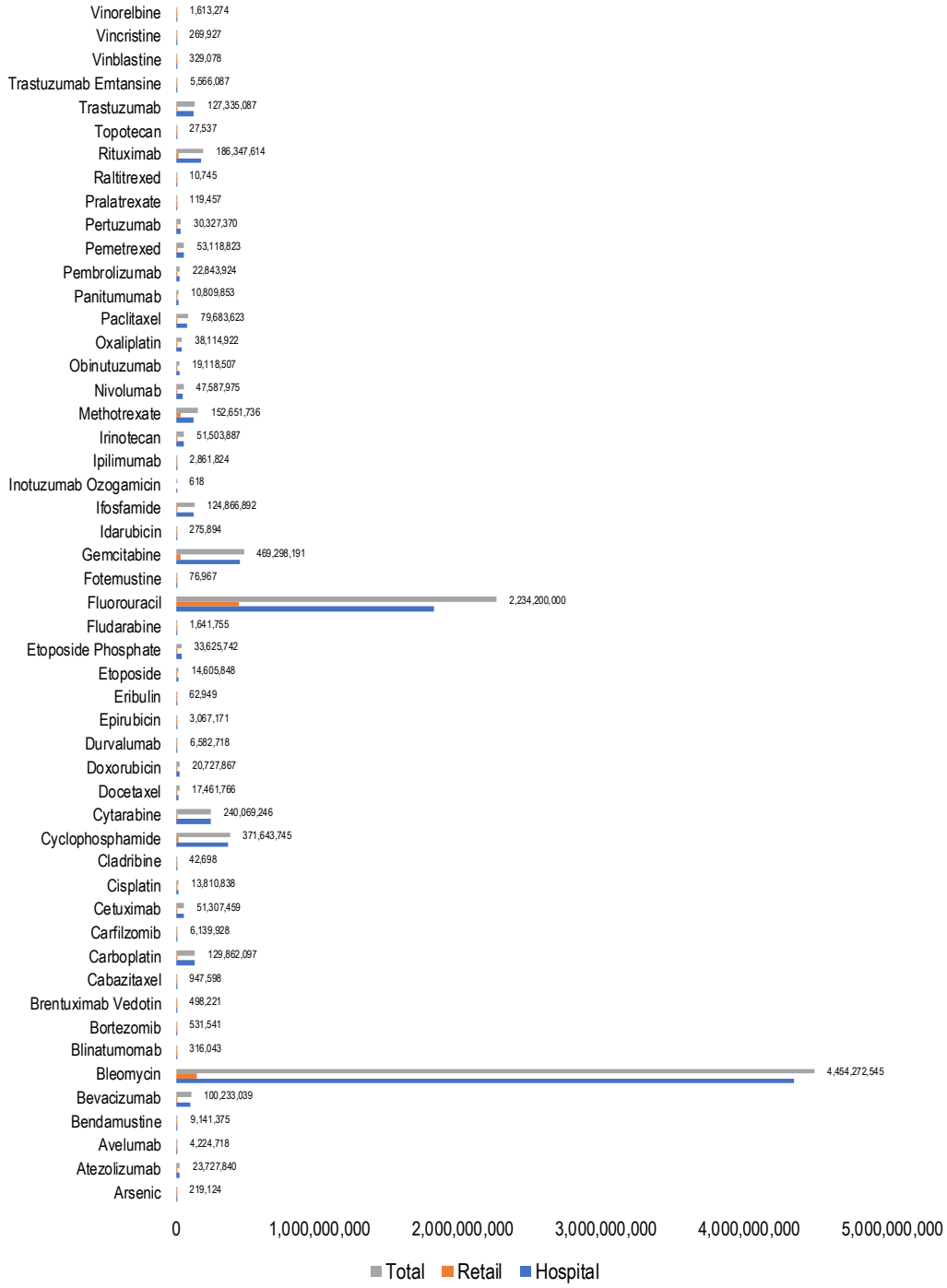
Setting	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Hospital	-	6,300	1,732,627	1,988,331	2,098,639	5,825,897
Retail	-	360	57,558	109,798	146,315	314,031
Total	-	6,660	1,790,185	2,098,129	2,244,954	6,139,928
Cetuximab						
Hospital	10,100,000	9,555,523	9,609,288	9,669,546	9,694,312	48,628,669
Retail	1,198,663	470,312	360,375	305,530	343,910	2,678,790
Total	11,298,663	10,025,835	9,969,663	9,975,076	10,038,222	51,307,459
Cisplatin						
Hospital	2,598,432	2,641,425	2,653,669	2,701,893	2,623,841	13,219,260
Retail	179,255	150,226	83,854	83,746	94,497	591,578
Total	2,777,687	2,791,651	2,737,523	2,785,639	2,718,338	13,810,838
Cladribine						
Hospital	8,909	7,902	6,334	9,899	7,501	40,545
Retail	720	269	125	564	475	2,153
Total	9,629	8,171	6,459	10,463	7,976	42,698
Cyclophosphamide						
Hospital	69,500,000	69,600,000	73,600,000	73,600,000	70,100,000	356,400,000
Retail	5,803,473	2,938,766	2,100,200	2,241,546	2,159,760	15,243,745
Total	75,303,473	72,538,766	75,700,200	75,841,546	72,259,760	371,643,745
Cytarabine						
Hospital	44,500,000	46,500,000	47,400,000	49,200,000	49,600,000	237,200,000
Retail	723,360	1,047,065	276,520	284,610	537,691	2,869,246
Total	45,223,360	47,547,065	47,676,520	49,484,610	50,137,691	240,069,246
Docetaxel						
Hospital	3,325,995	3,172,947	3,366,706	3,377,923	3,139,678	16,383,249
Retail	389,860	231,654	156,780	165,539	134,684	1,078,517
Total	3,715,855	3,404,601	3,523,486	3,543,462	3,274,362	17,461,766
Doxorubicin						
Hospital	3,539,243	3,750,005	4,030,161	4,212,907	4,209,549	19,741,865
Retail	307,407	181,819	138,924	195,827	162,025	986,002
Total	3,846,650	3,931,824	4,169,085	4,408,734	4,371,574	20,727,867
Durvalumab						
Hospital	-	-	-	3,703	6,439,335	6,443,038
Retail	-	-	-	-	139,680	139,680
Total	-	-	-	3,703	6,579,015	6,582,718
Epirubicin						
Hospital	990,453	765,115	505,972	352,717	255,336	2,869,593
Retail	101,898	49,195	23,274	11,631	11,580	197,578
Total	1,092,351	814,310	529,246	364,348	266,916	3,067,171
Eribulin						
Hospital	8,842	10,629	13,472	13,398	12,883	59,224
Retail	998	1,035	492	479	721	3,725
Total	9,840	11,664	13,964	13,877	13,604	62,949
Etoposide						
Hospital	3,109,103	6,368,389	1,783,310	1,374,773	1,270,637	13,906,212
Retail	219,503	322,677	90,396	44,550	22,510	699,636
Total	3,328,606	6,691,066	1,873,706	1,419,323	1,293,147	14,605,848
Etoposide Phosphate						
Hospital	7,348,671	2,154,335	7,659,010	7,748,653	7,785,539	32,696,208
Retail	350,980	66,912	125,671	192,744	193,227	929,534
Total	7,699,651	2,221,247	7,784,681	7,941,397	7,978,766	33,625,742
Fludarabine						
Hospital	374,117	300,754	325,502	330,177	264,971	1,595,521
Retail	20,541	7,973	8,867	4,557	4,296	46,234
Total	394,658	308,727	334,369	334,734	269,267	1,641,755
Fluorouracil						

Setting	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Hospital	300,000,000	334,000,000	360,000,000	389,000,000	418,000,000	1,801,000,000
Retail	28,800,000	71,900,000	91,500,000	115,000,000	126,000,000	433,200,000
Total	328,800,000	405,900,000	451,500,000	504,000,000	544,000,000	2,234,200,000
Fotemustine						
Hospital	16,745	31,117	3,916	7,304	10,923	70,005
Retail	1,327	2,503	1,872	-	1,260	6,962
Total	18,072	33,620	5,788	7,304	12,183	76,967
Gemcitabine						
Hospital	88,000,000	92,600,000	91,300,000	86,500,000	84,900,000	443,300,000
Retail	8,139,063	5,226,743	4,096,660	3,805,673	4,730,052	25,998,191
Total	96,139,063	97,826,743	95,396,660	90,305,673	89,630,052	469,298,191
Idarubicin						
Hospital	62,890	55,510	60,049	49,902	44,429	272,780
Retail	471	624	639	440	940	3,114
Total	63,361	56,134	60,688	50,342	45,369	275,894
Ifosfamide						
Hospital	26,400,000	24,400,000	24,800,000	24,100,000	22,500,000	122,200,000
Retail	917,540	711,212	225,040	419,600	393,500	2,666,892
Total	27,317,540	25,111,212	25,025,040	24,519,600	22,893,500	124,866,892
Inotuzumab Ozogamicin						
Hospital	-	-	-	278	340	618
Retail	-	-	-	-	-	-
Total	-	-	-	278	340	618
Ipilimumab						
Hospital	210,485	472,166	546,815	724,770	773,389	2,727,625
Retail	14,362	31,405	25,003	20,699	42,730	134,199
Total	224,847	503,571	571,818	745,469	816,119	2,861,824
Irinotecan						
Hospital	8,013,041	8,499,776	9,530,478	10,700,000	12,100,000	48,843,295
Retail	704,160	450,981	462,938	511,548	530,965	2,660,592
Total	8,717,201	8,950,757	9,993,416	11,211,548	12,630,965	51,503,887
Methotrexate						
Hospital	23,400,000	23,100,000	23,200,000	25,300,000	25,700,000	120,700,000
Retail	6,206,061	5,524,179	5,918,282	6,665,142	7,638,072	31,951,736
Total	29,606,061	28,624,179	29,118,282	31,965,142	33,338,072	152,651,736
Nivolumab						
Hospital	194,132	4,155,858	10,400,000	12,500,000	17,200,000	44,449,990
Retail	23,140	273,619	737,666	921,273	1,182,287	3,137,985
Total	217,272	4,429,477	11,137,666	13,421,273	18,382,287	47,587,975
Obinutuzumab						
Hospital	912,300	1,603,550	2,030,000	5,159,797	8,328,860	18,034,507
Retail	115,000	81,000	55,000	349,000	484,000	1,084,000
Total	1,027,300	1,684,550	2,085,000	5,508,797	8,812,860	19,118,507
Oxaliplatin						
Hospital	6,218,576	6,656,756	7,375,750	7,659,962	8,241,131	36,152,175
Retail	608,787	420,517	343,671	278,550	311,222	1,962,747
Total	6,827,363	7,077,273	7,719,421	7,938,512	8,552,353	38,114,922
Paclitaxel						
Hospital	12,600,000	14,100,000	15,500,000	16,200,000	17,100,000	75,500,000
Retail	1,448,517	920,211	580,900	573,010	660,985	4,183,623
Total	14,048,517	15,020,211	16,080,900	16,773,010	17,760,985	79,683,623
Panitumumab						
Hospital	1,422,991	2,048,774	2,104,091	2,269,511	2,402,510	10,247,877
Retail	154,662	188,955	79,269	57,360	81,730	561,976
Total	1,577,653	2,237,729	2,183,360	2,326,871	2,484,240	10,809,853
Pembrolizumab						

Setting	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Hospital	2,133,764	2,536,956	3,025,201	5,380,951	8,711,491	21,788,363
Retail	179,522	163,457	144,905	245,944	321,733	1,055,561
Total	2,313,286	2,700,413	3,170,106	5,626,895	9,033,224	22,843,924
Pemetrexed						
Hospital	7,672,891	7,733,338	8,623,639	10,400,000	16,400,000	50,829,868
Retail	811,625	371,030	243,555	347,680	515,065	2,288,955
Total	8,484,516	8,104,368	8,867,194	10,747,680	16,915,065	53,118,823
Pertuzumab						
Hospital	3,825,595	5,136,244	5,978,620	6,561,375	7,647,016	29,148,850
Retail	342,720	197,400	127,260	263,760	247,380	1,178,520
Total	4,168,315	5,333,644	6,105,880	6,825,135	7,894,396	30,327,370
Pralatrexate						
Hospital	-	-	23,959	34,150	47,144	105,253
Retail	-	-	1,380	10,120	2,704	14,204
Total	-	-	25,339	44,270	49,848	119,457
Raltitrexed						
Hospital	2,011	2,258	1,865	1,932	1,772	9,838
Retail	250	105	50	334	168	907
Total	2,261	2,363	1,915	2,266	1,940	10,745
Rituximab						
Hospital	35,300,000	36,300,000	35,600,000	33,600,000	33,900,000	174,700,000
Retail	3,282,434	2,109,113	1,766,077	2,044,737	2,445,253	11,647,614
Total	38,582,434	38,409,113	37,366,077	35,644,737	36,345,253	186,347,614
Topotecan						
Hospital	4,000	5,543	5,204	5,742	5,549	26,038
Retail	437	334	271	191	266	1,499
Total	4,437	5,877	5,475	5,933	5,815	27,537
Trastuzumab						
Hospital	21,200,000	23,500,000	24,700,000	25,800,000	26,500,000	121,700,000
Retail	1,748,278	958,150	603,219	1,023,782	1,301,658	5,635,087
Total	22,948,278	24,458,150	25,303,219	26,823,782	27,801,658	127,335,087
Trastuzumab Emtansine						
Hospital	935,281	1,016,111	948,833	874,314	1,548,370	5,322,909
Retail	111,362	42,262	11,856	31,530	46,168	243,178
Total	1,046,643	1,058,373	960,689	905,844	1,594,538	5,566,087
Vinblastine						
Hospital	67,844	59,668	55,325	63,337	68,325	314,499
Retail	4,903	3,409	1,846	2,164	2,257	14,579
Total	72,747	63,077	57,171	65,501	70,582	329,078
Vincristine						
Hospital	50,424	51,705	51,357	51,517	54,241	259,244
Retail	3,072	1,666	2,594	1,324	2,027	10,683
Total	53,496	53,371	53,951	52,841	56,268	269,927
Vinorelbine						
Hospital	334,181	311,624	328,801	300,751	247,166	1,522,523
Retail	36,151	15,838	15,981	10,417	12,364	90,751
Total	370,332	327,462	344,782	311,168	259,530	1,613,274

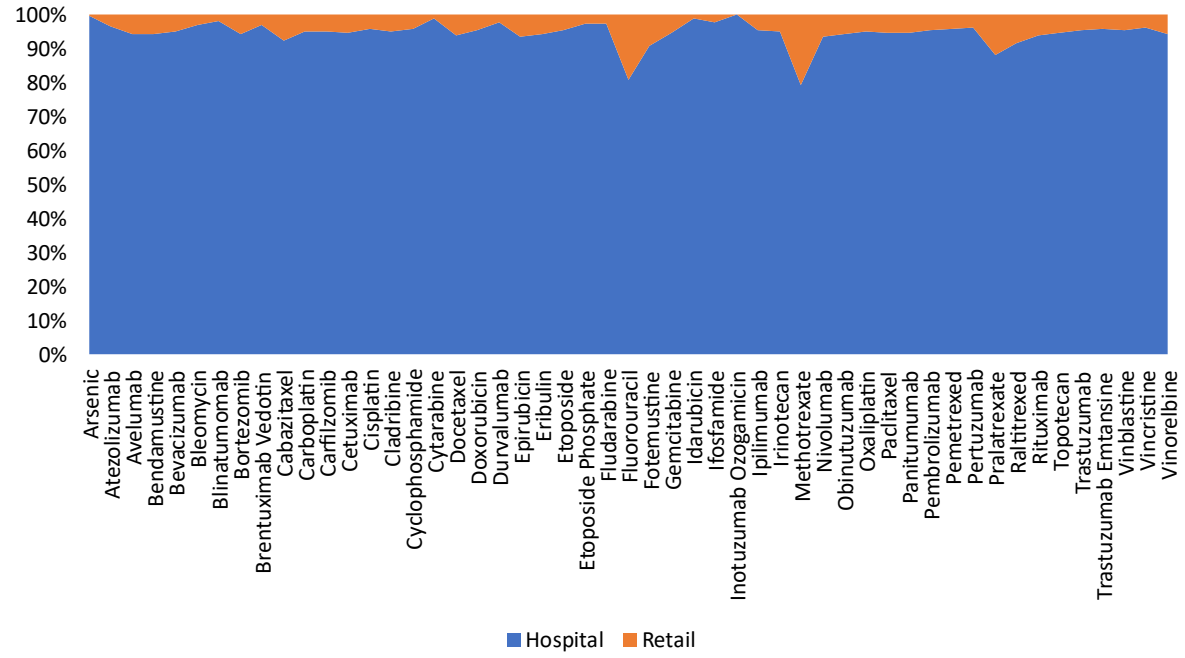
Source: Developed for this Review using in-market sales data (IQVIA).

Figure A53. Total units purchased by EFC-listed drug and pharmacy setting (2016-2020)



Source: Developed for this Review using in-market sales data (IQVIA).

Figure A54. Distribution of units purchased by EFC-listed drug and phamacy setting (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

A summary of the total units purchased by drug and compounding status is provided in Table A41 and Figure A55. Overall, approximately half of the products purchased by hospitals and pharmacies were purchased in compounding solutions.

Table A41. Total units purchased by EFC-listed drug and compounding status (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic						
Comp. Pack	16,490	17,385	23,912	26,096	30,241	114,124
Not comp.	9,700	9,200	19,200	36,700	30,200	105,000
Total	26,190	26,585	43,112	62,796	60,441	219,124
Atezolizumab						
Comp. Pack	-	-	806,400	3,128,240	8,422,320	12,356,960
Not comp.	-	-	1,605,600	3,404,400	6,339,840	11,349,840
Total	-	-	2,412,000	6,532,640	14,762,160	23,706,800
Avelumab						
Comp. Pack	-	-	-	715,975	1,392,143	2,108,118
Not comp.	-	-	-	835,600	1,281,000	2,116,600
Total	-	-	-	1,551,575	2,673,143	4,224,718
Bendamustine						
Comp. Pack	471,025	1,090,486	1,247,870	1,333,699	1,354,845	5,497,925
Not comp.	556,550	861,050	765,375	765,550	694,925	3,643,450
Total	1,027,575	1,951,536	2,013,245	2,099,249	2,049,770	9,141,375
Bevacizumab						
Comp. Pack	9,752,610	9,988,035	10,256,778	11,437,826	15,990,191	57,425,440
Not comp.	8,923,300	8,994,700	8,309,100	7,084,800	9,477,600	42,789,500
Total	18,675,910	18,982,735	18,565,878	18,522,626	25,467,791	100,214,940

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Bleomycin						
Comp. Pack	823,611,008	837,841,664	1,005,503,296	937,053,184	850,641,984	4,454,651,136
Not comp.	82,335	66,645	67,035	60,120	54,240	330,375
Total	823,693,343	837,908,309	1,005,570,331	937,113,304	850,696,224	4,454,981,511
Blinatumomab						
Comp. Pack	-	10,722	21,975	19,420	28,922	81,039
Not comp.	-	29,414	70,378	45,854	89,359	235,004
Total	-	40,136	92,353	65,274	118,281	316,043
Bortezomib						
Comp. Pack	53,038	56,531	57,914	64,915	74,030	306,428
Not comp.	54,760	46,244	41,092	41,392	41,625	225,113
Total	107,798	102,775	99,006	106,307	115,655	531,541
Brentuximab Vedotin						
Comp. Pack	8,982	13,892	27,397	32,988	48,012	131,271
Not comp.	42,100	84,000	83,200	81,300	76,350	366,950
Total	51,082	97,892	110,597	114,288	124,362	498,221
Cabazitaxel						
Comp. Pack	109,081	107,403	112,349	136,070	158,155	623,058
Not comp.	66,660	65,160	55,860	72,420	64,440	324,540
Total	175,741	172,563	168,209	208,490	222,595	947,598
Carboplatin						
Comp. Pack	14,981,798	15,996,151	17,431,288	18,382,892	19,884,768	86,676,897
Not comp.	9,185,050	8,255,900	8,685,550	8,371,000	8,656,950	43,154,450
Total	24,166,848	24,252,051	26,116,838	26,753,892	28,541,718	129,831,347
Carfilzomib						
Comp. Pack	-	-	1,135,245	1,484,319	1,556,504	4,176,068
Not comp.	-	6,660	654,940	613,810	688,450	1,963,860
Total	-	6,660	1,790,185	2,098,129	2,244,954	6,139,928
Cetuximab						
Comp. Pack	6,515,115	6,073,735	6,542,663	6,575,276	7,093,322	32,800,111
Not comp.	4,822,500	3,952,100	3,427,000	3,399,800	2,944,900	18,546,300
Total	11,337,615	10,025,835	9,969,663	9,975,076	10,038,222	51,346,411
Cisplatin						
Comp. Pack	1,644,937	1,701,851	1,780,223	1,944,939	1,892,988	8,964,938
Not comp.	1,132,750	1,089,800	957,300	840,700	825,350	4,845,900
Total	2,777,687	2,791,651	2,737,523	2,785,639	2,718,338	13,810,838
Cladribine						
Comp. Pack	4,259	3,671	4,099	5,613	4,726	22,368
Not comp.	5,370	4,500	2,360	4,850	3,250	20,330
Total	9,629	8,171	6,459	10,463	7,976	42,698
Cyclophosphamide						
Comp. Pack	59,939,956	59,245,312	61,605,848	61,429,064	59,642,296	301,862,476
Not comp.	15,382,500	13,244,000	14,141,000	14,375,000	12,615,000	69,757,500
Total	75,322,456	72,489,312	75,746,848	75,804,064	72,257,296	371,619,976
Cytarabine						
Comp. Pack	17,529,148	20,086,526	22,154,944	22,137,134	23,145,764	105,053,516
Not comp.	27,717,500	27,424,000	25,511,000	27,335,000	27,009,000	134,996,500
Total	45,246,648	47,510,526	47,665,944	49,472,134	50,154,764	240,050,016
Docetaxel						
Comp. Pack	2,587,695	2,445,021	2,579,426	2,653,322	2,547,582	12,813,046
Not comp.	1,128,160	959,580	944,060	890,140	726,780	4,648,720
Total	3,715,855	3,404,601	3,523,486	3,543,462	3,274,362	17,461,766
Doxorubicin						
Comp. Pack	2,274,320	2,549,204	2,690,770	2,882,254	2,947,514	13,344,062
Not comp.	1,572,330	1,382,620	1,478,315	1,526,480	1,424,060	7,383,805
Total	3,846,650	3,931,824	4,169,085	4,408,734	4,371,574	20,727,867

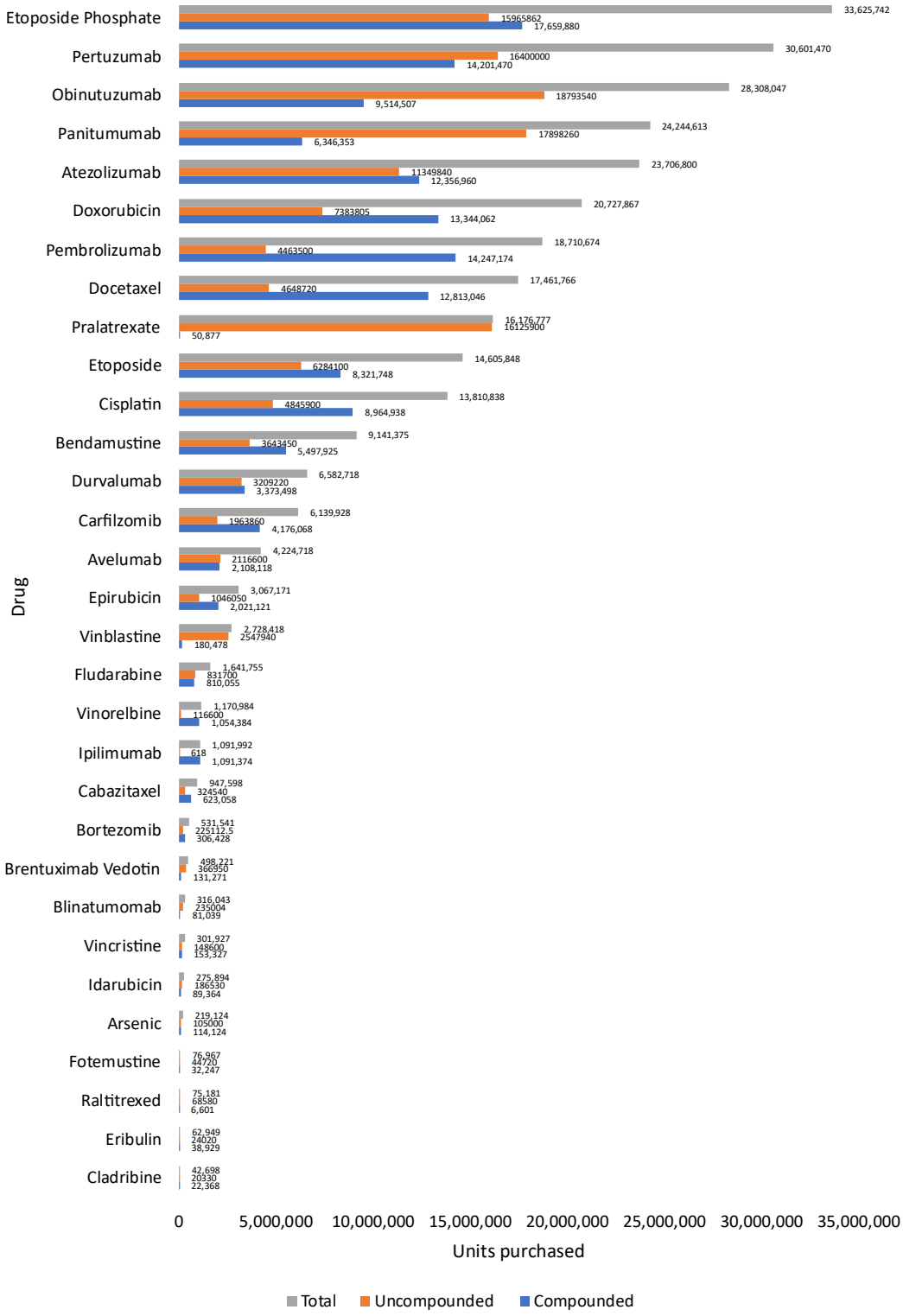
Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Durvalumab						
Comp. Pack	-	-	-	1,183	3,372,315	3,373,498
Not comp.	-	-	-	2,520	3,206,700	3,209,220
Total	-	-	-	3,703	6,579,015	6,582,718
Epirubicin						
Comp. Pack	666,351	525,010	373,446	264,048	192,266	2,021,121
Not comp.	426,000	289,300	155,800	100,300	74,650	1,046,050
Total	1,092,351	814,310	529,246	364,348	266,916	3,067,171
Eribulin						
Comp. Pack	4,840	6,986	9,092	9,214	8,797	38,929
Not comp.	5,000	4,678	4,872	4,663	4,807	24,020
Total	9,840	11,664	13,964	13,877	13,604	62,949
Etoposide						
Comp. Pack	1,166,706	4,103,866	1,292,906	946,723	811,547	8,321,748
Not comp.	2,161,900	2,587,200	580,800	472,600	481,600	6,284,100
Total	3,328,606	6,691,066	1,873,706	1,419,323	1,293,147	14,605,848
Etoposide Phosphate						
Comp. Pack	3,674,137	556,513	4,150,357	4,656,179	4,622,694	17,659,880
Not comp.	4,025,514	1,664,734	3,634,324	3,285,218	3,356,072	15,965,862
Total	7,699,651	2,221,247	7,784,681	7,941,397	7,978,766	33,625,742
Fludarabine						
Comp. Pack	173,808	167,327	170,269	159,184	139,467	810,055
Not comp.	220,850	141,400	164,100	175,550	129,800	831,700
Total	394,658	308,727	334,369	334,734	269,267	1,641,755
Fluorouracil						
Comp. Pack	241,274,000	267,886,384	292,126,560	323,686,752	364,035,648	1,489,009,344
Not comp.	87,845,000	138,264,992	159,797,504	179,504,992	180,102,496	745,514,984
Total	329,119,000	406,151,376	451,924,064	503,191,744	544,138,144	2,234,524,328
Fotemustine						
Comp. Pack	6,008	15,108	2,252	1,896	6,983	32,247
Not comp.	12,064	18,512	3,536	5,408	5,200	44,720
Total	18,072	33,620	5,788	7,304	12,183	76,967
Gemcitabine						
Comp. Pack	65,075,660	70,419,352	71,232,936	69,183,000	67,972,560	343,883,508
Not comp.	31,106,400	27,439,400	24,201,800	21,140,800	21,701,000	125,589,400
Total	96,182,060	97,858,752	95,434,736	90,323,800	89,673,560	469,472,908
Idarubicin						
Comp. Pack	18,421	17,089	21,038	17,007	15,809	89,364
Not comp.	44,940	39,045	39,650	33,335	29,560	186,530
Total	63,361	56,134	60,688	50,342	45,369	275,894
Ifosfamide						
Comp. Pack	14,035,887	13,963,587	13,354,267	13,591,048	13,627,650	68,572,439
Not comp.	13,299,000	11,127,000	11,712,000	10,914,000	9,263,000	56,315,000
Total	27,334,887	25,090,587	25,066,267	24,505,048	22,890,650	124,887,439
Inotuzumab Ozogamicin						
Not comp.	-	-	-	278	340	618
Total	-	-	-	278	340	618
Ipilimumab						
Comp. Pack	52,897	132,521	182,018	313,919	410,019	1,091,374
Not comp.	171,950	371,050	389,800	431,550	406,100	1,770,450
Total	224,847	503,571	571,818	745,469	816,119	2,861,824
Irinotecan						
Comp. Pack	5,854,201	6,511,157	7,403,196	8,379,999	9,589,659	37,738,212
Not comp.	2,863,000	2,439,600	2,590,220	2,836,395	3,009,239	13,738,454
Total	8,717,201	8,950,757	9,993,416	11,216,394	12,598,898	51,476,666
Methotrexate						

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Comp. Pack	10,200,163	9,321,781	10,625,077	11,621,250	11,479,525	53,247,796
Not comp.	19,368,310	19,280,632	18,471,416	20,316,432	21,872,678	99,309,468
Total	29,568,473	28,602,413	29,096,493	31,937,682	33,352,203	152,557,264
Nivolumab						
Comp. Pack	73,692	2,034,977	6,360,706	8,374,010	11,930,574	28,773,959
Not comp.	143,580	2,394,500	4,776,140	5,043,540	6,435,780	18,793,540
Total	217,272	4,429,477	11,136,846	13,417,550	18,366,354	47,567,499
Obinutuzumab						
Comp. Pack	324,300	718,550	774,000	2,824,797	4,872,860	9,514,507
Not comp.	703,000	966,000	1,311,000	2,684,000	3,940,000	9,604,000
Total	1,027,300	1,684,550	2,085,000	5,508,797	8,812,860	19,118,507
Oxaliplatin						
Comp. Pack	4,763,063	5,360,073	5,751,221	5,957,912	6,468,953	28,301,222
Not comp.	2,064,300	1,717,200	1,968,200	1,980,600	2,083,400	9,813,700
Total	6,827,363	7,077,273	7,719,421	7,938,512	8,552,353	38,114,922
Paclitaxel						
Comp. Pack	10,176,470	11,597,299	12,365,693	13,446,011	14,165,685	61,751,158
Not comp.	3,855,010	3,434,830	3,747,840	3,304,430	3,556,150	17,898,260
Total	14,031,480	15,032,129	16,113,533	16,750,441	17,721,835	79,649,418
Panitumumab						
Comp. Pack	774,453	1,204,729	1,312,760	1,422,171	1,632,240	6,346,353
Not comp.	803,200	1,033,000	870,600	904,700	852,000	4,463,500
Total	1,577,653	2,237,729	2,183,360	2,326,871	2,484,240	10,809,853
Pembrolizumab						
Comp. Pack	824,286	1,119,563	1,805,856	3,920,545	6,576,924	14,247,174
Not comp.	1,489,000	1,580,850	1,364,250	1,706,350	2,456,300	8,596,750
Total	2,313,286	2,700,413	3,170,106	5,626,895	9,033,224	22,843,924
Pemetrexed						
Comp. Pack	5,195,716	5,359,868	5,801,694	7,659,937	12,665,237	36,682,452
Not comp.	3,288,800	2,744,500	3,065,500	3,083,800	4,217,400	16,400,000
Total	8,484,516	8,104,368	8,867,194	10,743,737	16,882,637	53,082,452
Pertuzumab						
Comp. Pack	1,482,835	2,225,644	2,818,540	3,466,395	4,208,056	14,201,470
Not comp.	2,685,480	3,108,000	3,287,340	3,358,740	3,686,340	16,125,900
Total	4,168,315	5,333,644	6,105,880	6,825,135	7,894,396	30,327,370
Pralatrexate						
Comp. Pack	-	-	8,359	18,770	23,748	50,877
Not comp.	-	-	16,980	25,500	26,100	68,580
Total	-	-	25,339	44,270	49,848	119,457
Raltitrexed						
Comp. Pack	1,613	1,267	1,127	1,266	1,328	6,601
Not comp.	648	1,096	788	1,000	612	4,144
Total	2,261	2,363	1,915	2,266	1,940	10,745
Rituximab						
Comp. Pack	19,752,980	20,600,110	20,304,794	19,296,844	19,620,086	99,574,814
Not comp.	18,787,800	17,765,800	17,039,800	16,379,100	16,747,100	86,719,600
Total	38,540,780	38,365,910	37,344,594	35,675,944	36,367,186	186,294,414
Topotecan						
Comp. Pack	3,613	5,209	4,887	5,185	5,139	24,033
Not comp.	824	668	588	748	676	3,504
Total	4,437	5,877	5,475	5,933	5,815	27,537
Trastuzumab						
Comp. Pack	11,955,499	12,628,708	13,761,333	15,179,877	15,922,155	69,447,572
Not comp.	10,992,090	11,827,200	11,558,550	11,627,250	11,893,080	57,898,170
Total	22,947,589	24,455,908	25,319,883	26,807,127	27,815,235	127,345,742
Trastuzumab Emtansine						

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Comp. Pack	525,263	583,933	498,449	490,164	920,338	3,018,147
Not comp.	521,380	474,440	462,240	415,680	674,200	2,547,940
Total	1,046,643	1,058,373	960,689	905,844	1,594,538	5,566,087
Vinblastine						
Comp. Pack	38,347	34,677	29,871	38,701	38,882	180,478
Not comp.	34,400	28,400	27,300	26,800	31,700	148,600
Total	72,747	63,077	57,171	65,501	70,582	329,078
Vincristine						
Comp. Pack	30,171	29,256	31,886	31,096	30,918	153,327
Not comp.	23,325	24,115	22,065	21,745	25,350	116,600
Total	53,496	53,371	53,951	52,841	56,268	269,927
Vinorelbine						
Comp. Pack	228,282	201,992	228,502	210,518	185,090	1,054,384
Not comp.	142,050	125,470	116,280	100,650	74,440	558,890
Total	370,332	327,462	344,782	311,168	259,530	1,613,274

Source: Developed for this Review using in-market sales data (IQVIA).

Figure A55. Total units purchased by EFC-listed drug and compounding status (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

The total amount of cancer medicines (in mg or international units) purchased broken down by state is provided in Table A42 and Figure A56. Overall, states with the largest populations had the greatest consumption of EFC medicines.

Table A42. Total units purchased by EFC-listed drug and State and Territory (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
ACT						
Arsenic	-	2,584	394	999	4,487	8,464
Atezolizumab	-	-	8,400	123,600	242,640	374,640
Avelumab	-	-	-	15,170	520	15,690
Bendamustine	10,531	50,271	61,093	39,723	60,430	222,048
Bevacizumab	218,678	291,412	319,333	364,642	434,215	1,628,280
Bleomycin	42,500,000	43,800,000	69,600,000	57,700,000	22,800,000	236,000,000
Blinatumomab	-	-	1,470	2,981	-	4,451
Bortezomib	825	871	1,543	1,289	1,590	6,116
Brent. Vedotin	250	580	305	1,215	300	2,650
Cabazitaxel	2,384	2,996	3,576	2,139	2,864	13,959
Carboplatin	362,109	427,710	455,034	465,307	551,827	2,261,987
Carfilzomib	-	-	13,854	26,812	31,761	72,427
Cetuximab	126,605	190,345	112,302	256,829	160,737	846,818
Cisplatin	51,201	50,483	64,744	43,281	47,392	257,101
Cladribine	106	70	257	320	136	889
Cyclophosphamide	1,135,076	1,089,642	1,331,250	1,444,850	1,591,146	6,591,964
Cytarabine	1,112,444	1,074,670	784,324	1,518,098	785,256	5,274,792
Docetaxel	61,718	75,884	77,903	76,076	84,899	376,480
Doxorubicin	54,244	53,677	57,332	81,927	94,943	342,123
Durvalumab	-	-	-	-	68,810	68,810
Epirubicin	29,689	33,905	30,640	16,248	13,065	123,547
Eribulin	94	129	78	176	263	740
Etoposide	54,012	121,214	19,958	29,070	21,257	245,511
Etop. Phosphate	75,437	46,549	180,083	152,682	152,099	606,850
Fludarabine	5,350	3,288	6,022	2,927	5,810	23,397
Fluorouracil	3,700,473	5,183,762	6,107,825	8,096,147	8,426,709	31,500,000
Fotemustine	-	-	-	1,456	-	1,456
Gemcitabine	2,176,141	2,149,113	2,057,905	2,082,166	2,068,127	10,500,000
Idarubicin	1,965	1,957	1,555	1,231	1,276	7,984
Ifosfamide	740,252	569,948	559,540	504,174	1,108,635	3,482,549
Ipilimumab	450	400	3,172	4,589	9,125	17,736
Irinotecan	115,550	119,552	144,406	200,945	136,954	717,407
Methotrexate	406,621	313,847	350,726	610,002	517,304	2,198,499
Nivolumab	5,060	21,880	157,158	194,564	364,212	742,874
Obinutuzumab	12,000	16,000	61,000	130,000	348,000	567,000
Oxaliplatin	101,884	109,998	109,154	133,778	115,357	570,171
Paclitaxel	218,559	260,183	271,827	310,804	360,270	1,421,643
Panitumumab	-	5,980	1,960	50,483	55,620	114,043
Pembrolizumab	3,139	7,730	45,540	112,867	158,828	328,104
Pemetrexed	35,635	71,090	78,785	109,745	261,476	556,731
Pertuzumab	94,920	139,440	156,240	156,240	157,500	704,340
Pralatrexate	-	-	55	-	-	55
Raltitrexed	104	47	24	96	126	397
Rituximab	569,052	689,636	698,460	649,067	644,990	3,251,205
Topotecan	21	94	72	-	36	223
Trastuzumab	442,659	469,232	526,664	596,354	590,211	2,625,120
Trast. Emtansine	13,650	15,154	8,008	10,832	27,374	75,018

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Vinblastine	1,053	1,144	1,727	2,798	2,034	8,756
Vincristine	717	747	879	981	1,162	4,486
Vinorelbine	10,709	8,246	9,084	7,246	2,454	37,739
NSW						
Arsenic	11,418	10,789	17,610	15,944	13,644	69,405
Atezolizumab	-	-	508,800	1,755,240	4,178,160	6,442,200
Avelumab	-	-	-	583,813	1,023,407	1,607,220
Bendamustine	302,475	550,648	623,581	583,887	615,879	2,676,470
Bevacizumab	5,077,993	4,963,535	4,657,840	5,047,690	7,228,493	27,000,000
Bleomycin	443,000,000	381,000,000	437,000,000	391,000,000	332,000,000	1,980,000,000
Blinatumomab	-	7,849	34,052	15,065	24,546	81,511
Bortezomib	34,811	34,538	30,374	32,462	37,329	169,512
Brent. Vedotin	12,970	25,828	34,542	35,327	53,814	162,481
Cabazitaxel	46,098	37,632	46,983	47,611	50,787	229,111
Carboplatin	7,767,811	7,612,387	8,013,593	8,103,487	8,615,180	40,100,000
Carfilzomib	-	-	565,471	685,169	696,415	1,947,055
Cetuximab	4,160,962	3,744,021	3,386,821	3,231,180	2,753,767	17,300,000
Cisplatin	773,503	776,971	706,869	786,127	757,165	3,800,635
Cladribine	3,455	2,970	2,373	3,793	2,710	15,301
Cyclophosphamide	23,200,000	22,200,000	22,500,000	22,700,000	22,700,000	113,000,000
Cytarabine	13,500,000	14,100,000	13,200,000	15,000,000	16,900,000	72,800,000
Docetaxel	959,316	974,764	1,000,043	990,044	960,419	4,884,586
Doxorubicin	1,247,070	1,273,747	1,240,670	1,385,229	1,328,396	6,475,112
Durvalumab	-	-	-	600	2,125,353	2,125,953
Epirubicin	301,665	223,683	156,856	97,421	81,366	860,991
Eribulin	2,445	3,025	3,809	3,788	3,787	16,854
Etoposide	1,245,930	2,282,143	643,958	571,663	503,772	5,247,466
Etop. Phosphate	2,074,951	691,443	2,329,664	2,294,172	2,336,402	9,726,632
Fludarabine	96,111	73,266	91,266	82,540	69,214	412,397
Fluorouracil	85,700,000	115,000,000	124,000,000	145,000,000	155,000,000	625,000,000
Fotemustine	8,477	22,262	2,212	2,312	4,303	39,566
Gemcitabine	30,100,000	29,900,000	27,500,000	27,400,000	26,200,000	141,000,000
Idarubicin	13,445	13,008	15,002	13,395	12,320	67,170
Ifosfamide	7,945,081	7,922,414	7,898,208	8,032,856	7,236,400	39,000,000
Inot. Ozogamicin	-	-	-	43	86	129
Ipilimumab	62,877	175,602	165,537	241,070	252,491	897,577
Irinotecan	2,438,497	2,696,820	2,746,510	3,120,471	3,396,892	14,400,000
Methotrexate	8,786,263	9,595,027	8,906,434	10,800,000	11,300,000	49,300,000
Nivolumab	53,773	1,297,180	3,177,067	3,877,046	5,192,509	13,600,000
Obinutuzumab	444,200	526,900	528,000	1,431,700	2,523,400	5,454,200
Oxaliplatin	2,097,007	2,243,726	2,111,712	2,328,444	2,449,126	11,200,000
Paclitaxel	4,380,067	4,715,056	4,716,550	4,929,964	5,281,523	24,000,000
Panitumumab	418,093	607,171	653,115	662,810	760,648	3,101,837
Pembrolizumab	907,871	998,083	970,711	1,813,682	2,799,717	7,490,064
Pemetrexed	2,466,895	2,335,669	2,683,848	3,100,747	5,053,367	15,600,000
Pertuzumab	1,073,715	1,433,104	1,559,380	1,740,060	2,229,000	8,035,259
Pralatrexate	-	-	8,917	18,912	20,410	48,239
Raltitrexed	913	868	570	875	536	3,762
Rituximab	11,300,000	11,100,000	10,100,000	9,702,120	11,100,000	53,300,000
Topotecan	1,078	1,236	1,619	1,175	1,077	6,185
Trastuzumab	7,125,512	7,388,266	7,385,175	7,867,030	7,820,644	37,600,000
Trast. Emtansine	330,291	346,455	287,984	247,804	497,174	1,709,708
Vinblastine	22,008	16,059	13,897	17,528	17,705	87,197
Vincristine	15,489	13,561	14,582	14,068	15,240	72,940
Vinorelbine	89,657	65,933	68,593	69,439	58,842	352,464
NT						

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Arsenic	1,801	539	-	-	-	2,340
Avelumab	-	-	-	-	12,000	12,000
Bendamustine	6,981	9,368	-	-	-	16,349
Bevacizumab	128,927	106,114	9,600	30,944	16,670	292,255
Bleomycin	15,300	8,445	-	-	-	23,745
Bortezomib	334	306	-	-	-	640
Cabazitaxel	567	227	-	-	-	794
Carboplatin	147,665	109,411	3,076	5,405	970	266,527
Cetuximab	159,946	97,932	-	6,090	6,420	270,388
Cisplatin	30,122	15,433	-	272	-	45,827
Cladribine	55	-	-	-	-	55
Cyclophosphamide	346,771	198,014	16,346	10,196	6,024	577,351
Cytarabine	259,710	224,980	-	-	-	484,690
Docetaxel	38,559	11,746	806	1,113	-	52,224
Doxorubicin	17,048	15,184	825	364	602	34,023
Durvalumab	-	-	-	-	10,000	10,000
Epirubicin	14,352	1,711	-	-	-	16,063
Eribulin	18	11	-	-	-	29
Etoposide	1,511	20,816	-	1,795	1,430	25,552
Etop. Phosphate	53,148	3,233	-	167	-	56,548
Fludarabine	2,447	492	-	-	-	2,939
Fluorouracil	2,149,550	2,200,941	405,288	770,870	830,275	6,356,924
Gemcitabine	486,832	361,098	-	3,780	-	851,710
Idarubicin	401	381	-	-	-	782
Ifosfamide	137,421	73,575	-	-	-	210,996
Ipilimumab	3,525	1,185	-	-	4,200	8,910
Irinotecan	68,986	70,554	-	7,119	3,863	150,522
Methotrexate	70,136	89,319	33,845	34,980	33,010	261,290
Nivolumab	447	8,697	927	10,860	79,400	100,331
Obinutuzumab	-	6,000	-	-	-	6,000
Oxaliplatin	61,148	44,701	1,041	4,603	244	111,737
Paclitaxel	89,400	63,659	7,356	2,315	2,150	164,880
Panitumumab	10,234	-	-	1,852	32,252	44,338
Pembrolizumab	5,388	5,108	400	6,768	70,000	87,664
Pemetrexed	10,780	45,213	-	-	1,000	56,993
Pertuzumab	70,560	29,820	5,880	8,820	6,300	121,380
Raltitrexed	27	-	-	-	-	27
Rituximab	133,220	119,490	700	4,700	25,600	283,710
Topotecan	-	27	-	-	-	27
Trastuzumab	197,462	116,395	9,030	6,042	7,530	336,459
Trast. Emtansine	1,752	7,090	-	-	-	8,842
Vinblastine	323	205	-	-	-	528
Vincristine	120	114	-	-	-	234
Vinorelbine	1,013	975	-	-	-	1,988
QLD						
Arsenic	12,489	11,390	21,314	28,600	22,946	96,739
Atezolizumab	-	-	505,200	1,269,720	3,192,840	4,967,760
Avelumab	-	-	-	437,812	799,011	1,236,823
Bendamustine	213,310	469,955	542,268	540,739	595,791	2,362,063
Bevacizumab	4,231,809	4,200,131	4,025,935	3,659,017	5,438,374	21,600,000
Bleomycin	194,000,000	223,000,000	199,000,000	175,000,000	152,000,000	943,000,000
Blinatumomab	-	4,762	10,548	4,391	14,771	34,471
Bortezomib	22,908	22,947	21,022	22,102	25,324	114,302
Brent. Vedotin	9,971	11,433	19,607	18,002	16,148	75,161
Cabazitaxel	40,048	42,577	36,956	47,452	52,029	219,062
Carboplatin	5,661,560	5,763,064	6,191,322	6,499,219	6,765,199	30,900,000

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Carfilzomib	-	1,380	458,604	564,015	586,194	1,610,193
Cetuximab	2,555,259	2,127,942	1,982,047	1,684,017	2,016,066	10,400,000
Cisplatin	667,050	651,174	653,971	728,165	671,957	3,372,317
Cladribine	1,887	1,450	1,315	1,814	1,655	8,121
Cyclophosphamide	16,700,000	16,300,000	17,000,000	16,400,000	16,200,000	82,600,000
Cytarabine	9,788,061	11,800,000	12,700,000	11,300,000	10,700,000	56,200,000
Docetaxel	845,916	734,999	787,696	803,750	785,141	3,957,502
Doxorubicin	804,147	806,858	903,091	926,829	946,752	4,387,677
Durvalumab	-	-	-	-	1,686,661	1,686,661
Epirubicin	189,993	149,556	96,508	61,960	51,569	549,586
Eribulin	2,273	3,354	3,961	3,768	3,534	16,890
Etoposide	952,266	1,606,511	556,924	318,261	203,401	3,637,363
Etop. Phosphate	1,363,767	273,948	1,571,282	1,911,121	1,880,269	7,000,387
Fludarabine	108,484	103,546	89,847	85,106	75,062	462,045
Fluorouracil	77,300,000	97,200,000	111,000,000	122,000,000	127,000,000	535,000,000
Fotemustine	-	1,791	1,872	-	720	4,383
Gemcitabine	22,300,000	22,400,000	22,400,000	20,900,000	18,900,000	107,000,000
Idarubicin	16,668	15,394	17,702	13,910	11,441	75,115
Ifosfamide	6,056,984	5,959,803	4,652,533	6,164,455	5,820,233	28,700,000
Inot. Ozogamicin	-	-	-	74	27	101
Ipilimumab	66,767	104,622	132,916	169,438	213,952	687,695
Irinotecan	1,676,954	1,707,428	2,164,131	2,477,290	2,777,096	10,800,000
Methotrexate	5,961,662	4,872,692	5,468,712	7,182,682	6,897,083	30,400,000
Nivolumab	77,654	1,145,732	2,710,789	3,292,927	4,529,967	11,800,000
Obinutuzumab	175,000	370,900	415,000	1,381,100	2,641,160	4,983,160
Oxaliplatin	1,616,513	1,600,260	1,798,755	1,780,806	1,874,879	8,671,213
Paclitaxel	3,797,568	4,031,046	4,288,434	4,280,098	4,488,203	20,900,000
Panitumumab	520,257	693,496	691,689	588,831	620,965	3,115,238
Pembrolizumab	498,274	649,358	812,326	1,374,642	2,121,560	5,456,160
Pemetrexed	2,205,373	2,001,085	1,956,341	2,653,726	3,859,821	12,700,000
Pertuzumab	829,080	1,064,700	1,226,400	1,371,300	1,539,216	6,030,696
Pralatrexate	-	-	6,602	12,958	11,080	30,640
Raltitrexed	624	356	551	655	610	2,796
Rituximab	8,543,867	9,053,560	8,801,540	7,599,172	7,995,605	42,000,000
Topotecan	1,781	3,120	2,157	2,929	2,794	12,781
Trastuzumab	4,523,781	5,046,415	5,360,359	5,696,042	6,370,334	27,000,000
Trast. Emtansine	223,754	239,203	216,554	190,474	349,811	1,219,796
Vinblastine	15,237	15,659	14,228	12,323	14,579	72,026
Vincristine	12,259	13,129	11,072	11,751	11,714	59,925
Vinorelbine	83,417	83,387	92,951	77,599	66,943	404,297
SA						
Arsenic	-	-	1,200	12,400	13,600	27,200
Atezolizumab	-	-	234,000	504,080	1,483,560	2,221,640
Avelumab	-	-	-	81,000	152,265	233,265
Bendamustine	125,630	211,370	207,439	241,188	202,826	988,453
Bevacizumab	1,637,912	1,839,289	1,729,602	1,758,975	2,386,814	9,352,592
Bleomycin	48,090	36,300,000	34,300,000	53,100,000	60,800,000	185,000,000
Blinatumomab	-	5,783	3,960	7,506	8,609	25,857
Bortezomib	9,290	7,647	7,827	9,905	7,884	42,552
Brent. Vedotin	5,700	16,200	10,800	6,958	7,300	46,958
Cabazitaxel	19,329	16,791	12,297	23,302	28,007	99,726
Carboplatin	1,500,469	1,571,834	1,823,290	1,934,579	2,200,557	9,030,729
Carfilzomib	-	-	97,973	100,615	184,521	383,109
Cetuximab	427,541	390,788	617,846	771,601	793,205	3,000,981
Cisplatin	161,267	157,778	202,168	201,065	183,773	906,051
Cladribine	430	276	601	554	657	2,518

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Cyclophosphamide	6,285,792	5,515,779	5,699,453	6,282,048	4,643,036	28,400,000
Cytarabine	2,881,700	2,636,632	3,366,483	3,046,360	3,999,460	15,900,000
Docetaxel	220,840	182,909	189,532	187,092	165,433	945,806
Doxorubicin	261,730	269,137	310,795	348,593	354,889	1,545,144
Durvalumab	-	-	-	-	491,766	491,766
Epirubicin	75,848	69,667	49,384	52,304	35,943	283,146
Eribulin	668	871	690	680	829	3,738
Etoposide	130,825	584,943	13,400	20,350	27,700	777,218
Etop. Phosphate	506,081	87,201	617,043	716,112	684,135	2,610,572
Fludarabine	30,691	18,789	29,923	18,636	20,748	118,787
Fluorouracil	19,800,000	22,800,000	25,800,000	31,200,000	43,100,000	143,000,000
Fotemustine	1,440	2,288	600	-	1,076	5,404
Gemcitabine	6,318,305	5,564,426	5,999,289	6,639,240	8,793,216	33,300,000
Idarubicin	5,070	4,740	4,490	3,270	4,239	21,809
Ifosfamide	2,304,236	1,480,650	2,055,100	1,970,600	1,964,700	9,775,286
Inot. Ozogamicin	-	-	-	38	21	59
Ipilimumab	8,755	17,218	29,376	38,195	49,502	143,046
Irinotecan	673,464	640,777	635,320	764,912	1,029,568	3,744,041
Methotrexate	2,300,653	2,196,267	2,494,343	3,097,392	3,158,069	13,200,000
Nivolumab	5,220	298,078	791,872	934,509	1,227,207	3,256,886
Obinutuzumab	104,000	198,000	191,000	674,000	951,000	2,118,000
Oxaliplatin	398,199	465,073	646,181	608,021	785,709	2,903,183
Paclitaxel	795,386	914,823	1,115,871	1,279,719	1,489,908	5,595,707
Panitumumab	222,971	191,979	185,504	259,702	365,604	1,225,760
Pembrolizumab	118,910	151,155	220,139	483,974	677,141	1,651,319
Pemetrexed	628,395	650,755	807,720	782,632	1,178,887	4,048,389
Pertuzumab	338,560	507,360	564,480	638,820	723,240	2,772,460
Pralatrexate	-	-	2,800	2,620	3,966	9,386
Raltitrexed	253	363	143	160	63	982
Rituximab	3,272,145	2,822,415	2,842,361	2,902,380	2,302,737	14,100,000
Topotecan	349	418	194	308	140	1,409
Trastuzumab	1,805,601	1,844,516	2,067,776	2,006,608	1,738,631	9,463,132
Trast. Emtansine	99,928	87,994	90,568	84,905	131,227	494,622
Vinblastine	5,427	4,196	3,708	4,332	5,648	23,311
Vincristine	3,663	3,691	4,092	3,956	3,700	19,102
Vinorelbine	22,823	32,072	28,948	25,903	24,448	134,194
TAS						
Arsenic	48	811	225	2,932	3,524	7,540
Atezolizumab	-	-	34,800	118,800	288,360	441,960
Avelumab	-	-	-	59,570	100,570	160,140
Bendamustine	49,010	72,038	61,310	93,975	58,900	335,233
Bevacizumab	357,270	452,137	388,709	371,730	530,898	2,100,744
Bleomycin	53,970	4,716,045	58,700,000	38,300,000	30,800,000	133,000,000
Blinatumomab	-	774	3,529	1,761	7,164	13,228
Bortezomib	2,483	2,034	2,009	2,644	2,412	11,582
Brent. Vedotin	1,200	1,700	4,260	2,715	3,985	13,860
Cabazitaxel	3,504	2,190	4,067	5,851	6,740	22,352
Carboplatin	567,420	571,758	615,184	585,596	669,464	3,009,422
Carfilzomib	-	1,800	24,115	39,023	28,678	93,616
Cetuximab	290,850	156,995	242,480	272,580	415,540	1,378,445
Cisplatin	53,499	48,834	45,981	56,730	54,718	259,762
Cladribine	169	60	-	253	197	679
Cyclophosphamide	1,454,110	1,718,884	1,530,204	1,499,704	1,606,327	7,809,229
Cytarabine	1,214,598	938,019	889,982	1,261,505	1,422,791	5,726,895
Docetaxel	98,016	88,734	82,734	90,635	84,781	444,900
Doxorubicin	67,719	86,139	89,575	96,504	108,413	448,350

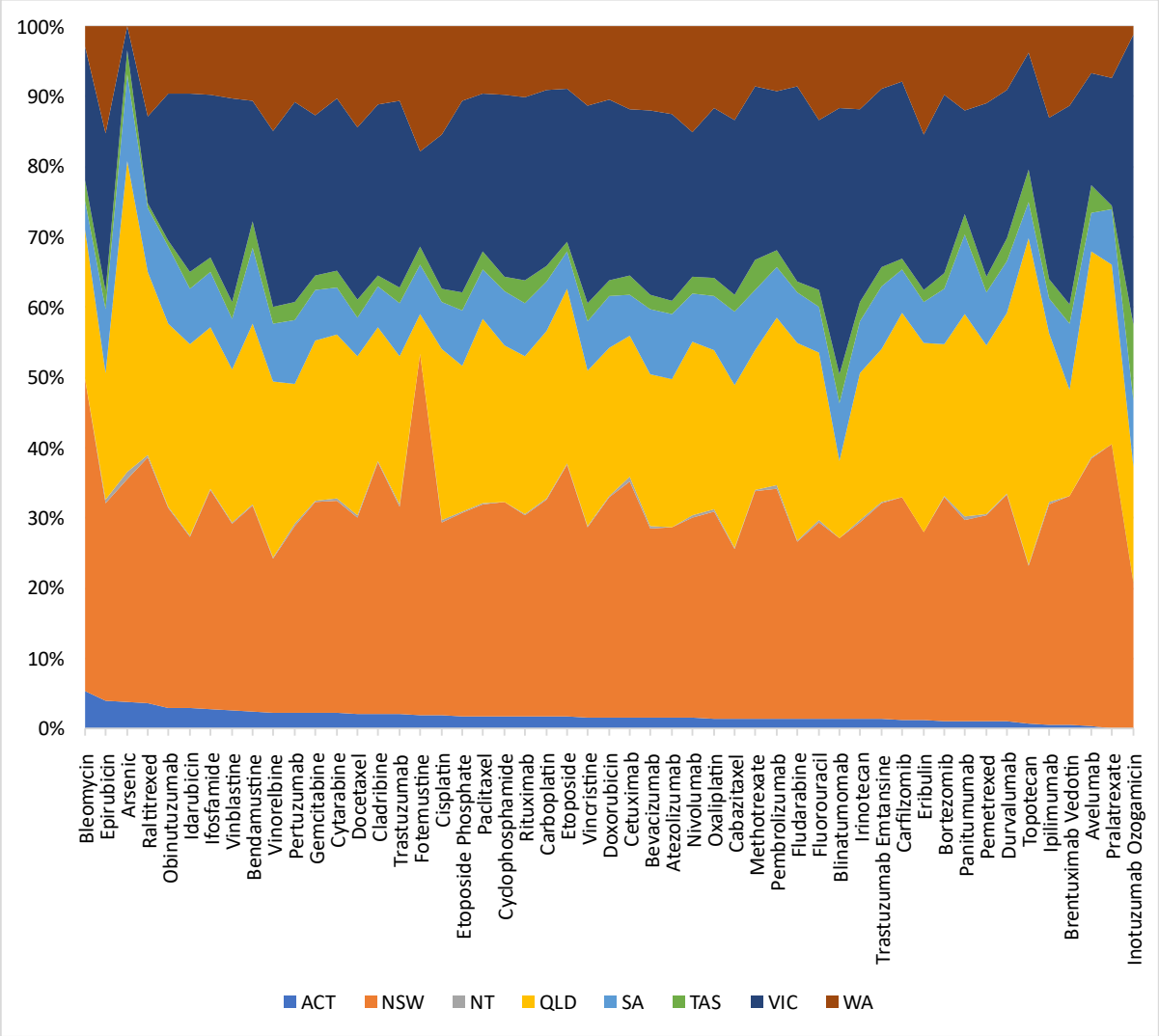
Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Durvalumab	-	-	-	-	210,280	210,280
Epirubicin	20,733	21,916	12,163	12,881	7,425	75,118
Eribulin	100	192	280	230	242	1,044
Etoposide	20,450	162,343	4,859	1,032	4,550	193,234
Etop. Phosphate	187,126	47,309	212,110	232,156	209,409	888,110
Fludarabine	6,856	5,344	3,290	4,940	4,414	24,844
Fluorouracil	6,667,380	9,797,491	11,200,000	12,800,000	15,900,000	56,400,000
Fotemustine	570	600	-	832	-	2,002
Gemcitabine	1,763,556	1,783,522	1,862,393	1,986,956	2,132,853	9,529,280
Idarubicin	1,794	1,198	906	1,579	1,229	6,706
Ifosfamide	507,738	639,160	480,890	409,550	517,000	2,554,338
Inot. Ozogamicin	-	-	-	-	66	66
Ipilimumab	3,700	11,390	19,470	24,745	19,659	78,964
Irinotecan	201,470	241,034	282,012	300,920	419,629	1,445,065
Methotrexate	1,599,744	1,197,064	1,076,118	1,237,094	1,318,167	6,428,186
Nivolumab	440	103,558	260,117	311,399	452,340	1,127,854
Obinutuzumab	-	11,000	18,000	57,000	67,000	153,000
Oxaliplatin	171,990	199,575	205,875	190,317	244,939	1,012,696
Paclitaxel	296,714	315,465	452,173	437,156	493,982	1,995,490
Panitumumab	59,960	91,560	51,756	42,246	66,890	312,412
Pembrolizumab	39,306	54,336	85,445	144,888	222,098	546,073
Pemetrexed	181,970	157,585	211,205	284,915	375,742	1,211,417
Pertuzumab	147,840	149,100	145,740	165,060	173,460	781,200
Pralatrexate	-	-	230	355	-	585
Raltitrexed	36	39	-	-	-	75
Rituximab	1,071,280	1,194,733	1,208,398	1,253,078	1,360,956	6,088,445
Topotecan	320	170	106	285	392	1,273
Trastuzumab	568,161	621,201	470,078	609,826	636,812	2,906,078
Trast. Emtansine	43,330	21,320	26,550	22,240	36,212	149,652
Vinblastine	1,515	2,348	1,253	1,108	1,652	7,876
Vincristine	1,078	1,060	1,359	1,489	2,002	6,988
Vinorelbine	8,556	5,581	7,597	10,478	6,044	38,256
VIC						
Arsenic	434	472	2,369	1,921	2,240	7,436
Atezolizumab	-	-	698,400	1,876,800	3,709,560	6,284,760
Avelumab	-	-	-	286,240	393,240	679,480
Bendamustine	219,632	369,007	312,089	364,028	300,456	1,565,212
Bevacizumab	5,131,557	4,918,919	4,981,980	4,948,341	6,200,172	26,200,000
Bleomycin	144,000,000	134,000,000	175,000,000	166,000,000	230,000,000	848,000,000
Blinatumomab	-	18,134	31,056	27,603	42,863	119,655
Bortezomib	26,228	25,523	26,568	27,399	29,411	135,129
Brent. Vedotin	14,441	25,901	29,833	37,721	32,951	140,847
Cabazitaxel	43,112	48,626	41,628	51,435	51,039	235,840
Carboplatin	6,052,200	6,073,364	6,540,433	6,768,779	7,169,766	32,600,000
Carfilzomib	-	3,480	467,869	536,741	537,461	1,545,551
Cetuximab	2,234,277	2,071,722	2,330,932	2,678,135	2,840,149	12,200,000
Cisplatin	607,284	632,240	609,803	605,292	592,397	3,047,016
Cladribine	2,334	2,265	1,523	2,701	1,556	10,379
Cyclophosphamide	19,100,000	18,300,000	20,100,000	19,800,000	18,400,000	95,800,000
Cytarabine	12,300,000	11,700,000	11,100,000	12,400,000	11,500,000	59,000,000
Docetaxel	900,356	813,145	884,303	919,516	772,609	4,289,929
Doxorubicin	1,002,851	1,004,620	1,092,235	1,131,492	1,111,451	5,342,649
Durvalumab	-	-	-	3,103	1,390,523	1,393,626
Epirubicin	313,546	170,166	94,068	66,474	47,897	692,151
Eribulin	2,415	2,418	3,196	3,101	2,782	13,912
Etoposide	626,257	1,268,847	486,702	379,676	424,077	3,185,559

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Etop. Phosphate	2,618,291	759,720	1,917,846	1,939,848	1,946,609	9,182,314
Fludarabine	114,100	83,426	85,618	103,361	71,433	457,938
Fluorouracil	87,600,000	98,600,000	108,000,000	120,000,000	123,000,000	537,000,000
Fotemustine	5,713	3,351	688	-	700	10,452
Gemcitabine	21,600,000	22,300,000	22,900,000	20,100,000	20,400,000	107,000,000
Idarubicin	18,865	13,915	14,199	10,972	12,027	69,978
Ifosfamide	6,224,615	5,207,607	6,668,021	6,244,782	4,690,084	29,000,000
Inot. Ozogamicin	-	-	-	117	139	256
Ipilimumab	39,908	127,848	139,117	163,737	185,473	656,083
Irinotecan	2,533,041	2,336,219	2,736,277	3,096,621	3,424,514	14,100,000
Methotrexate	8,218,659	7,744,180	7,112,805	6,699,331	7,710,440	37,500,000
Nivolumab	40,258	882,173	2,214,632	2,701,423	3,987,926	9,826,412
Obinutuzumab	154,000	395,750	563,000	1,338,997	1,546,300	3,998,047
Oxaliplatin	1,583,149	1,628,049	1,889,691	1,958,494	2,114,771	9,174,154
Paclitaxel	3,068,361	3,404,836	3,707,685	3,857,617	3,850,478	17,900,000
Panitumumab	240,920	352,976	338,845	419,470	245,165	1,597,376
Pembrolizumab	498,340	591,193	682,731	1,233,876	2,150,109	5,156,249
Pemetrexed	1,841,488	1,875,686	2,200,636	2,842,957	4,352,761	13,100,000
Pertuzumab	1,152,480	1,459,920	1,755,600	2,026,215	2,187,040	8,581,255
Pralatrexate	-	-	2,995	7,330	11,393	21,718
Raltitrexed	168	211	311	282	354	1,326
Rituximab	10,100,000	9,661,544	9,758,206	9,781,661	9,320,588	48,600,000
Topotecan	698	669	1,138	1,066	1,026	4,597
Trastuzumab	6,071,468	6,431,073	6,877,613	7,177,198	7,381,730	33,900,000
Trast. Emtansine	259,058	264,618	229,177	240,695	416,484	1,410,032
Vinblastine	20,827	18,229	16,078	19,023	21,611	95,768
Vincristine	15,194	14,854	15,146	14,737	15,989	75,920
Vinorelbine	104,617	78,580	86,787	74,429	59,978	404,391
WA						
Arsenic	-	-	-	-	-	-
Atezolizumab	-	-	422,400	884,400	1,667,040	2,973,840
Avelumab	-	-	-	87,970	192,130	280,100
Bendamustine	100,006	218,879	205,465	235,709	215,488	975,547
Bevacizumab	1,891,764	2,211,198	2,452,879	2,341,287	3,232,155	12,100,000
Bleomycin	88,785	15,700,000	32,800,000	56,400,000	22,600,000	127,000,000
Blinatumomab	-	2,836	7,739	5,968	20,328	36,870
Bortezomib	10,920	8,911	9,665	10,508	11,707	51,709
Brent. Vedotin	6,550	16,250	11,250	12,350	9,864	56,264
Cabazitaxel	20,699	21,524	22,702	30,700	31,129	126,754
Carboplatin	2,107,614	2,122,523	2,474,906	2,391,521	2,568,756	11,700,000
Carfilzomib	-	-	162,299	145,754	179,924	487,977
Cetuximab	1,382,175	1,246,090	1,297,235	1,074,644	1,052,338	6,052,482
Cisplatin	433,761	458,738	453,987	364,707	410,936	2,122,129
Cladribine	1,193	1,080	390	1,028	1,065	4,756
Cyclophosphamide	7,062,927	7,226,196	7,470,055	7,718,182	7,060,580	36,500,000
Cytarabine	4,101,304	5,063,610	5,646,623	4,942,647	4,887,259	24,600,000
Docetaxel	591,134	522,420	500,469	475,236	421,080	2,510,339
Doxorubicin	391,841	422,462	474,562	437,796	426,128	2,152,789
Durvalumab	-	-	-	-	595,622	595,622
Epirubicin	146,525	143,706	89,627	57,060	29,651	466,569
Eribulin	1,827	1,664	1,950	2,134	2,167	9,742
Etoposide	297,355	644,249	147,905	97,476	106,960	1,293,945
Etop. Phosphate	820,850	311,844	956,653	695,139	769,843	3,554,329
Fludarabine	30,619	20,576	28,403	37,224	22,586	139,408
Fluorouracil	46,300,000	55,100,000	65,100,000	63,300,000	70,600,000	300,000,000
Fotemustine	1,872	3,328	416	2,704	5,384	13,704

Drug	*2016*	*2017*	*2018*	*2019*	*2020*	*2016-2020*
Gemcitabine	11,500,000	13,400,000	12,600,000	11,200,000	11,100,000	59,800,000
Idarubicin	5,153	5,541	6,834	5,985	2,837	26,350
Ifosfamide	3,418,560	3,237,430	2,751,975	1,178,631	1,553,598	12,100,000
Inot. Ozogamicin	-	-	-	6	1	7
Ipilimumab	38,865	65,306	82,230	103,695	81,717	371,813
Irinotecan	1,009,239	1,138,373	1,284,760	1,248,116	1,410,382	6,090,870
Methotrexate	2,224,736	2,594,019	3,653,510	2,295,101	2,463,533	13,200,000
Nivolumab	34,420	672,179	1,824,284	2,094,822	2,532,793	7,158,498
Obinutuzumab	138,100	160,000	309,000	496,000	736,000	1,839,100
Oxaliplatin	797,473	785,891	957,012	934,049	967,328	4,441,753
Paclitaxel	1,385,425	1,327,061	1,553,637	1,652,768	1,755,321	7,674,212
Panitumumab	105,218	294,567	260,491	301,477	337,096	1,298,849
Pembrolizumab	242,058	243,450	352,814	456,198	833,771	2,128,291
Pemetrexed	1,113,980	967,285	928,659	969,015	1,799,583	5,778,522
Pertuzumab	461,160	550,200	692,160	718,620	878,640	3,300,780
Pralatrexate	-	-	3,740	2,095	2,999	8,834
Raltitrexed	136	479	316	198	251	1,380
Rituximab	3,548,659	3,769,020	3,927,675	3,783,766	3,653,923	18,700,000
Topotecan	190	143	189	170	350	1,042
Trastuzumab	2,212,945	2,538,810	2,623,188	2,848,027	3,269,343	13,500,000
Trast. Emtansine	74,880	76,539	101,848	108,894	136,256	498,417
Vinblastine	6,357	5,237	6,280	8,389	7,353	33,616
Vincristine	4,976	6,215	6,821	5,859	6,461	30,332
Vinorelbine	49,540	52,688	50,822	46,074	40,821	239,945

Source: Developed for this Review using in-market sales data (IQVIA).

Figure A56. Distribution of units purchased by State and Territory (2016 - 2020)



Source: Developed for this Review using in-market sales data (IQVIA).

Factors affecting price per mg

The factors affecting the price per unit per medicine were investigated by applying a series of hierarchical linear regression models which sought to examine the impact on the price per unit of various explanatory variables, taking into account that information was available on multiple levels for a given medicine (e.g. multiple manufacturers or multiple pack presentations). The results from those analyses are summarised as:

- Number of manufacturers: for each additional manufacturer available in the Australian market, the price per unit was reduced by $0.82 (p-value ≤ 0.05; see Equation 1). However, this result was no longer observed when the number of manufactures was dichotomised as

one or more; there was no significant relationship between the price per unit and manufacturer number (see Equation 2).

- Location of sales: there was no significant difference in the price paid per unit between states (see Equation 3).
- Number of packs: in general, the price per unit decreases by $0.15 for each additional unique pack ID available (p-value ≤ 0.05; see Equation 4).
- Year: on average the price paid per unit reduced by $1.95 each year (p-value<0.05; see Equation 5).
- Compounding status: hospitals and pharmacies save $4.98 per unit (p-value ≤ 0.05) when they purchase drugs in compounded solution (see Equation 6).
- Purchasing channel: on average retail pharmacies pay $1.23 per unit more than hospitals do (p-value <0.05; see Equation 7). This difference was not attenuated by controlling for the total units purchased (see Equation 8).

Equation 1. Impact of manufacturer number on price per unit.

```
. mixed Permg N_Manufacturer i.Year || Molecule: || Manufacturer:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood =  -422947.2
Iteration 1:   log likelihood = -422941.99
Iteration 2:   log likelihood = -422941.62
Iteration 3:   log likelihood = -422941.62

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548

        Grouping information
------------------------------------------------------------------------------
 Group variable |     No. of       Observations per group
                |     groups    Minimum    Average    Maximum
----------------+-------------------------------------------------------------
        Molecule |         51         67    1,559.8      8,502
    Manufacturer |        131          1      607.2      4,030
------------------------------------------------------------------------------

                                                Wald chi2(5)      =     301.20
Log likelihood = -422941.62                     Prob > chi2       =     0.0000

------------------------------------------------------------------------------
        Permg | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
--------------+---------------------------------------------------------------
N_Manufacturer |  -.8211938   .2247563    -3.65   0.000    -1.261708   -.3806794
              |
         Year |
         2017 |  -1.793933   .5673411    -3.16   0.002    -2.905901   -.6819643
         2018 |  -4.290491   .5763846    -7.44   0.000    -5.420184   -3.160798
         2019 |  -8.835707   .5761903   -15.33   0.000    -9.965019   -7.706395
         2020 |  -6.806794   .5801388   -11.73   0.000    -7.943845   -5.669743
              |
        _cons |    272.798   226.8223     1.20   0.229    -171.7656    717.3616
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects parameters |   Estimate   Std. err.      [95% conf. interval]
----------------------------+-------------------------------------------------
Molecule: Identity          |
                 var(_cons) |    2623834     519625       1779771     3868198
----------------------------+-------------------------------------------------
Manufacturer: Identity      |
                 var(_cons) |   5.145671   1.723559       2.668882    9.920984
----------------------------+-------------------------------------------------
              var(Residual) |   2407.339    12.0776       2383.784    2431.128
------------------------------------------------------------------------------
LR test vs. linear model: chi2(2) = 3.1e+05                   Prob > chi2 = 0.0000
```

Notes: Fixed effects: Number of manufactures and year. Random effects: Manufacturer and molecule.

Equation 2. Impact of manufacturer (one or more) on price per unit

```
. mixed Permg Generic i.Year || Molecule: || Manufacturer:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422953.31
Iteration 1:   log likelihood = -422948.21
Iteration 2:   log likelihood = -422947.95
Iteration 3:   log likelihood = -422947.95

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548

        Grouping information
-------------------------------------------------------------
 Group variable |     No. of       Observations per group
                |      groups    Minimum    Average    Maximum
----------------+--------------------------------------------
       Molecule |          51         67    1,559.8      8,502
   Manufacturer |         131          1      607.2      4,030
-------------------------------------------------------------

                                                Wald chi2(5)      =     288.85
Log likelihood = -422947.95                     Prob > chi2       =     0.0000

------------------------------------------------------------------------------
       Permg | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
     Generic |      .81194   1.002745     0.81   0.418    -1.153404    2.777284
             |
        Year |
        2017 |   -1.610229   .5655733    -2.85   0.004    -2.718732   -.5017261
        2018 |   -3.997649   .5712894    -7.00   0.000    -5.117356   -2.877942
        2019 |   -8.535659   .5709016   -14.95   0.000    -9.654605   -7.416712
        2020 |   -6.430096   .5702623   -11.28   0.000    -7.547789   -5.312402
             |
       _cons |     270.328   226.8516     1.19   0.233    -174.2929    714.9489
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects parameters |   Estimate   Std. err.     [95% conf. interval]
----------------------------+-------------------------------------------------
Molecule: Identity          |
                  var(_cons) |    2624520   519760.6       1780236     3869208
----------------------------+-------------------------------------------------
Manufacturer: Identity      |
                  var(_cons) |   5.507755   1.823745      2.878208    10.53967
----------------------------+-------------------------------------------------
               var(Residual) |   2407.668   12.07938      2384.109     2431.46
------------------------------------------------------------------------------
LR test vs. linear model: chi2(2) = 3.1e+05               Prob > chi2 = 0.0000

Note: LR test is conservative and provided only for reference.
```

Notes: Fixed effects: Number of manufacturers (dichotomised) and year. Random effects: Manufacturer and molecule.

Equation 3. Impact of state on price paid per unit

```
. mixed Permg i.Year ib2.State || Molecule:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422959.73
Iteration 1:   log likelihood = -422959.73

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548
Group variable: Molecule                        Number of groups  =         51
                                                Obs per group:
                                                              min =         67
                                                              avg =    1,559.8
                                                              max =      8,502
                                                Wald chi2(11)     =     283.67
Log likelihood = -422959.73                     Prob > chi2       =     0.0000
```

Permg	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
Year						
2017	-1.494214	.5634599	-2.65	0.008	-2.598575	-.3898525
2018	-3.694591	.5651392	-6.54	0.000	-4.802243	-2.586938
2019	-8.066516	.559566	-14.42	0.000	-9.163245	-6.969786
2020	-5.964402	.5578816	-10.69	0.000	-7.05783	-4.870975
State						
ACT	.5933908	.8115831	0.73	0.465	-.9972829	2.184065
NT	1.900973	1.342138	1.42	0.157	-.72957	4.531515
QLD	-.7364603	.5847006	-1.26	0.208	-1.882452	.4095318
SA	-.5393436	.6449092	-0.84	0.403	-1.803342	.7246552
TAS	.7180474	.7573711	0.95	0.343	-.7663726	2.202467
VIC	-.5484689	.5799959	-0.95	0.344	-1.68524	.5883021
WA	.030636	.6128219	0.05	0.960	-1.170473	1.231745
_cons	270.5781	226.8241	1.19	0.233	-173.989	715.1452

Random-effects parameters	Estimate	Std. err.	[95% conf.	interval]
Molecule: Identity				
var(_cons)	2623891	519588.3	1779873	3868142
var(Residual)	2409.566	12.08588	2385.994	2433.37

LR test vs. linear model: chibar2(01) = 3.1e+05 Prob >= chibar2 = 0.0000

Notes: Fixed effects: State and year. Random effects: Molecule.

Equation 4. Impact of number of unique pack IDs on price per unit

```
. mixed Permg  N_PFC Year || Molecule:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422991.02
Iteration 1:   log likelihood = -422991.02

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548
Group variable: Molecule                        Number of groups  =         51
                                                Obs per group:
                                                              min =         67
                                                              avg =    1,559.8
                                                              max =      8,502
                                                Wald chi2(2)      =     220.89
Log likelihood = -422991.02                     Prob > chi2       =     0.0000
```

Permg	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
N_PFC	-.1524893	.0690687	-2.21	0.027	-.2878615	-.017117
Year	-1.87914	.1264448	-14.86	0.000	-2.126968	-1.631313
_cons	4059.607	341.4515	11.89	0.000	3390.375	4728.84

Random-effects parameters	Estimate	Std. err.	[95% conf.	interval]
Molecule: Identity				
var(_cons)	2623387	519488.6	1779532	3867400
var(Residual)	2411.463	12.0954	2387.873	2435.287

LR test vs. linear model: chibar2(01) = 3.1e+05 Prob >= chibar2 = 0.0000

Notes: Fixed effects: Number of packs and year. Random effects: Molecule.

Equation 5. Impact of time on price paid per unit

```
. mixed Permg Year || Molecule: ||  Manufacturer:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422983.56
Iteration 1:   log likelihood = -422978.42
Iteration 2:   log likelihood = -422978.17
Iteration 3:   log likelihood = -422978.17

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548

        Grouping information

-------------------------------------------------------------
 Group variable |     No. of       Observations per group
                |      groups    Minimum    Average    Maximum
----------------+--------------------------------------------
        Molecule |          51         67    1,559.8      8,502
    Manufacturer |         131          1      607.2      4,030
-------------------------------------------------------------

                                                Wald chi2(1)      =     227.94
Log likelihood = -422978.17                     Prob > chi2       =     0.0000

------------------------------------------------------------------------------
       Permg | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
        Year |  -1.945332   .1288486   -15.10   0.000    -2.197871   -1.692794
       _cons |    4192.27   345.0752    12.15   0.000     3515.935    4868.605
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects parameters |   Estimate   Std. err.      [95% conf. interval]
----------------------------+-------------------------------------------------
Molecule: Identity          |
                  var(_cons) |   2624244   519705.9       1780050     3868801
----------------------------+-------------------------------------------------
Manufacturer: Identity      |
                  var(_cons) |   5.238266   1.762157       2.70921     10.1282
----------------------------+-------------------------------------------------
               var(Residual) |   2409.54   12.08872      2385.963     2433.35
------------------------------------------------------------------------------
LR test vs. linear model: chi2(2) = 3.1e+05                   Prob > chi2 = 0.0000
```

Notes: Fixed effects: Year. Random effects: Manufacturer and molecule.

Equation 6. Impact of compounding status on price paid per unit

```
. mixed Permg  i.CompoundedFlag Year || Molecule:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422901.92
Iteration 1:   log likelihood = -422901.92  (backed up)

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548
Group variable: Molecule                        Number of groups  =         51
                                                Obs per group:
                                                              min =         67
                                                              avg =    1,559.8
                                                              max =      8,502
                                                Wald chi2(2)      =     399.80
Log likelihood = -422901.92                     Prob > chi2       =     0.0000
```

Permg	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
CompoundedFlag						
Not compounded	-4.980282	.3678495	-13.54	0.000	-5.701254	-4.25931
Year	-1.807877	.1251427	-14.45	0.000	-2.053152	-1.562602
_cons	3917.698	339.4831	11.54	0.000	3252.323	4583.073

Random-effects parameters	Estimate	Std. err.	[95% conf.	interval]
Molecule: Identity				
var(_cons)	2624690	519744.9	1780417	3869315
var(Residual)	2406.063	12.06831	2382.525	2429.833

LR test vs. linear model: chibar2(01) = 3.1e+05 Prob >= chibar2 = 0.0000

Notes: Fixed effects: Compounding status year. Random effects: molecule

Equation 7. Impact of retail status on price paid per unit

```
.  mixed Permg i.Channel Year || Molecule:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422988.86
Iteration 1:   log likelihood = -422988.86

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548
Group variable: Molecule                        Number of groups  =         51
                                                Obs per group:
                                                              min =         67
                                                              avg =    1,559.8
                                                              max =      8,502
                                                Wald chi2(2)      =     225.23
Log likelihood = -422988.86                     Prob > chi2       =     0.0000
```

Permg	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
Channel						
Retail	1.230802	.4057991	3.03	0.002	.4354503	2.026154
Year	-1.832403	.1252878	-14.63	0.000	-2.077963	-1.586844
_cons	3964.089	339.6818	11.67	0.000	3298.325	4629.854

Random-effects parameters	Estimate	Std. err.	[95% conf.	interval]
Molecule: Identity				
var(_cons)	2623871	519584.3	1779860	3868113
var(Residual)	2411.332	12.09474	2387.743	2435.154

Notes: Fixed effects: channel status and year. Random effects: drug

Equation 8. Impact of retail status and total units purchased on price paid per unit

```
. mixed Permg i.Channel mgTotal Year || Molecule:

Performing EM optimization ...

Performing gradient-based optimization:
Iteration 0:   log likelihood = -422988.86
Iteration 1:   log likelihood = -422988.86  (backed up)

Computing standard errors ...

Mixed-effects ML regression                     Number of obs     =     79,548
Group variable: Molecule                        Number of groups  =         51
                                                Obs per group:
                                                              min =         67
                                                              avg =    1,559.8
                                                              max =      8,502
                                                Wald chi2(3)      =     225.23
Log likelihood = -422988.86                     Prob > chi2       =     0.0000
```

Permg	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
Channel						
Retail	1.229722	.406274	3.03	0.002	.4334398	2.026005
mgTotal	-9.59e-09	1.74e-07	-0.05	0.956	-3.51e-07	3.32e-07
Year	-1.832334	.1252941	-14.62	0.000	-2.077906	-1.586762
_cons	3963.951	339.6907	11.67	0.000	3298.17	4629.733

Random-effects parameters	Estimate	Std. err.	[95% conf.	interval]
Molecule: Identity				
var(_cons)	2623856	519580	1779851	3868087
var(Residual)	2411.332	12.09474	2387.743	2435.154

LR test vs. linear model: chibar2(01) = 3.1e+05 Prob >= chibar2 = 0.0000

Notes: Fixed effects: channel status, total units purchased and year. Random effects: drug

Appendix 8. Analysis of TGA Safety Data

Overview

The purpose of this analysis was to examine the rates of off-label use of cancer medicines listed on the EFC, which were potentially associated with causing adverse events (AEs). Additionally, this analysis sought to identify the impact listing cancer medicines on the EFC had on rates of AEs associated with off-label use.

Method

An analysis of spontaneous AEs related to cancer medicines listed on the EFC was undertaken using data extracted from the TGA's Database of Adverse Event Notifications (DAEN) website [49]. Medicines were selected for analysis if they were on the EFC list, had a TGA indication that was consistent with the PBS indication and did not have a general benefit listing. This resulted in the inclusion of 40 EFC medicines. A summary of reasons for the inclusion or exclusion of EFC-medicines from the analysis is provided in Table A43, Table A44 and Table A45.

Table A43. EFC molecules included in the analysis of DAEN data

Drug	*TGA indication*	*PBS indication*
Arsenic (Trioxide)	• Acute promyelocytic leukaemia (induction of remission and consolidation)	• Acute promyelocytic leukaemia (induction of remission and consolidation)
Bendamustine (Hydrochloride)	• Treatment of chronic lymphocytic leukaemia • Previously untreated indolent CD20-positive, stage III-IV Non-Hodgkin's lymphoma (*in combination*) • Previously untreated CD20-positive, stage III-IV Mantle Cell Lymphoma (*in combination*) • Relapsed/refractory indolent non-Hodgkin's lymphoma	• Previously untreated stage III or IV mantle cell lymphoma • Follicular lymphoma • Previously untreated stage II bulky or stage III or IV indolent non-Hodgkin's lymphoma
Bevacizumab (Recombinant)	• Metastatic Colorectal Cancer • Locally recurrent or metastatic Breast Cancer • Advanced, metastatic or recurrent non-squamous non-small cell lung cancer • Advanced and/or metastatic renal cell cancer • Grade IV glioma • Epithelial ovarian, fallopian tube or primary peritoneal cancer • Recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer • Cervical cancer	• Epithelial ovarian, fallopian tube or primary peritoneal cancer • Advanced carcinoma of cervix • Relapsed or recurrent glioblastoma • Stage IV (metastatic) non-small cell lung cancer • Advanced (unresectable) Barcelona Clinic Liver Cancer Stage B or Stage C hepatocellular carcinoma • Metastatic colorectal cancer

Drug	*TGA indication*	*PBS indication*
Blinatumomab (Recombinant)	• relapsed or refractory B-cell precursor acute lymphoblastic leukaemia	• Acute lymphoblastic leukaemia
Bortezomib	• Multiple myeloma • Induction therapy prior to high dose chemotherapy with autologous stem cell rescue • Treatment of adult patients with previously untreated mantle cell lymphoma	• Multiple myeloma
Brentuximab Vedotin (Recombinant)	• Hodgkin lymphoma • Peripheral T-cell lymphoma • Cutaneous T cell lymphoma	• CD30 positive systemic anaplastic large cell lymphoma • Relapsed or Refractory Hodgkin lymphoma • CD30 positive cutaneous T-cell lymphoma
Cabazitaxel	• Metastatic castration resistant prostate cancer previously treated with a docetaxel containing regimen (*in combination with prednisone or prednisolone*)	• Castration resistant metastatic carcinoma of the prostate
Carboplatin	• Advanced ovarian carcinoma of epithelial origin. • Small cell lung carcinoma • Carcinoma of the head and neck • Carcinoma of the testis • Paediatric cerebral tumours • Soft tissue sarcoma • Neuroblastoma	• Not reported
Carfilzomib	• Relapsed or refractory multiple myeloma	• Multiple myeloma
Cetuximab (Recombinant)	• Colorectal cancer • Squamous cell cancer of the head and neck	• Metastatic colorectal cancer • Stage III, IVa or IVb squamous cell cancer of the larynx, oropharynx or hypopharynx
Cisplatin	• Metastatic non-seminomatous germ cell carcinoma • Advanced stage, refractory ovarian carcinoma • Advanced stage, refractory bladder carcinoma • Refractory squamous cell carcinoma of the head and neck.	• Not reported
Cladribine	• Hairy Cell Leukaemia • B-cell chronic lymphocytic leukaemia • Relapsing-remitting multiple sclerosis • lymphoplasmacytic lymphoma (second line)	• Relapsing remitting multiple sclerosis • Hairy cell leukaemia
Cyclophosph…	• Malignant lymphomas • Neuroblastoma (patients with disseminated disease); adenocarcinoma of the ovary, retinoblastoma.	• Not reported

Drug	*TGA indication*	*PBS indication*
	• Carcinoma of the breast; malignant neoplasms of the lung	
Cytarabine	• Induction and maintenance of remission in acute myelocytic leukaemia • Acute lymphocytic leukaemia • Chronic myelocytic leukaemia (blast phase) • Meningeal Leukaemia	• Not reported
Docetaxel	• Breast Cancer • Non-Small Cell Lung Cancer • Hormone Refractory Prostate Cancer • Gastric Adenocarcinoma • Squamous cell carcinoma of the head and neck cancer	• Not reported
Doxorubicin (Hydrochloride)	• Advanced epithelial ovarian cancer • AIDS-related Kaposi's sarcoma • Metastatic breast cancer	• Advanced epithelial ovarian cancer • Metastatic breast cancer
Durvalumab (Recombinant)	• Urothelial carcinoma • Locally advanced non-small cell lung cancer • Small cell lung cancer	• Unresectable Stage III non-small cell lung cancer
Epirubicin (Hydrochloride)	• Breast cancer • Gastric cancer • Ovarian cancer • Small cell lung cancer • Lymphoma (non-Hodgkin’s lymphoma) • Advanced/metastatic soft tissue sarcoma • Superficial bladder cancer (Tis, Ta)	• Not reported
Eribulin (Mesilate)	• Locally advanced or metastatic breast cancer • Unresectable liposarcoma	• Locally advanced or metastatic breast cancer • Advanced (unresectable and/or metastatic) liposarcoma
Etoposide	• Small cell carcinoma of the lung • Acute monocytic and myelomonocytic leukaemia • Hodgkin's disease • Non-Hodgkin's lymphoma	• Not reported
Etoposide Phosphate	• Small cell carcinoma of the lung • Acute monocytic and myelomonocytic leukaemia • Hodgkin's disease • Non-Hodgkin's lymphoma • Testicular tumour	• Not reported
Fludarabine (Phosphate)	• B - cell chronic lymphocytic leukaemia	• Not reported
Fluorouracil	• Palliative treatment of malignant tumours, particularly of the breast, colon or rectum	• Not reported

Drug	*TGA indication*	*PBS indication*
	• Treatment of gastric, primary hepatic, pancreatic, uterine (cervical particularly), ovarian and bladder carcinomas.	
Fotemustine	• Disseminated malignant melanoma including cerebral metastases	• Metastatic malignant melanoma
Gemcitabine (Hydrochloride) Idarubicin (Hydrochloride)	• Non-small cell lung cancer, pancreatic cancer, biliary tract cancer, uroepithelial cancer, inoperable or recurrent breast cancer, ovarian cancer progressing after chemotherapy, recurrence or refractory malignant lymphoma	• Not reported
Ifosfamide	• Acute myelogenous leukaemia	• Acute myelogenous leukaemia
Gemcitabine (Hydrochloride)	• Germ cell tumours, sarcomas, lymphomas • Anti-tumour activity has been shown in ovarian and cervical cancers. • Some activity has also been seen in lung and breast cancer	• Not reported
Inotuzumab Ozogamicin (Recombinant)	• Acute lymphoblastic leukaemia	• Acute lymphoblastic leukaemia
Ipilimumab (Recombinant)	• Melanoma • Renal Cell Carcinoma • Non-Small Cell Lung Cancer • Malignant Pleural Mesothelioma	• Unresectable Stage III or Stage IV malignant melanoma • Stage IV clear cell variant renal cell carcinoma • Stage IV (metastatic) non-small cell lung cancer
Irinotecan (Hydrochloride)	• Metastatic carcinoma of the colon or rectum • Non-small-cell lung cancer • Small-cell lung cancer • Cervical cancer • Ovarian cancer • Inoperable or recurrent gastric cancer • Esophageal cancer.	• Not reported
Nivolumab (Recombinant)	• Melanoma • Non-Small Cell Lung Cancer • Malignant Pleural Mesothelioma • Renal Cell Carcinoma • Classical Hodgkin Lymphoma • Squamous Cell Carcinoma of the Head and Neck • Urothelial Carcinoma • Hepatocellular Carcinoma • Oesophageal Squamous Cell Carcinoma	• Unresectable Stage III or Stage IV malignant melanoma • Resected Stage IIIB, IIIC, IIID or Stage IV malignant melanoma • Locally advanced or metastatic non-small cell lung cancer • Stage IV (metastatic) non-small cell lung cancer • Stage IV clear cell variant renal cell carcinoma • Recurrent or metastatic squamous cell carcinoma of the oral cavity, pharynx or larynx
Obinutuzumab (Recombinant)	• Chronic lymphocytic leukaemia • Follicular lymphoma	• Chronic lymphocytic leukaemia • Stage II bulky or Stage III/IV follicular lymphoma • Follicular lymphoma

Drug	*TGA indication*	*PBS indication*
		• Chronic lymphocytic leukaemia or small lymphocytic lymphoma
Oxaliplatin	• Adjuvant treatment of stage III (Duke's C) colon cancer • Treatment of advanced colorectal cancer • Treatment of patients with advanced esophagogastric cancer (in combination with epirubicin and either capecitabine or fluorouracil). • Inoperable pancreatic cancer • Gastric cancer	• Not reported
Paclitaxel	• Ovarian cancer • Non-small cell lung cancer • Metastatic breast cancer	• Not reported
Panitumumab (Recombinant)	• Metastatic colorectal cancer	• Metastatic colorectal cancer
Panitumumab (Recombinant)	• Melanoma • Non-small cell lung cancer • Head and Neck Squamous Cell Cancer • Classical Hodgkin Lymphoma • Primary mediastinal B-Cell Lymphoma • Urothelial carcinoma • Microsatellite instability-high or mismatch repair deficient cancer • Endometrial carcinoma • Renal Cell Carcinoma	• Unresectable Stage III or Stage IV malignant melanoma • Resected Stage IIIB, Stage IIIC or Stage IIID malignant melanoma • Relapsed or Refractory Hodgkin lymphoma • Stage IV (metastatic) non-small cell lung cancer • Locally advanced (Stage III) or metastatic (Stage IV) urothelial cancer • Relapsed or refractory primary mediastinal B-cell lymphoma
Pemetrexed (Disodium)	• Malignant Pleural Mesothelioma • Non-Small Cell Lung Cancer	• Not reported
Pralatrexate	• Treatment of adult patients with peripheral T-cell lymphoma	• Relapsed or chemotherapy refractory Peripheral T-cell Lymphoma
Raltitrexed	• Palliative treatment of advanced colorectal cancer	• Advanced colorectal cancer
Topotecan (Hydrochloride)	• Small cell lung carcinoma • Metastatic carcinoma of the ovary • Histologically confirmed Stage IV-B, recurrent, or persistent carcinoma of the cervix (in combination with cisplatin)	• Not reported
Vinblastine (Sulfate)	• Treatment of Hodgkin’s Disease (in combination) • Treatment of advanced testicular carcinoma (in combination) • Palliative treatment of lymphocytic lymphoma, histiocytic lymphoma, advanced stages of mycosis fungoides, Kaposi's sarcoma and Histiocytosis X • Treatment of choriocarcinoma and carcinoma of the breast • Advanced testicular germ-cell cancers (in combination)	• Not reported

Drug	*TGA indication*	*PBS indication*
Vincristine (Sulfate)	• Treatment of acute leukaemia • Treatment of Hodgkin's disease, non-Hodgkin's malignant lymphomas, rhabdomyosarcoma, neuroblastoma, Wilm's tumour, osteogenic sarcoma, mycosis fungoides, Ewing's sarcoma, carcinoma of the uterine cervix, breast cancer, malignant melanoma, oat-cell carcinoma of the lung and gynaecological tumours of childhood (in combination)	• Not reported
Vinorelbine (Bitartrate)	• Treatment of advanced breast cancer • Treatment for advanced non-small cell lung cancer	• Advanced breast cancer • Locally advanced or metastatic non-small cell lung cancer

Table A44. EFC medicines excluded from the analysis (TGA indication is broader than the PBS indication)

Drug	*TGA indication*	*PBS indication*
Atezolizumab (Recombinant)	• Non-small cell lung cancer • Small cell lung cancer • Urothelial carcinoma • Triple-negative breast cancer • Hepatocellular carcinoma	• Non-small cell lung cancer • Small cell lung cancer • Hepatocellular carcinoma
Avelumab (Recombinant)	• Metastatic Merkel cell carcinoma • Urothelial carcinoma • Advanced renal cell carcinoma *(in combination with axitinib)*	• Metastatic Merkel cell carcinoma (stage IV)
Bleomycin (Sulfate)	• Squamous cell carcinoma of the skin, head and neck and oesophagus • Squamous cell carcinoma of the penis, larynx and uterine cervix • Choriocarcinoma and embryonal cell carcinoma of the testis • Advanced Hodgkin's disease and in some cases of other lymphomas	• Germ cell neoplasms
Fluorouracil (Sodium Salt)	• Not applicable	• Not applicable
Pertuzumab (Recombinant)	• Early Breast Cancer • Metastatic Breast Cancer	• Metastatic (Stage IV) HER2 positive breast cancer

Table A45. EFC medicines excluded from the analysis (listing of IV formulation on multiple sections of the PBS)

Drug	*TGA indication*	*PBS indication*
Doxorubicin (Hydrochloride) – Pegylated	• Advanced epithelial ovarian cancer • AIDS-related Kaposi's sarcoma • Metastatic breast cancer	• Advanced epithelial ovarian cancer • Metastatic breast cancer
Methotrexate	• Breast cancer and gestational choriocarcinoma • Non-Hodgkin's lymphoma	• Severe active rheumatoid arthritis • Severe psoriasis

Drug	*TGA indication*	*PBS indication*
	• Leukemia advanced stages (III and IV, Peters Staging System) of lymphosarcoma • Osteogenic sarcoma, acute leukaemia, bronchogenic carcinoma and epidermoid carcinoma of the head and neck (high dose) • Severe psoriasis and severe rheumatoid arthritis	
Methotrexate (Disodium)	• Not applicable	• Not applicable
Rituximab (Recombinant)	• Non-Hodgkin's Lymphoma • Chronic Lymphocytic Leukaemia • Rheumatoid Arthritis • Granulomatosis with polyangiitis (Wegener's) and Microscopic polyangiitis	• Previously untreated or relapsed/refractory CD20 positive lymphoid cancer • Previously untreated or relapsed/refractory CD20 positive acute lymphoblastic leukaemia • Relapsed or refractory Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma • Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma • Severe active granulomatosis with polyangiitis (Wegeners granulomatosis) • Severe active microscopic polyangiitis
Trastuzumab Emtansine (Recombinant)	• Metastatic breast cancer • Early breast cancer • Locally Advanced Breast Cancer • Advanced Gastric Cancer	• Metastatic (Stage IV) HER2 positive breast cancer • Early HER2 positive breast cancer
Trastuzumab (Recombinant)	• Metastatic breast cancer • Early breast cancer • Locally Advanced Breast Cancer • Advanced Gastric Cancer	• Metastatic (Stage IV) HER2 positive breast cancer • Early HER2 positive breast cancer • Metastatic (Stage IV) HER2 positive adenocarcinoma of the stomach or gastro-oesophageal junction

The period of analysis was restricted to January 2016 and December 2020, with data extracted in June 2021.

DAEN

The TGA's DAEN is a publicly available database that contains AE reports, medication error reports and product quality complaints resulting in AEs that were submitted to the TGA. The database is designed to support the TGA's post-marketing safety surveillance program for medicines. AEs and medication errors in the database are coded using terms in the Medical Dictionary for Regulatory Activities (MedRA) [49].

There are a number of limitations to the DAEN and its use:

- there is no certainty that the reported event was due to the medicine. The TGA does not require that a causal relationship between medicine and event be proven, and reports do not always contain enough detail to properly evaluate an event [49].
- the TGA does not receive reports for every AE or medication error that occurs with a product [49].
- there are duplicate reports of events within the database, where the same event may have been reported separately by a consumer and by the sponsor.

For these reasons, the DAEN data cannot be used to calculate the incidence of an adverse event or medication error in the Australian population [49].

Method of statistical analysis

Disproportionality analysis was used to identify medicines with higher or lower than expected rates of off-label use (as defined in Table A46). This method is commonly used in pharmacovigilance studies and by medicines authorities (such as the World Health Organisation, the Food and Drug Administration, the European Medicines Agency and the TGA) to identify or confirm a suspected adverse event [70]. Calculations of measures of disproportionality are based upon a two-by-two contingency table (see Table A46).

Table A46. Example of calculating the reporting odds ratio using disproportionality analysis

Drug AE	*Drug of interest*	*Other drugs*	*Total*
AE of interest	DE	dE	E
Other AEs	De	de	e
Total	D	d	N

Source: [70d70f]
Abbreviations: AE, adverse event; D, the number of adverse events reported for the drug of interest; E, the total number times the adverse event occurred; DE, both the drug of interest was used and the event of interest occurred; de, neither the drug of interest was used nor the event occurred; dE, the drug was not used but the event occurred; the drug was used but the event did not occur; E, sum of the events of interest that occurred; e, sum of other events that occurred; N, total number events that occurred

From these data, a reporting odds ratio (ROR) may be calculated using the following formula [70d70f]:

$$ROR = \frac{DE\ x\ de}{dE\ x\ De}$$

A ROR ≥ 2 indicates a clinically significant higher-than-expected rate of reported off-label use in a given year [70d70f]. A ROR ≤ 0.25 indicates a clinically significant, lower-than-expected rate of

reported off-label use in a given year[70d70f]. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is in range with expectations [70d70f]. To account for clustering that can occur with repeated measures data, logistic regression with clustering on the case ID was employed. As drugs other than the drug of interest could be causing the AE, this was included as a fixed effect in the analysis.

Results

The extracted data comprised 6,268 unique case reports of AEs involving at least one EFC-listed medicine. Given that cancer patients often receive a combination regimen (for example, carfilzomib is typically given in combination with dexamethasone for multiple myeloma), some of the spontaneous AE reports involved more than one EFC-medicine. This resulted in a total of 8,899 unique case reports of AEs and EFC-medicine combinations (hereby referred to as instances). Hence, the data had a repeated measures design.

Off-label Use

Of the 8,899 instances reported, 931 contained MedRA search terms that were suggestive of off-label use and/or medication errors (see Table A47). These search terms were further defined into deliberate off-label use (96%, N = 891/931) and non-deliberate / unclear off-label use (4%, N = 50/931). The list of MedRA search terms was verified by a clinical expert.

Table A47. Reported off-label use of EFC-listed drugs by adverse event type (2016 - 2020)

MedRA Search Term	*Deliberate*	*Non-deliberate/ unclear*	*Total*
Accidental overdose	-	2 (5%)	2 (<1%)
Drug effective for an unapproved indication	2 (<1%)	-	2 (<1%)
Drug ineffective for an unapproved indication	8 (1%)	-	8 (1%)
Drug monitoring procedure incorrectly performed	-	3 (8%)	3 (<1%)
Inappropriate schedule of product administration	12 (1%)	-	12 (1%)
Incorrect dose administered	-	3 (8%)	3 (<1%)
Incorrect drug administration rate	-	3 (8%)	3 (<1%)
Incorrect product administration duration	-	1 (3%)	1 (<1%)
Incorrect route of product administration	-	9 (23%)	9 (1%)
Intentional product misuse	1 (<1%)	-	1 (<1%)
Intentional product use issue	117 (13%)	-	117 (13%)
Intercepted drug administration error	-	1 (3%)	1 (<1%)
Off label use	441 (49%)	-	441 (47%)
Prescribed overdose	2 (<1%)	-	2 (<1%)
Prescribed underdose	5 (1%)	-	5 (1%)
Product administered to the patient of inappropriate age	3 (<1%)	-	3 (<1%)
Product administration error	-	1 (3%)	1 (<1%)

MedRA Search Term	*Deliberate*	*Non-deliberate/ unclear*	*Total*
Product dose omission issue	-	7 (18%)	7 (1%)
Product storage error	-	6 (15%)	6 (1%)
Product use in	1 (<1%)	-	1 (<1%)
Product use is unapproved in	1 (<1%)	-	1 (<1%)
Product use in an unapproved indication	241 (27%)	-	241 (26%)
Product use issue	56 (6%)	-	56 (6%)
Product used for unknown indication	1 (<1%)	-	1 (<1%)
Wrong product administered	-	2 (5%)	2 (<1%)
Wrong technique in the product usage process	-	2 (5%)	2 (<1%)
Total	*891 (100%)*	*40 (100%)*	*931 (100%)*

Source: Developed for this Review using data from the DAEN.
Abbreviations: EFC, Efficient Funding of Chemotherapy; MedRA, Medical Dictionary for Regulatory Activities

Almost all of the reported instances of off-label use were characterised as 'deliberate' (99%, N = 891/931) (see Table A48).

Table A48. Off-label use (deliberate, non-deliberate/unclear) of EFC-listed drugs (2016 - 2020)

Category	Number (%)
Uniquely identified cases	6,268
Instances†	8,899
Instances associated with off-label use	931 (10%)
Deliberate	891 (10%)
Non-deliberate/unclear	40 (<1%)
Other adverse event reported	7,968 (90%)

Source: Developed for this Review using data from the DAEN.
Abbreviations: EFC, Efficient Funding of Chemotherapy.

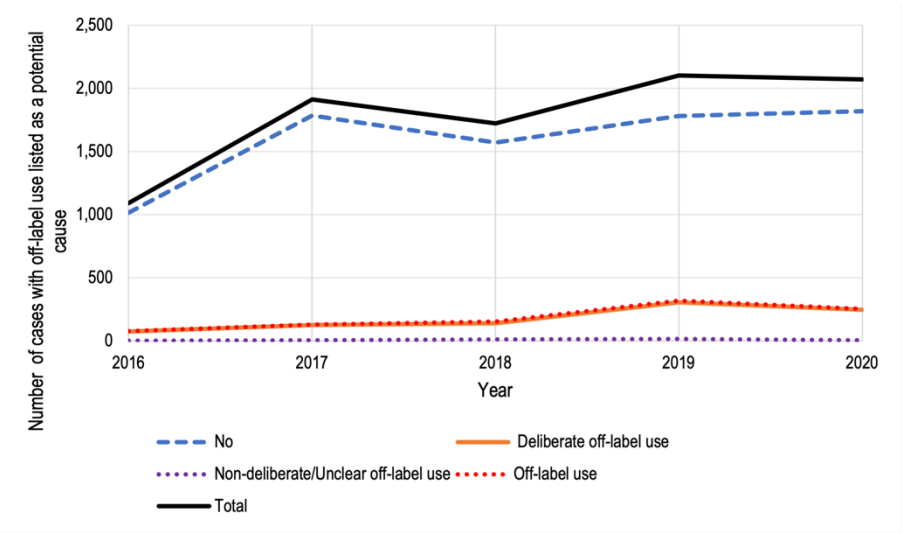
A breakdown of instances of off-label use by year reveals an apparent spike in the proportion of reported off-label use in 2019 (see Table A49). As in the aggregate, the vast majority of each year's reported off-label use may be considered deliberate. Overall, the number of reported instances of off-label use has increased since 2016 (see Figure A57).

Table A49. Off-label use by year (2016-2020)

Year	*Off-label use*	*Deliberate*	*Non-deliberate /unclear*	*Other adverse events*	*Total*
2016	76 (7%)	74 (7%)	2 (0%)	1014 (93%)	1090 (100%)
2017	130 (7%)	125 (7%)	5 (0%)	1783 (93%)	1913 (100%)
2018	153 (9%)	141 (8%)	12 (1%)	1570 (91%)	1723 (100%)
2019	320 (15%)	304 (14%)	16 (1%)	1781 (85%)	2101 (100%)
2020	252 (12%)	247 (12%)	5 (0%)	1820 (88%)	2072 (100%)
Total	931 (10%)	891 (10%)	40 (0%)	7968 (90%)	8899 (100%)

Source: Developed for this Review using data from the DAEN.

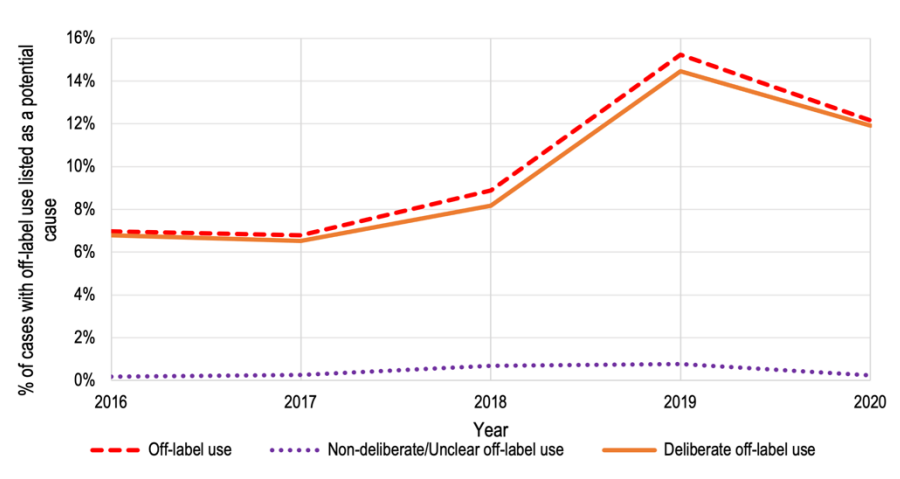
Figure A57. Reported cases of off-label use by year (2016 - 2020)



Source: Developed for this Review using DAEN data.

The annual proportion of cases associated with off-label use is summarised in Figure A58, showing an increase in the proportion of AE associated with off-label use in 2019.

Figure A58. The proportion of reported adverse events associated with off-label use (2016-2020)



Source: Developed for this Review using DAEN data.

Disproportionality analysis: Off-label use by year (exposure)

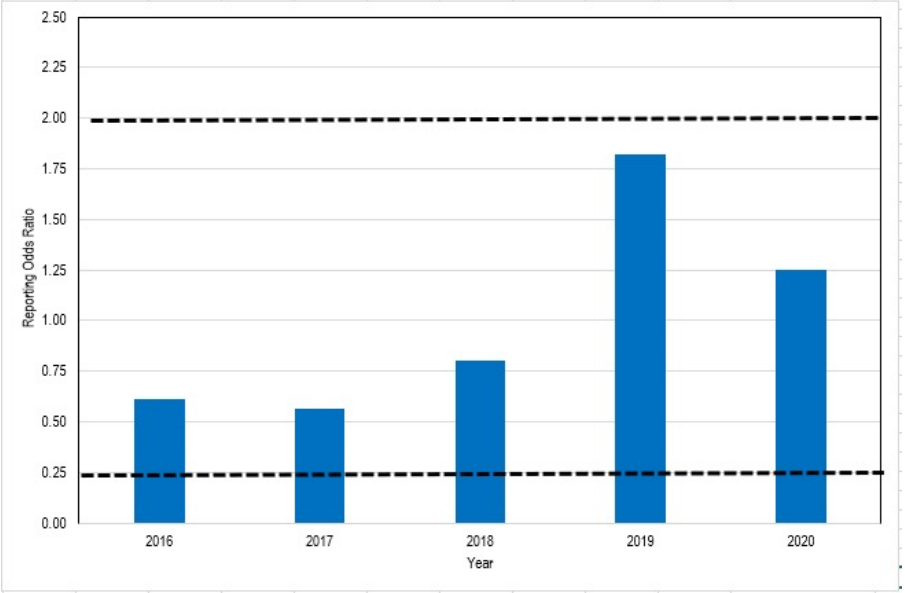
A disproportionality analysis was undertaken to examine clinically significant between-year differences in the reporting of off-label use in the period 2016-2020. As shown by the results in Table A50 and Figure A59, there was a statistically significant decrease in the rate of reported off-label use in 2016 and 2017 and a statistically significant increase in the rate of off-label use in 2019. However, the ROR did not cross the bounds for disproportionality (i.e. ≤ 0.25 or ≥ 2.00) for either year. This suggested there was no clinically significant change in the rates of off-label over the timeframe.

Table A50. Disproportionality analysis: off-label use by year (2016 - 2020)

Year	*ROR (95% CI)*	*p-value*
2016	0.61 (0.43, 0.86)	0.01*
2017	0.56 (0.42, 0.75)	0.00*
2018	0.80 (0.60, 1.07)	0.13
2019	1.82 (1.41, 2.35)	0.00*
2020	1.25 (0.93, 1.69)	0.13

Source: Developed for this Review using DAEN data.
Abbreviations: CI, confidence interval; ROR, reporting odds ratio.
Notes: * indicates a result is statistically significant at p-value ≤ 0.05; A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use in a given year. A ROR ≤ 0.25 indicates a clinically significant lower-than-*expected rate of reported off-label use in a given year. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other years; Ordinary least squares (OLS) regression was used with clustering on the case ID as the data was not clustered.*

Figure A59. Disproportionality analysis: reporting odds ratio of off-label use by year (2016 - 2020)



Source: Developed for this Review using DAEN data.
Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use in a given year. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use in a given year. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other years

Reported off-label use by drug (exposure) for the period 2016-2020

Disproportionality analysis was also undertaken to assess whether there was clinically significant higher or lower-than-expected reporting of off-label use for each EFC-listed drug relative to all other EFC-listed drugs in the period 2016-2020 (see Table A51).

Table A51. Disproportionality analysis: reported off-label use by EFC-listed drug (2016 - 2020)

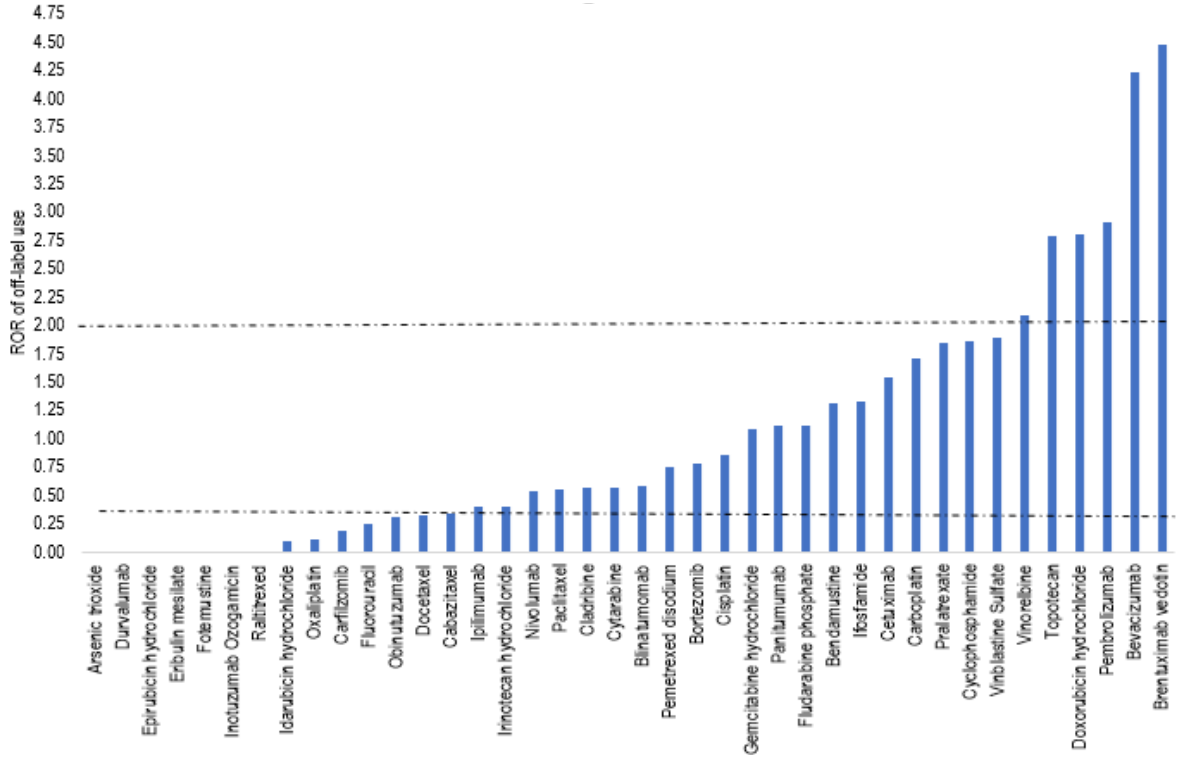
Drug	*Off-label use*	*Other Adverse Events*	*Total*	*Reporting Odds Ratio (95% CI)*
Arsenic trioxide	0 (0%)	19 (100%)	19 (100%)	0 (0, 0)
Bendamustine	15 (13%)	98 (87%)	113 (100%)	1.32 (0.64, 2.69)
Bevacizumab	112 (31%)	249 (69%)	361 (100%)	4.24 (3.19, 5.63) **
Blinatumomab	6 (6%)	87 (94%)	93 (100%)	0.59 (0.25, 1.36)
Bortezomib	36 (8%)	389 (92%)	425 (100%)	0.78 (0.49, 1.24)
Brentuximab vedotin	17 (34%)	33 (66%)	50 (100%)	4.47 (2.46, 8.13) **
Cabazitaxel	1 (4%)	25 (96%)	26 (100%)	0.34 (0.05, 2.53)
Carboplatin	65 (16%)	335 (84%)	400 (100%)	1.71 (1.26, 2.32) **
Carfilzomib	6 (2%)	272 (98%)	278 (100%)	0.18 (0.08, 0.42) **
Cetuximab	21 (15%)	118 (85%)	139 (100%)	1.54 (0.93, 2.52)
Cisplatin	18 (9%)	179 (91%)	197 (100%)	0.86 (0.5, 1.46)
Cladribine	8 (6%)	119 (94%)	127 (100%)	0.57 (0.26, 1.28)
Cyclophosphamide	114 (17%)	557 (83%)	671 (100%)	1.86 (1.47, 2.35) **
Cytarabine	23 (6%)	336 (94%)	359 (100%)	0.58 (0.37, 0.9) *
Docetaxel	14 (4%)	350 (96%)	364 (100%)	0.33 (0.19, 0.57) **

Drug	*Off-label use*	*Other Adverse Events*	*Total*	*Reporting Odds Ratio (95% CI)*
Doxorubicin hydrochloride	118 (23%)	391 (77%)	509 (100%)	2.81 (2.19, 3.61) **
Durvalumab	0 (0%)	127 (100%)	127 (100%)	0 (0, 0)
Epirubicin hydrochloride	0 (0%)	39 (100%)	39 (100%)	0 (0, 0)
Eribulin mesilate	0 (0%)	18 (100%)	18 (100%)	0 (0, 0)
Fludarabine phosphate	19 (12%)	145 (88%)	164 (100%)	1.12 (0.64, 1.97)
Fluorouracil	7 (3%)	236 (97%)	243 (100%)	0.25 (0.11, 0.58) **
Fotemustine	0 (0%)	1 (100%)	1 (100%)	0 (0, 0)
Gemcitabine hydrochloride	15 (11%)	119 (89%)	134 (100%)	1.08 (0.56, 2.09)
Idarubicin hydrochloride	3 (1%)	249 (99%)	252 (100%)	0.1 (0.03, 0.31) **
Ifosfamide	14 (13%)	90 (87%)	104 (100%)	1.34 (0.71, 2.53)
Inotuzumab Ozogamicin	0 (0%)	9 (100%)	9 (100%)	0 (0, 0)
Ipilimumab	23 (5%)	470 (95%)	493 (100%)	0.4 (0.26, 0.62) **
Irinotecan hydrochloride	10 (7%)	133 (93%)	143 (100%)	0.41 (0.06, 3)
Nivolumab	69 (6%)	1031 (94%)	1100 (100%)	0.54 (0.41, 0.71) **
Obinutuzumab	5 (3%)	143 (97%)	148 (100%)	0.31 (0.11, 0.87) *
Oxaliplatin	5 (1%)	403 (99%)	408 (100%)	0.12 (0.05, 0.3) **
Paclitaxel	46 (6%)	710 (94%)	756 (100%)	0.55 (0.38, 0.8) **
Panitumumab	6 (12%)	45 (88%)	51 (100%)	1.11 (0.38, 3.25)
Pembrolizumab	115 (25%)	342 (75%)	457 (100%)	2.92 (2.3, 3.69) **
Pemetrexed disodium	3 (8%)	33 (92%)	36 (100%)	0.76 (0.23, 2.47)
Pralatrexate	2 (18%)	9 (82%)	11 (100%)	1.85 (0.24, 14.28)
Raltitrexed	0 (0%)	1 (100%)	1 (100%)	0 (0, 0)
Topotecan	4 (25%)	12 (75%)	16 (100%)	2.78 (0.54, 14.38)
Vinblastine Sulfate	5 (19%)	22 (81%)	27 (100%)	1.90 (0.62, 5.8)
Vinorelbine	6 (20%)	24 (80%)	30 (100%)	2.09 (0.7, 6.2)

Source: Developed for this Review using DAEN data.
Abbreviations: CI, confidence interval; ROR, reporting odds ratio
Notes: * indicates a result is statistically significant at p-value ≤ 0.05; ** statistically significant at p-value ≤ 0.01.

As shown in Table A51 and Figure A60, the drugs (1) brentuximab vedotin, (2) bevacizumab, (3) doxorubicin hydrochloride, (5) pembrolizumab, (6) topotecan, and (7) vinorelbine had potentially clinically significant, higher-than-expected rates of reported off-label use relative to other EFC-listed drugs in the period 2016-2020 (ROR ≥ 2). In the same period, the drugs: (1) arsenic (trioxide), (2) durvalumab (3) epirubicin hydrochloride, (4) eribulin mesilate, (5) fotemustine, (6) inotuzumab ozogamicin, (7) raltitrexed, (8) idarubicin hydrochloride, (9) oxaliplatin, (10) carfilzomib, and (11) fluorouracil had potentially clinically significant, lower-than-expected rates of reported off-label use relative to other EFC-listed drugs (ROR ≤ 0.25).

Figure A60. Disproportionality analysis: reported off-label use by EFC-listed drug (2016 - 2020)



Source: Developed for this Review using DAEN data.
Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use for a given drug. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use for a given drug. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other drugs.

When the rates of off-label use for EFC-drugs was examined by the year of reporting, substantial variation in rates of off-label use was observed between years (see Table A52 and Figure A61).

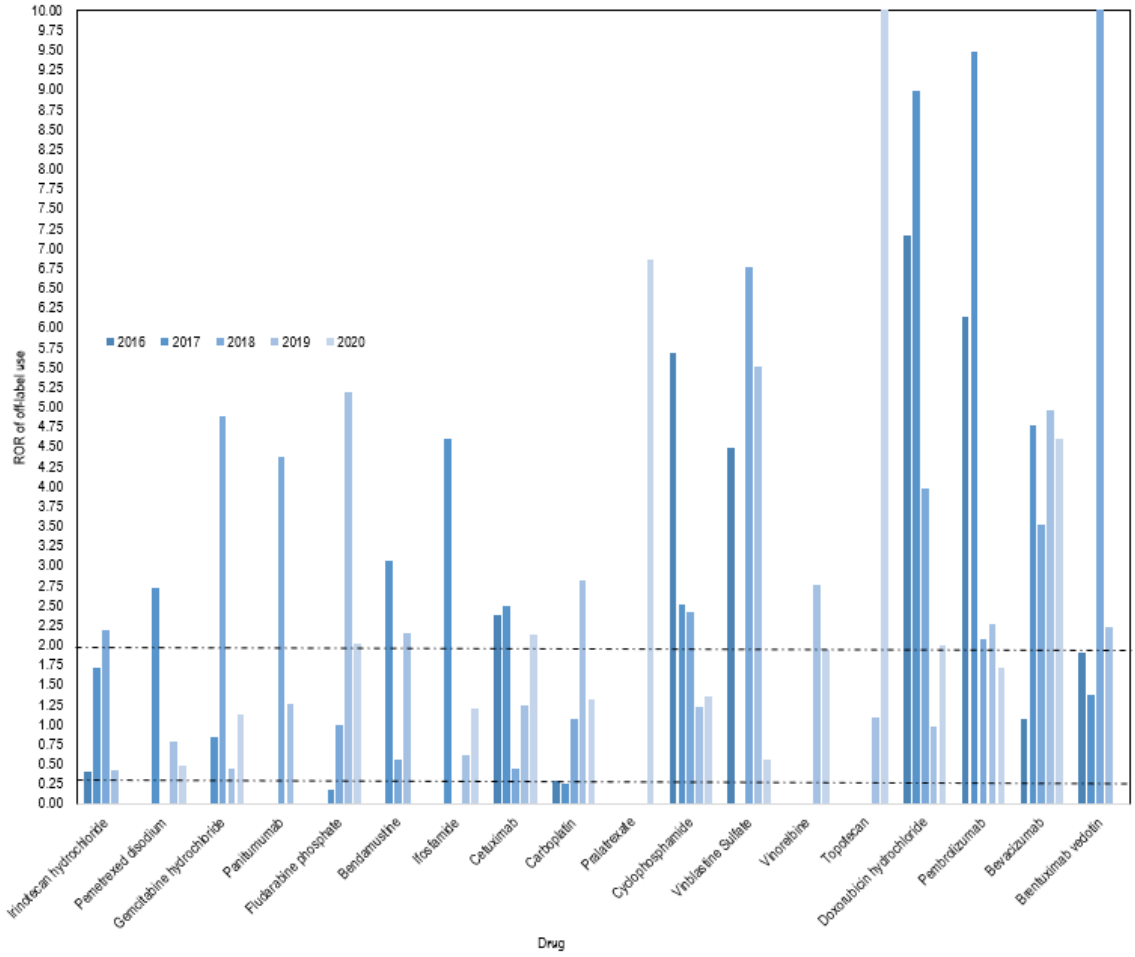
Table A52. Disproportionality analysis: reported off-label use by EFC-listed drug and year (2016 - 2020)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
Arsenic trioxide	N = 2, 0 (0, 0)	N = 0, 0 (0, 0)	N = 5, 0 (0, 0)	N = 5, 0 (0, 0)	N = 7, 0 (0, 0)
Bendamustine	N = 10, 0 (0, 0)	N = 28, 3.06 (0.86, 10.91)	N = 38, 0.56 (0.13, 2.4)	N = 29, 2.15 (0.72, 6.39)	N = 8, 0 (0, 0)
Bevacizumab	N = 54, 1.07 (0.37, 3.13)	N = 58, 4.77 (2.27, 10) **	N = 49, 3.53 (1.52, 8.17) **	N = 124, 4.96 (3.3, 7.47) **	N = 76, 4.61 (2.45, 8.68) **
Blinatumomab	N = 15, 0 (0, 0)	N = 12, 0 (0, 0)	N = 27, 1.29 (0.38, 4.4)	N = 19, 1.04 (0.3, 3.65)	N = 20, 0 (0, 0)
Bortezomib	N = 26, 1.11 (0.15, 8.48)	N = 98, 0.27 (0.04, 2)	N = 105, 0.72 (0.25, 2.07)	N = 98, 1.09 (0.53, 2.24)	N = 98, 0.72 (0.3, 1.75)
Brentuximab vedotin	N = 8, 1.92 (0.23, 16.02)	N = 11, 1.37 (0.17, 10.91)	N = 22, 16.11 (6.6, 39.31) **	N = 7, 2.23 (0.43, 11.67)	N = 2, 0 (0, 0)
Cabazitaxel	N = 1, 0 (0, 0)	N = 6, 0 (0, 0)	N = 13, 0.85 (0.11, 6.59)	N = 3, 0 (0, 0)	N = 3, 0 (0, 0)
Carboplatin	N = 45, 0.29 (0.04, 2.14)	N = 54, 0.25 (0.03, 1.83)	N = 63, 1.08 (0.41, 2.83)	N = 126, 2.82 (1.89, 4.2) **	N = 112, 1.31 (0.74, 2.34)
Carfilzomib	N = 11, 0 (0, 0)	N = 81, 0.17 (0.02, 1.21)	N = 78, 0.4 (0.12, 1.3)	N = 53, 0.21 (0.05, 0.89) *	N = 55, 0 (0, 0)
Cetuximab	N = 27, 2.39 (0.8, 7.2)	N = 33, 2.51 (0.95, 6.63)	N = 24, 0.44 (0.06, 3.33)	N = 33, 1.24 (0.45, 3.45)	N = 22, 2.15 (0.77, 6.02)
Cisplatin	N = 27, 0.51 (0.07, 3.55)	N = 41, 0 (0, 0)	N = 29, 1.66 (0.58, 4.76)	N = 38, 0.84 (0.33, 2.14)	N = 62, 1.07 (0.43, 2.7)
Cladribine	N = 4, 0 (0, 0)	N = 0, 0 (0, 0)	N = 14, 0 (0, 0)	N = 50, 0.61 (0.24, 1.58)	N = 59, 0.38 (0.08, 1.72)
Cyclophosphamide	N = 57, 5.69 (3.07, 10.56) **	N = 125, 2.52 (1.45, 4.38) **	N = 106, 2.42 (1.34, 4.37) **	N = 129, 1.22 (0.72, 2.08)	N = 254, 1.37 (0.93, 2.02)
Cytarabine	N = 14, 0 (0, 0)	N = 181, 0.07 (0.01, 0.49) **	N = 31, 0.7 (0.17, 2.91)	N = 58, 0.89 (0.43, 1.85)	N = 75, 1.39 (0.72, 2.71)
Docetaxel	N = 68, 0 (0, 0)	N = 80, 0 (0, 0)	N = 75, 0.57 (0.2, 1.57)	N = 82, 0.51 (0.23, 1.14)	N = 59, 0.38 (0.12, 1.23)
Doxorubicin	N = 45, 7.16 (3.68, 13.95) **	N = 71, 8.99 (5.16, 15.66) **	N = 73, 3.98 (2.19, 7.23) **	N = 87, 0.98 (0.48, 1.98)	N = 233, 2.01 (1.35, 3.01) **
Durvalumab	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 24, 0 (0, 0)	N = 57, 0 (0, 0)	N = 46, 0 (0, 0)
Epirubicin	N = 4, 0 (0, 0)	N = 12, 0 (0, 0)	N = 3, 0 (0, 0)	N = 7, 0 (0, 0)	N = 13, 0 (0, 0)
Eribulin	N = 1, 0 (0, 0)	N = 3, 0 (0, 0)	N = 1, 0 (0, 0)	N = 7, 0 (0, 0)	N = 6, 0 (0, 0)
Fludarabine	N = 10, 0 (0, 0)	N = 76, 0.18 (0.02, 1.29)	N = 34, 0.99 (0.3, 3.24)	N = 21, 5.19 (1.87, 14.4) **	N = 23, 2.03 (0.74, 5.54)
Fluorouracil	N = 27, 0 (0, 0)	N = 53, 0 (0, 0)	N = 27, 0.39 (0.05, 2.81)	N = 64, 0.27 (0.08, 0.85) *	N = 72, 0.31 (0.07, 1.35)
Fotemustine	N = 1, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)
Gemcitabine	N = 21, 0 (0, 0)	N = 17, 0.86 (0.12, 6.36)	N = 19, 4.89 (1.6, 14.97) **	N = 40, 0.45 (0.1, 1.99)	N = 37, 1.13 (0.36, 3.59)
Idarubicin	N = 3, 0 (0, 0)	N = 184, 0 (0, 0)	N = 33, 0 (0, 0)	N = 8, 0.79 (0.1, 6.38)	N = 24, 0.65 (0.15, 2.79)
Ifosfamide	N = 2, 0 (0, 0)	N = 4, 4.6 (0.48, 43.68)	N = 6, 0 (0, 0)	N = 50, 0.61 (0.24, 1.53)	N = 42, 1.21 (0.41, 3.6)
Inotuzumab Ozogamicin	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 3, 0 (0, 0)	N = 6, 0 (0, 0)	N = 0, 0 (0, 0)
Ipilimumab	N = 55, 0.24 (0.03, 1.72)	N = 105, 0 (0, 0)	N = 126, 0.24 (0.07, 0.74) *	N = 112, 0.36 (0.16, 0.78)	N = 95, 1.05 (0.55, 1.99)
Irinotecan	N = 33, 0.41 (0.06, 3)	N = 18, 1.73 (0.4, 7.5)	N = 23, 2.19 (0.62, 7.8)	N = 42, 0.42 (0.1, 1.88)	N = 27, 0 (0, 0)
Nivolumab	N = 183, 0.26 (0.09, 0.73) *	N = 187, 0.59 (0.26, 1.35)	N = 253, 0.3 (0.14, 0.63) **	N = 267, 0.49 (0.3, 0.78) **	N = 210, 1.02 (0.62, 1.68)
Obinutuzumab	N = 26, 1.77 (0.51, 6.18)	N = 42, 0.68 (0.1, 4.7)	N = 29, 0.68 (0.1, 4.7)	N = 24, 0 (0, 0)	N = 27, 0 (0, 0)
Oxaliplatin	N = 73, 0 (0, 0)	N = 73, 0 (0, 0)	N = 59, 0.34 (0.08, 1.4)	N = 105, 0.1 (0.02, 0.41) **	N = 98, 0.14 (0.02, 0.98) *
Paclitaxel	N = 128, 0 (0, 0)	N = 113, 0.11 (0.02, 0.82) *	N = 152, 0 (0, 0)	N = 206, 1.13 (0.74, 1.72)	N = 157, 0.59 (0.29, 1.23)
Panitumumab	N = 14, 0 (0, 0)	N = 6, 0 (0, 0)	N = 10, 4.37 (0.85, 22.46)	N = 16, 1.27 (0.27, 6.04)	N = 5, 0 (0, 0)
Pembrolizumab	N = 85, 6.15 (3.23, 11.69) **	N = 119, 9.48 (5.73, 15.7) **	N = 150, 2.08 (1.25, 3.45) **	N = 103, 2.27 (1.36, 3.78) **	N = 107, 1.72 (0.97, 3.04)
Pemetrexed	N = 0, 0 (0, 0)	N = 6, 2.74 (0.32, 23.75)	N = 7, 0 (0, 0)	N = 8, 0.78 (0.1, 6.36)	N = 15, 0.49 (0.06, 3.72)

Drug	*2016*	*2017*	*2018*	*2019*	*2020*
Pralatrexate	N = 0, 0 (0, 0)	N = 3, 0 (0, 0)	N = 1, 0 (0, 0)	N = 3, 0 (0, 0)	N = 4, 6.86 (0.67, 70.61)
Raltitrexed	N = 1, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)	N = 0, 0 (0, 0)
Topotecan	N = 2, 0 (0, 0)	N = 0, 0 (0, 0)	N = 4, 0 (0, 0)	N = 6, 1.1 (0.13, 9.45)	N = 4, 20.66 (1.32, 324.08) *
Vinblastine Sulfate	N = 4, 4.49 (0.48, 42.26)	N = 3, 0 (0, 0)	N = 5, 6.77 (0.71, 64.58)	N = 2, 5.51 (0.34, 87.97)	N = 13, 0.57 (0.07, 4.39)
Vinorelbine	N = 3, 0 (0, 0)	N = 10, 0 (0, 0)	N = 2, 0 (0, 0)	N = 6, 2.76 (0.5, 15.15)	N = 9, 1.95 (0.26, 14.63)

Source: Developed for this Review using DAEN data.
Abbreviation: CI, confidence interval; N, number of instances; ROR, reporting odds ratio.
Notes: * indicates statistically significant at p-value ≤ 0.05; ** statistically significant at p-value ≤ 0.01.

Figure A61. Subset of EFC-drugs with disproportionally high rates of off-label use in any year



Source: Developed for this Review using DAEN data.

Note: Dotted lines indicate the bounds for clinical significance. A ROR ≥ 2 indicates a clinically significant, higher-than-expected rate of reported off-label use for a given drug. A ROR ≤ 0.25 indicates a clinically significant lower-than-expected rate of reported off-label use for a given drug. A ROR between 0.25 and 2 indicates a rate of reported off-label use that is proportionally consistent with all other drugs.

Impact of EFC-listing on off-label use

The descriptive statistics for off-label use before and after the EFC listing of cancer medicines is presented in Table A53.

Table A53. Off-label-use after EFC-listing and before EFC-listing

	EFC-Listed			*Not EFC-listed*		
Drug	*No*	*Off-label*	*Total*	*No*	*Off-label*	*Total*
Arsenic (Trioxide)	18 (100%)	0 (0%)	18 (100%)	1 (100%)	0 (0%)	1 (100%)
Bendamustine	98 (87%)	15 (13%)	113 (100%)	0 (0%)	0 (0%)	0 (0%)
Bevacizumab	249 (69%)	113 (31%)	362 (100%)	0 (0%)	0 (0%)	0 (0%)
Blinatumomab	66 (90%)	7 (10%)	73 (100%)	21 (100%)	0 (0%)	21 (100%)
Bortezomib	389 (92%)	36 (8%)	425 (100%)	0 (0%)	0 (0%)	0 (0%)
Brentuximab vedotin	33 (66%)	17 (34%)	50 (100%)	0 (0%)	0 (0%)	0 (0%)
Cabazitaxel	25 (96%)	1 (4%)	26 (100%)	0 (0%)	0 (0%)	0 (0%)
Carboplatin	335 (84%)	66 (16%)	401 (100%)	0 (0%)	0 (0%)	0 (0%)
Carfilzomib	181 (97%)	5 (3%)	186 (100%)	91 (99%)	1 (1%)	92 (100%)
Cetuximab	118 (85%)	21 (15%)	139 (100%)	0 (0%)	0 (0%)	0 (0%)
Cisplatin	178 (90%)	20 (10%)	198 (100%)	0 (0%)	0 (0%)	0 (0%)
Cladribine	117 (92%)	10 (8%)	127 (100%)	0 (0%)	0 (0%)	0 (0%)
Cyclophosphamide	557 (83%)	114 (17%)	671 (100%)	0 (0%)	0 (0%)	0 (0%)
Cytarabine	336 (94%)	23 (6%)	359 (100%)	0 (0%)	0 (0%)	0 (0%)
Docetaxel	350 (96%)	14 (4%)	364 (100%)	0 (0%)	0 (0%)	0 (0%)
Doxorubicin	391 (77%)	118 (23%)	509 (100%)	0 (0%)	0 (0%)	0 (0%)
Durvalumab	39 (100%)	0 (0%)	39 (100%)	88 (100%)	0 (0%)	88 (100%)
Epirubicin	39 (100%)	0 (0%)	39 (100%)	0 (0%)	0 (0%)	0 (0%)
Eribulin mesilate	18 (100%)	0 (0%)	18 (100%)	0 (0%)	0 (0%)	0 (0%)
Fludarabine phosphate	145 (88%)	19 (12%)	164 (100%)	0 (0%)	0 (0%)	0 (0%)
Fluorouracil	234 (96%)	9 (4%)	243 (100%)	0 (0%)	0 (0%)	0 (0%)
Fotemustine	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Gemcitabine	119 (89%)	15 (11%)	134 (100%)	0 (0%)	0 (0%)	0 (0%)
Idarubicin	249 (99%)	3 (1%)	252 (100%)	0 (0%)	0 (0%)	0 (0%)
Ifosfamide	90 (87%)	14 (13%)	104 (100%)	0 (0%)	0 (0%)	0 (0%)
Inotuzumab Ozogamicin	3 (100%)	0 (0%)	3 (100%)	6 (100%)	0 (0%)	6 (100%)
Ipilimumab	470 (95%)	23 (5%)	493 (100%)	0 (0%)	0 (0%)	0 (0%)
Irinotecan	133 (93%)	10 (7%)	143 (100%)	0 (0%)	0 (0%)	0 (0%)
Nivolumab	1002 (93%)	70 (7%)	1072 (100%)	29 (100%)	0 (0%)	29 (100%)
Obinutuzumab	143 (97%)	5 (3%)	148 (100%)	0 (0%)	0 (0%)	0 (0%)
Oxaliplatin	402 (99%)	6 (1%)	408 (100%)	0 (0%)	0 (0%)	0 (0%)
Paclitaxel	709 (94%)	49 (6%)	758 (100%)	0 (0%)	0 (0%)	0 (0%)
Panitumumab	45 (88%)	6 (12%)	51 (100%)	0 (0%)	0 (0%)	0 (0%)
Pembrolizumab	428 (76%)	136 (24%)	564 (100%)	0 (0%)	0 (0%)	0 (0%)
Pemetrexed disodium	33 (92%)	3 (8%)	36 (100%)	0 (0%)	0 (0%)	0 (0%)
Pralatrexate	6 (75%)	2 (25%)	8 (100%)	3 (100%)	0 (0%)	3 (100%)
Raltitrexed	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Topotecan	12 (75%)	4 (25%)	16 (100%)	0 (0%)	0 (0%)	0 (0%)
Vinblastine Sulfate	52 (84%)	10 (16%)	62 (100%)	0 (0%)	0 (0%)	0 (0%)
Vinorelbine	24 (80%)	6 (20%)	30 (100%)	0 (0%)	0 (0%)	0 (0%)

Source: Developed for this Review using DAEN data.

The data in Table A53 shows that all cases of off-label use occurred after EFC-listing. However, as

patients generally cannot access cancer medicines with Government funding, the use of these medicines was generally limited. With the exception of doxorubicin and vinblastine sulfate, the date EFC listing was the same as the date of PBS-listing. Patients who accessed carfilzomib and durvalumab likely accessed these medicines through compassionate use programs or partook in clinical trials.

Impact of EFC-listing on off-label use vs. general schedule listing

Doxorubicin and vinblastine sulfate were listed on the general schedule of the PBS until January 2013. After this date, these drugs were added to the EFC. To examine the impact EFC-listing had on these medicines, additional data from the DEAN database were collected for the year 2010 to 2020. The rates of off-label use for 2010-2012 (pre-EFC listing) and 2013-2020 (post-EFC listing) were then compared. A breakdown of instances of off-label use by year for these drugs from 2010 to 2020 is presented in Table A54.

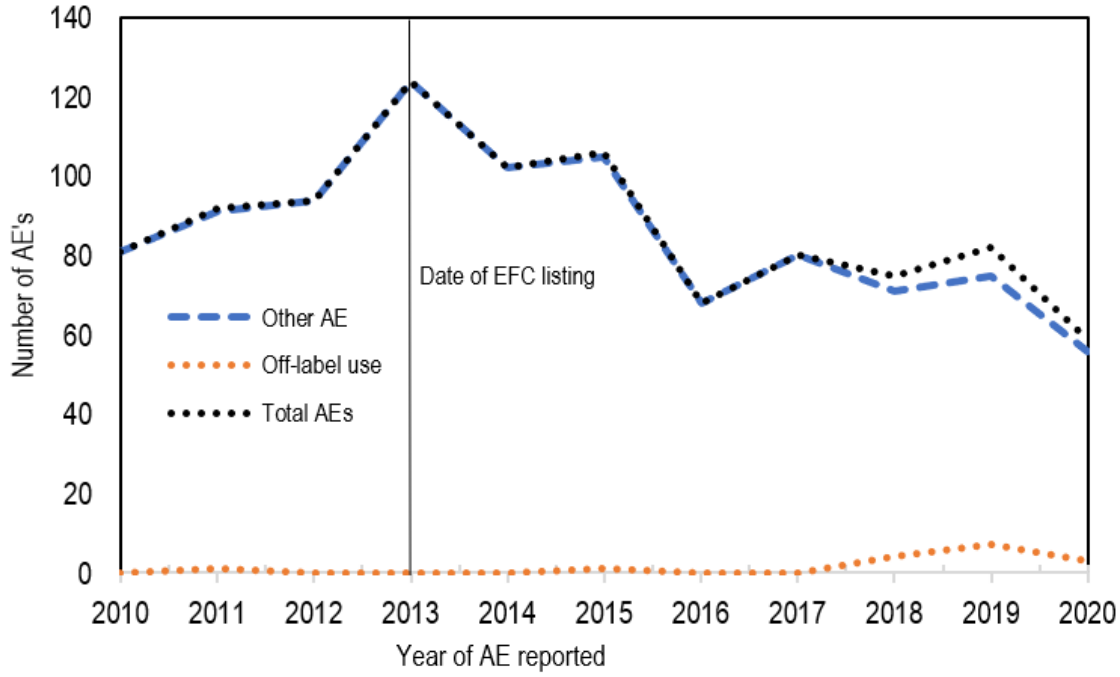
Table A54. Off-label-use before and after EFC-listing

Year	*Doxorubicin*			*Vinblastine Sulfate*			*Total*		
	No	*Off-label*	*Total*	*No*	*Off-label*	*Total*	*No*	*Off-label*	*Total*
				Drug listed on the PBS under the general schedule					
2010	81 (100%)	0 (0%)	81 (100%)	0 (0%)	0 (0%)	0 (0%)	81 (100%)	0 (0%)	81 (100%)
2011	91 (99%)	1 (1%)	92 (100%)	0 (0%)	0 (0%)	0 (0%)	91 (99%)	1 (1%)	92 (100%)
2012	94 (100%)	0 (0%)	94 (100%)	3 (100%)	0 (0%)	3 (100%)	97 (100%)	0 (0%)	97 (100%)
				Drug listed on the EFC					
2013	124 (100%)	0 (0%)	124 (100%)	4 (100%)	0 (0%)	4 (100%)	128 (100%)	0 (0%)	128 (100%)
2014	102 (100%)	0 (0%)	102 (100%)	0 (0%)	0 (0%)	0 (0%)	102 (100%)	0 (0%)	102 (100%)
2015	105 (99%)	1 (1%)	106 (100%)	1 (100%)	0 (0%)	1 (100%)	106 (99%)	1 (1%)	107 (100%)
2016	68 (100%)	0 (0%)	68 (100%)	6 (75%)	2 (25%)	8 (100%)	74 (97%)	2 (3%)	76 (100%)
2018	80 (100%)	0 (0%)	80 (100%)	7 (100%)	0 (0%)	7 (100%)	87 (100%)	0 (0%)	87 (100%)
2019	71 (95%)	4 (5%)	75 (100%)	6 (60%)	4 (40%)	10 (100%)	77 (91%)	8 (9%)	85 (100%)
2020	75 (91%)	7 (9%)	82 (100%)	2 (50%)	2 (50%)	4 (100%)	77 (90%)	9 (10%)	86 (100%)
2020	56 (95%)	3 (5%)	59 (100%)	23 (92%)	2 (8%)	25 (100%)	79 (94%)	5 (6%)	84 (100%)
Total	*947 (98%)*	*16 (2%)*	*963 (100%)*	*52 (84%)*	*10 (16%)*	*62 (100%)*	*999 (97%)*	*26 (3%)*	*1025 (100%)*

Source: Developed for this Review using DAEN data.

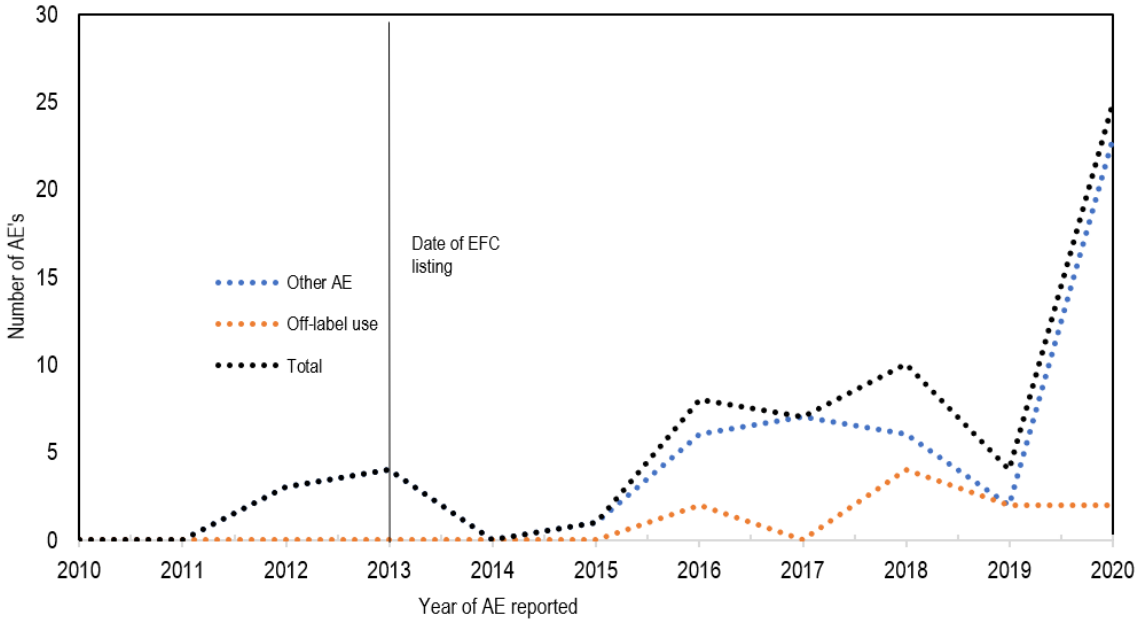
Overall, the listing of these medicines on the EFC appeared to have a negligible impact on their use, as the number of instances of off-label use was relatively stable between 2010-2015 (see Figure A62 and Figure A63). However, after 2016, the number of cases with off-label use increased.

Figure A62. Off-label use by year, doxorubicin (2016 - 2020)



Source: Developed for this Review using DAEN data.

Figure A63. Off-label use by year, vinblastine sulfate (2016 - 2020)



Source: Developed for this Review using DAEN data.

Disproportionality analysis was used to test the impact of changing doxorubicin and vinblastine sulfate from a general PBS-listing to an EFC-listing (see Table A55). The general listing period was 2010 to 2012, whilst the EFC-listing period was 2013- 2020. Based on these data, the ROR for

doxorubicin and doxorubicin + vinblastine sulfate suggested EFC-listing increased the rates of off-label. However, when the post-EFC listing period was limited to 2013-2015, EFC-listing had no impact on the rates of off-label use.

Table A55. Disproportionality analysis: reported off-label use by EFC-listing status, doxorubicin and vinblastine sulfate

EFC-listing	*Doxorubicin*			*Vinblastine Sulfate*			*Doxorubicin + Vinblastine Sulfate*		
	No	*Off-label*	*ROR (95% CI)*	*No*	*Off-label*	*ROR (95% CI)*	*No*	*Off-label*	*ROR (95% CI)*
				Period of analysis: 2010-2020					
Gen. listing (2010-13)	266 (100%)	1 (<1%)	Ref.	3 (100%)	0 (0%)	Ref.	269 (100%)	1 (<1%)	Ref.
EFC listing (2013-20)	681 (98%)	15 (2%)	5.86 (0.77, 44.62)	49 (83%)	10 (17%)	NE	730 (97%)	25 (3%)	9.21 (1.21, 70.30) *
				Period of analysis: 2010-2015					
Gen. listing (2010-13)	266 (100%)	1 (<1%)	Ref.	3 (100%)	0 (0%)	Ref.	269 (100%)	1 (<1%)	Ref.
EFC-listing (2013-15)	399 (100%)	1 (<1%)	0.67 (0.04, 10.72)	11 (85%)	2 (15%)	NE	410 (99%)	3 (1%)	1.97 (0.17, 22.84)

Source: Developed for this Review using DAEN data.
Abbreviations: CI, confidence interval; NE, not estimable; ROR, reporting odds ratio.
Notes: * indicates statistically significant at p-value ≤ 0.05; ** statistically significant at p-value ≤ 0.01.

Appendix 9. Per-mg Pricing Model

Aims

The aim of this analysis was to model the cost to Government for the five years from 1 July 2016 to 30 June 2021 under the EFC's extant per-vial costing compared to an alternate, per-mg basis for remuneration. Three case studies were chosen for assessment in the analysis:

- cabazitaxel for prostate cancer [4376H (public) 7236W (private)]. This medicine was included on the basis of input from the stakeholder consultations that there had been extensive vial sharing affecting the use of this medication on the PBS.
- avelumab for merkel cell carcinoma. [11671G (public, continuing); 11679Q (private, initial); 11685B (private, continuing); 11965M (public, initial). This medicine was included on the basis of being a recently listed monoclonal antibody (i.e., non-cytotoxic) for which use comprised both mg per kg dosing (as the predominant form of utilisation) and flat-based dosing.
- bortezomib for multiple myeloma [12219D (private) and 12227M (public), available from 2021]. The following item codes were for various restrictions for multiple myeloma in public hospitals: 04403R, 04429D, 04706Q, 04712B, 04713C, 04725Q, 04732C, 12227M; and private hospitals: 07238Y, 07268M, 07269N, 07271Q, 07272R, 07274W, 07275X, 12219D]. This medicine was included as a third case study, being a medicine prescribed on a mg per m^2 BSA basis.

Structure of the model

The standard 'Utilisation and Cost Model Workbook' was adapted for this analysis (see Table A56). A summary of the data inputs and changes made to the relevant workbook are provided below.

Table A56. Excel worksheets in use from the Utilisation and Cost Model Workbook

Sheet name	*Description and location of data input*
0. Title	Define the structure of the model
1. Overview	Define General Information; Regulatory information; Existing listings of this medicine; Economics /SPA /RSA; Patients counts/costs
2e. Scripts – market	2.Identify the expected substitutable medicines in the current PBS market – include services volumes for the first full calendar year. 3. Estimate the number of scripts - include services volumes for year 2016 to 2021. The estimated annual rate of growth [0%], proportion applicable to indication [100%], proportion affected by the proposed medicine [100%] 4. Methods and assumptions
4b. Impact – affected (pub)	2. Cost of individual forms/strengths – adjust co-payment calculation to initial script 3. Identify the costs for all forms / strengths of the affected medicines

Sheet name	*Description and location of data input*
	4. Methods and assumptions
5. Impact - net	Provide a summary of the published prices
References	First year of listing. Relevant cells J42:J46
Reference	Pricing calculator D21-845017 Mark-ups v38 – eff 1 Jul 21 – External, spreadsheet named 'Reference'. Relevant cells are in B33:H38

Abbreviations: PBS, pharmaceutical benefits scheme; pub, published; RSA, risk-sharing arrangement; SPA, special pricing arrangements.

Using the 'Utilisation and Cost Model Workbook' the structure of the model was defined in the *Worksheet 0. Title* as follows:

- Identify the script source: Market share
- Script split source: Current market
- Proposed listing results in: Substitution
- Affected medicine has SPA: No for cabazitaxel and bortezomib and Yes for avelumab.

Methods and inputs

Assumptions: A market share approach was taken using patient level utilisation data as provided from the Department of Health. No modelling of expenditure growth or forwards estimates was undertaken. The analysis was conducted at the DPMA level, noting that the impact of moving to per mg pricing as the basis for reimbursement will be different for avelumab given that it is supplied under a special pricing arrangement, but details of the effective price were not known (see Pricing Inputs).

Data Sources: Five years of utilisation data for the relevant PBS items were utilised (1 July 2016 to 30 June 2021). The dataset included service volumes by line item along with form and strength, quantity supplied (mg or mcg), pharmacy approval type and repeat script flag. The PBS data were cross-referenced to the PBS item report data of services processed from Services Australia.

The PBS database does not report the actual dose strengths used as the basis for the estimation of the most efficient combination of vials; rather, due to a reporting anomaly, for PBS items with multiple strengths, only the first strength per PBS Item as it appears on the PBS schedule is shown in the PBS database. Accordingly, the analyses presented in this section do not utilise the medicine strengths as contained in the PBS database, relying on the recorded dose reimbursed per service and the total number of services per medicine, as follows:

1. Cabazitaxel: There are three cabazitaxel brands - Cabazitaxel Ever Pharma (6 ml injection, 6 ml vial), Cabazitaxel Juno (1.5 ml injection) and Jevtana (1.5 ml injection). Cabazitaxel Ever Pharma was listed on the PBS 01/07/2021 and no data were available during the study period[4]. Data were only available for concentrated injection 60 mg (as acetone solvate) in 1.5 mL, with diluent reflecting Cabazitaxel Juno or Jevtana (note, the brand used was not provided in the PBS database).
2. Avelumab: There is one strength of avelumab listed on the PBS with brand name Bavencio® (200 mg/10 ml injection, 10 ml vial). Avelumab is administered in a dose of 10 mg/kg intravenously over 60 minutes once every 2 weeks or 800 mg administered intravenously over 60 minutes every 2 weeks. Data on avelumab use were available from 2019 onwards (reflecting the time from which this medicine was listed on the PBS).
3. Bortezomib: There are three strengths of bortezomib on the PBS - 1 mg, 3 mg and 3.5 mg. A 2.5 mg vial was recently approved but not available during the study period. The Janssen Velcade® formulation may be administered intravenously (at a concentration of 1 mg/mL) as a 3-5 second bolus injection or subcutaneously (at a concentration of 2.5 mg/mL). Data on Janssen Velcade® were available for the entire study period (given that it is the innovator brand), whereas data on the use of the Juno Pharmaceuticals Juno® brand were available from 2021 (note, the brand used was not provided in the PBS database). For the costing, the bortezomib 3 mg vial was used in the analysis (the price per mg was the same across the 1 mg, 3 mg and 3.5 mg strengths).

The required inputs were obtained from a number of data sources. The PBS line level database analysis relied on the date supplied variable *[spply_dt],* which was converted into half years (e.g. 2021h1 indicating scripts supplied from 1 January 2021 to 30 June 2021). Within the database, the medicine item code *[itm_cd]* and drug name *[drg_schdl_nm]* were used to identify the medicine and item of interest.

- script volumes for each line item by time from PBS line level database
- patient category *[ptnt_ctgry_drvd_cd]* split for each line item from PBS data line level database

[4] https://www.pbs.gov.au/medicinestatus/document/483.html

- public/private/community split for each line item from PBS line level database using item code (public/private only) and pharmacy approval type *[phrmcy_apprvl_typ_cd]*
- average mg per service using quantity supplied *[pbs_rgltn24_adjst_qty]* from PBS line level database
- proportion of services initial or repeat scripts *[srt_rpt_ind]* from PBS line level database
- approved ex-manufacturer price (AEMP) from the PBS website[5]
- published dispensed price for maximum amount (DPMA) from PBS website[6]
- fees and mark-ups for EFC from the PBS website[7].

Service Utilisation Inputs: The service volumes for each of the medicines by line item are presented in Table A57. The estimated script volumes for years 2016 (half year) to 2021 (half year) were hardcoded into Section 3 of the *Worksheet 2e. Scripts – market* in the Excel workbook.

Table A57. Script volumes by line item

Line item	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
Cabazitaxel							
04376H public	604	1,110	1,232	1,582	1,820	949	7,297
07236W private	1,582	2,995	3,101	3,534	3,803	1,885	16,900
Total							*24,197*
Avelumab							
11671G public	-	-	-	119	500	318	937
11679Q private	-	-	-	873	806	348	2,027
11685B private	-	-	-	448	1,481	813	2,742
11695M public	-	-	-	419	320	164	903
Total							*6,609*
Bortezomib							
04403R public	3,471	5,827	5,110	7,223	8,964	1,463	32,058
04429D public	491	759	856	1,626	1,963	213	5,908
04706Q public	1,523	2,432	1,897	2,453	3,004	329	11,638
04712B public	88	201	149	295	390	27	1,150
04713C public	717	1,285	1,071	1,217	907	60	5,257
04725Q public	88	122	162	118	170	-	660
04732C public	1,088	1,970	2,276	2,642	1,991	70	10,037
07238Y private	6,684	11,768	11,770	12,176	15,606	4,394	62,398
07268M private	2,098	3,464	3,356	4,896	5,660	712	20,186

[5] https://www.pbs.gov.au/pbs/industry/pricing/ex-manufacturer-price

[6] https://www.pbs.gov.au/medicine/item/4376H-7236W

https://www.pbs.gov.au/medicine/item/12219D-12227M

https://www.pbs.gov.au/medicine/item/11671G-11679Q-11685B-11695M

[7] https://www.pbs.gov.au/info/healthpro/explanatory-notes/front/fee

Line item	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*Total*
07269N private	229	490	357	711	949	87	2,823
07271Q private	1,375	3,720	2,616	2,004	1,582	337	11,634
07272R private	74	298	356	388	354	60	1,530
07274W private	805	1,738	1,936	2,822	2,699	587	10,587
07275X private	2,672	5,128	6,109	3,838	2,680	176	20,603
12219D private	-	-	-	-	-	11,019	11,019
12227M public	-	-	-	-	-	9,145	9,145
Total							*216,633*

Note: Developed for this Review using PBS line level data.

Data were applied for the first full calendar for which data were available, 2017 for cabazitaxel and bortezomib and 2019 for avelumab. Service volumes were entered into Section 2 of the *Worksheet 2e. Scripts – market* in the Excel workbook (Table A58.).

Table A58. Line item by patient category

Line item	*General - Ordinary*	*General - Safety Net*	*Concessional - Ordinary*	*Concessional - Free*	*RPBS - Ordinary*	*RPBS - Safety Net*	*Total*
Cabazitaxel (2017)							
04376H – public	266	10	780	49	5	0	1,110
07236W - private	942	34	1,794	87	129	9	2,995
Total							*4,105*
Avelumab (2019)							
11671G public	24	0	95	0	0	0	119
11679Q private	300	0	496	30	47	0	873
11685B private	124	0	286	7	30	1	448
11695M public	62	0	329	21	7	0	419
Total							*1,859*
Bortezomib (2017)							
04403R public	1,346	25	4,052	369	35	0	5,827
04429D public	120	4	510	98	27	0	759
04706Q public	489	25	1,744	138	36	0	2,432
04712B public	29	0	154	17	1	0	201
04713C public	253	0	924	105	3	0	1,285
04725Q public	36	0	86	0	0	0	122
04732C public	1,013	0	885	44	28	0	1,970
07238Y private	2,842	116	7,685	748	309	68	11,768
07268M private	1,036	24	2,084	222	92	6	3,464
07269N private	151	1	275	48	15	0	490
07271Q private	1,277	39	2,045	255	104	0	3,720
07272R private	93	8	175	16	0	6	298
07274W private	202	12	1,290	189	45	0	1,738
07275X private	3,252	25	1,661	117	73	0	5,128
12219D private	0	0	0	0	0	0	0
12227M public	0	0	0	0	0	0	0
Total							*39,202*

Abbreviations: RPBS, repatriation pharmaceutical benefits scheme.
Note: Year in parentheses indicates first full calendar year of data available.
Developed for this Review using PBS line level data.

The analysis relied on the pharmacy approval type to determine the split amongst public, private and community pharmacy mark-ups. The PBS database reported the pharmacy approval type: 0 - Community pharmacy, F Community pharmacy (flagged as a friendly society), H - private hospital Y - public hospital (reform arrangements, see Table A59). Overall, based on the pharmacy approval type 30%, 28% and 37% were supplied in public hospitals for cabazitaxel, avelumab and bortezomib, respectively. The public and private split was cross-referenced using the item code method. The derived public/private split for each medicine was estimated from the PBS data based on the item codes for the first full calendar year for which data were available for that medicine. The item code designation does not identify supply via pharmacy setting. Using the item code designation 30%, 28% and 35% were supplied in public hospitals for cabazitaxel, avelumab and bortezomib, respectively. Further, some of the bortezomib 'private hospital' item codes were provided in public hospitals so that public hospital supply is marginally higher with the pharmacy approval type method, compared to the item code method. Overall, only minor differences were seen between the two methods, and the pharmacy approval type was relied on for the costing model.

Table A59. Line item by drug and pharmacy setting

Line item	*Community Pharmacy*	*Community Pharmacy: Friendly Soc.*	*Private Hospital*	*Public Hospital*	*Total*
Cabazitaxel					
04376H public	0	0	0	7,297	7,297
07236W private	9,693	57	7,150	0	16,900
Total	*9,693*	*57*	*7,150*	*7,297*	*24,197*
Avelumab					
11671G public	0	0	0	937	937
11679Q private	1,295	0	732	0	2,027
11685B private	1,795	0	947	0	2,742
11695M public	0	0	0	903	903
Total	*3,090*	*0*	*1,679*	*1,840*	*6,609*
Bortezomib					
04403R public	17	0	34	32,007	32,058
04429D public	6	0	12	5,890	5,908
04706Q public	17	0	39	11,582	11,638
04712B public	10	0	11	1,129	1,150
04713C public	1	0	0	5,256	5,257
04725Q public	5	0	0	655	660
04732C public	12	1	2	10,022	10,037
07238Y private	42,675	121	17,150	2,452	62,398
07268M private	13,186	102	6,321	577	20,186
07269N private	1,901	0	826	96	2,823
07271Q private	8,298	0	2,866	470	11,634
07272R private	1,062	0	438	30	1,530
07274W private	7,271	19	2,951	346	10,587
07275X private	14,632	54	4,687	1,230	20,603
12219D private	7,150	10	3,853	6	11,019

Line item	Community Pharmacy	Community Pharmacy: Friendly Soc.	Private Hospital	Public Hospital	Total
12227M public	0	0	0	9,145	9,145
Total	*96,243*	*307*	*39,190*	*80,893*	*216,633*

Note: Developed for this Review using PBS line level data.

Pricing Inputs: The fees and mark-ups relevant to the EFC medicines are presented in Table A60. The fees are indexed annually on 1 July each year. Currently, there are no wastage, container or dangerous drug fees payable for EFC items.

Table A60. Fees and mark-ups relevant for EFC

					Sens analysis	
Fee/mark-up	*Pub*	*Priv*	*Comm*	*Base case*	*10% increase*	*25% increase*
Ready prepared dispensing fee		√	√	$7.78	$8.56	$9.73
Distribution fee		√	√	$27.75	$30.53	$34.69
Diluent fee		√	√	$5.50	$6.05	$6.88
Preparation fee	√	√	√	$86.28	$94.91	$107.85
AHI mark-up s85 & s100 EFCs94 - Private		√		1.40%	1.54%	1.75%
Tier 1 PTP $0 to $100			√	$4.30	$4.73	$5.38
Tier 2 PTP $100 to $2000, % exceeding $100			√	5.00%	5.50%	6.25%

Abbreviations: AHI, Administration, Handling and Infrastructure; Comm, community; EFC, efficient funding of chemotherapy; Priv, private; PTP, price to pharmacist; Pub, public; Sens, sensitivity.
Note: Fees as of 1 July 2021
Developed for this Review using PBS line level data.

The following mark-ups were applied for all three medicines:

- (s94) Public hospital pharmacies which are authorised to supply PBS-subsidised chemotherapy medicines are only eligible for the preparation fee. Section 94 – public hospital mark-ups: preparation fee equated to $86.28.
- (s94) Private hospital mark-ups: distribution fee, diluent fee, preparation fee and ready prepared and Administration, Handling and Infrastructure (AHI) fee mark-up percentage s100 EFC mark-up for $0 to $99,999 and equated to $127.31 excluding the 1.4% AHI.
- (s90) Community pharmacy mark-ups: distribution fee, diluent fee, preparation fee and ready prepared. In addition, pharmacy mark-up based on Tier 1 with a price to pharmacy (PTP) between $0 to $100 and equated to $131.61 excluding the 5% mark-up for Tier 2 mark-up between PTP and $100.

The effective price for avelumab was unknown; while this may effect the quantum of the reduction in the cost to Government due to a change to per mg pricing as the basis for reimbursement, it is

unlikely to influence the proportional change.

Co-payment Inputs: From 1 January 2021, co-payments are $41.30 for general (non-concessional) patients or $6.60 for concession card holders. The co-payments were applied to initial scripts which was 30% for cabazitaxel, 17% for avelumab and 10% for bortezomib. This was multiplied by the existing formula in the less co-payments rows in the "Section 2. Cost of individual forms/strengths" in the *Workbook 4.b. Impact – affected (pub).*

The estimation of the weighted DPMA was based on the weighted average of public hospital, private hospital and community pharmacy supply of the medicines (Table A61). The community s90 mark-ups were estimated but could not be verified. The effective price of bortezomib was unknown. The calculated published prices using the mark-ups were based on applying the revised mark-ups to the AEMP, adjusted for the relevant maximum amount. The sensitivity analysis assuming the public hospital DPMA were equivalent to private hospital DPMA under the assumption of no public/private item code distinction resulted in a slightly higher weighted DPMA.

Table A61. Estimation of weighted DPMA and co-payments

		DPMA				Co-payment[1]		Sensitivity
Medicine	*AEMP*	*Public*	*Private*	*Community*	*Weighted*	*PBS*	*RPBS*	*DPMA Weighted*[2]
Cabazitaxel	$946.16	$1,032.44	$1,086.72	$1,120.08	$1,083.79	($16.95)	($6.18)	$1,100.16
		30.16%	29.55%	40.29%				
Avelumab	$1,357.36	$8,230.44	$8,385.47	$8,433.63	$8,364.83	($16.36)	($6.52)	$8,407.99
		27.84%	25.40%	46.75%				
Bortezomib	$518.72	$605.00	$653.29	$671.27	$643.27	($17.18)	($5.98)	$661.30
		37.34%	18.09%	44.57%				

Source: Developed for this Review using PBS line level data.
Abbreviations: AEMP, approved ex-manufacturer price; DPMA, dispensed price for maximum amount; PBS, pharmaceutical benefits scheme; RPBS, repatriation pharmaceutical benefits scheme.
Note: [1] Co-payments in parentheses are negative values. [2] The weighted DMPA for the sensitivity analysis assumes the removal between public and private item codes with the mark-ups for private hospital and community pharmacy only.

Price per mg calculations: In this section, the method used to estimate a price per service that would reflect the average mg dosed per supply of service is summarised. This analysis captured what the net cost to Government would be if only the quantity supplied (in mgs or mcgs) was reimbursed. The base case of this analysis assumed that the full vial contents can be utilised, however, in reality there would be some amount of drug that cannot be extracted (due to overage), dependent on drug viscosity, container, extraction equipment and operator technique.

The average dose per service was calculated using the quantity supplied from the available PBS data (Table *A62*). For cabazitaxel, the mean quantity supplied for all services was 38 mg (SD: 6.9 mg)

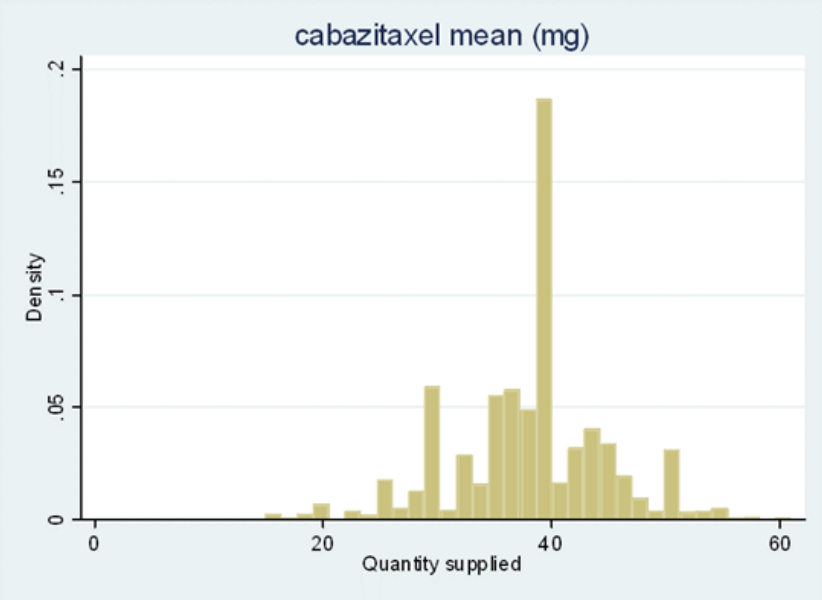
(Figure A64). For avelumab, overall the mean quantity supplied was 825 mg (SD 187.1 mg) (Figure A65). Avelumab is a weight based dose with the option of an 800 mg flat based dose, however, when excluding the 800 mg dose (on the assumption that these services may have represented flat based dosing), the mean dose increased marginally to 827 mg (SD 194.9 mg). The base case analysis relied on the full dataset including the 800 mg dosing. For bortezomib, overall the mean quantity supplied was 2.4 mg (SD 0.45 mg) (Figure A66).

Table A62. Average dose per service

Item	*Mean*	*SD*	*Min*	*Max*	*n*
Cabazitaxel, mg	38.23	6.90	1	61	24,197
Avelumab, mg	824.70	187.09	4	1,600	6,609
Avelumab, mg exclude 800 mg dosing	826.86	194.93	4	1,600	6,079
Bortezomib, mcg, all strengths	2396.55	454.96	1	28,500	216,633
Bortezomib, mcg, 1 mg vial	2407.28	450.71	1	28,500	161,755
Bortezomib, mcg, 3.5 mg vial	2364.94	465.82	1	12,000	54,878

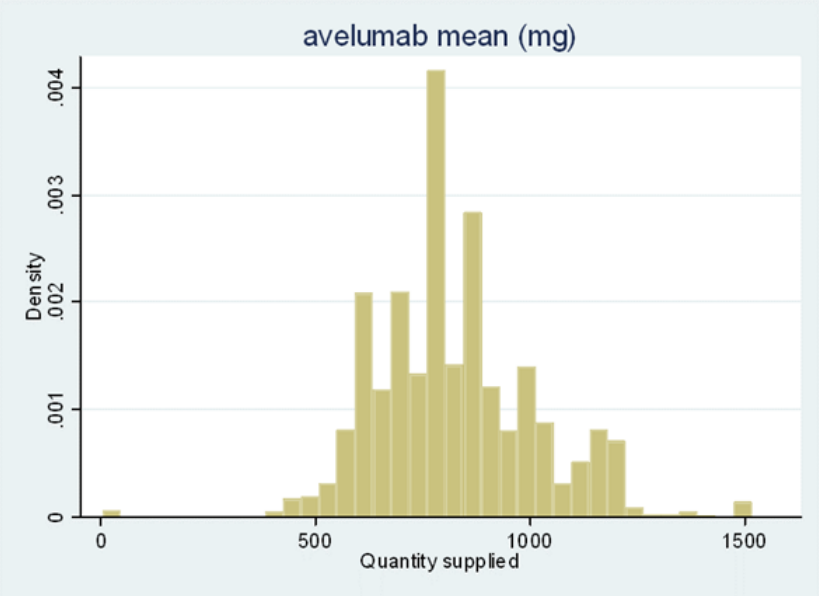
Note: Developed for this Review using PBS line level data.

Figure A64. Quantity supplied (mg), cabazitaxel



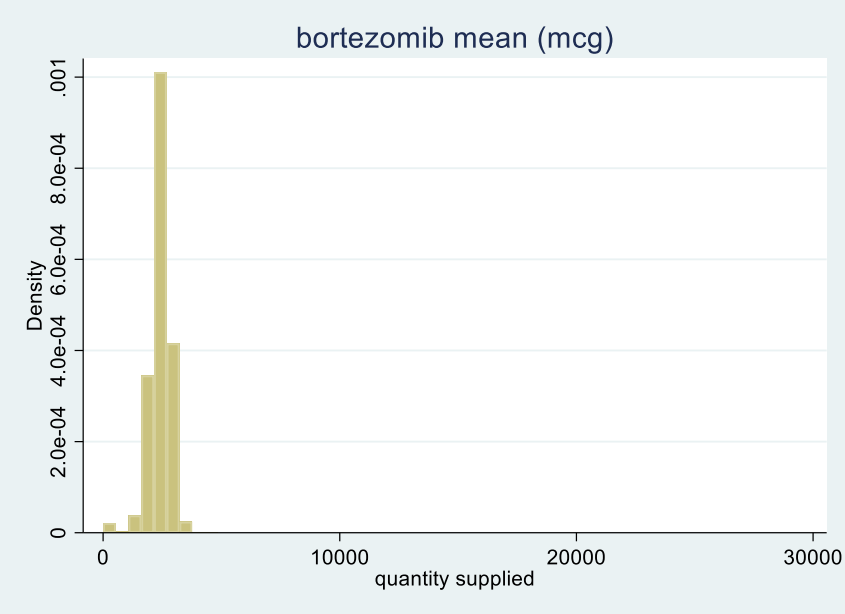
Note: Developed for this Review using PBS line level data.

Figure A65. Quantity supplied (mg), avelumab



Note: Developed for this Review using PBS line level data.

Figure A66. Quantity supplied (mcg), bortezomib



Note: Developed for this Review using PBS line level data.

The estimation of the pack price (at the AEMP level) was based on the following formula.

$$Pack\ price\ on\ a\ per\ mg\ basis = \left(\frac{AEMP}{Maximum\_quantity}\right) \times average\ mg\ per\ service$$

The components of the resulting pack price, at the DPMA (taking into account fees and mark-ups in the various settings) are presented in Table A63.

Table A63. Price per mg calculation

	AEMP $	*Vial size* mg	*Max quantity* mg	*AEMP/max quantity* mg	*Average mg per service* mg	*Price per mg* $	*DPMA public* $	*DPMA private* $	*DPMA s90* $
Cabazitaxel	$946.16	60	55	$17.20	38.23	$657.67	$743.90	$794.14	$817.11
Avelumab	$1,357.36	200	1200	$1.13	824.71	$932.86	$5,683.41	$5,802.79	$5,835.67
Bortezomib[a]	$518.72	3	3	$172.91	2.39	$414.38	$500.66	$547.49	$561.71

Source: Developed for this Review using PBS line level data.
Notes: [a] The AEMP applied was 3 mg. Price per mg was the same across the 1 mg, 3 mg and 3.5 mg strengths.

Sensitivity analyses: Three parameters were varied in sensitivity analyses within the model:

1. The extent to which per mg pricing applies to services. In recognition that not all drug within vials can be utilised, the proportion of services for which per mg pricing would apply was varied. This might reflect the extent to which facilities are able to participate in vial sharing (either due to volume constraints or due to medicines not being sufficiently stable to allow drug to be combined across multiple patients, potentially occurring on different days). A wastage factor (i.e. the proportion of use to which per mg pricing would not apply) was tested at 5%, 10%, 20% and 30% using the 'Weighted DPMA' value (base case 100%, i.e. 0% wastage) in *Workbook 4b.Impact – affected (pub)* (Table A64).

Table A64. Weighted DPMA based on per-mg pricing substitution

Weighted DPMA	*Cabazitaxel*	*Avelumab*	*Bortezomib*
Per vial, 100%	$1,083.79	$8,364.83	$643.27
Per mg, 100%	$788.24	$5,737.82	$536.34
Per mg, 95%	$803.02	$5,869.17	$541.69
Per mg, 90%	$817.80	$6,000.52	$547.03
Per mg, 80%	$847.35	$6,263.22	$557.73
Per mg, 70%	$876.91	$6,525.92	$568.42

Abbreviation: DPMA, dispensed price for maximum amount.
Note: Developed for this Review using PBS line level data.

2. The quantum of EFC fees and mark-ups applied. The impact of increasing fee and mark-ups (by 10% and 25%) under the current policy and under a price per mg policy was tested.
3. Consistency of EFC fees across private and public hospitals. The impact of increasing public hospital fees to be consistent with those of private hospitals under the current policy and under a price per mg policy was tested.

Results

The net costs to the PBS/RPBS for the three medicines over the full calendar years from 2017 to 2020 are presented in Table 20. Under the assumption of no public/private distinction in item codes the net cost to government resulted in a 102%, 101% and 103% increase for cabazitaxel, avelumab and bortezomib, respectively.

The cost to government on a per mg pricing basis was 73%, 69% and 83% of the cost under EFC funding for cabazitaxel, avelumab and bortezomib respectively (Table 20). This represents reductions of 27%, 31% and 17% respectively. Under the no item code distinction (removal of the distinction between public and private hospital item codes) and a per mg pricing, the total cost to Government reduced to 74%, 70% and 86%, for cabazitaxel, avelumab and bortezomib, respectively. Similarly, overall increase in mark-up and fees by 25%, resulted in a 103%, 100% and 104% change for cabazitaxel, avelumab and bortezomib, respectively. Under the per mg pricing and with a 25% increase in mark-up and fees, the total cost to Government reduced to 76%, 69% and 88% for cabazitaxel, avelumab and bortezomib, respectively. Therefore, an increase in mark-ups by 25% (and to a lesser extent 10%) or the removal of public hospital item codes, erodes the cost reduction to government from moving to per mg pricing.

Table A65. Net cost PBS/RPBS based on full calendar year, base case

Item	*2017*	*2018*	*2019*	*2020*	*Sum at 4 years (million)*	*Change*[1]
Cabazitaxel						
Base case	$4,428,539	$4,674,509	$5,519,221	$6,066,178	$20.69	100%
No public/private distinction	$4,495,729	$4,745,431	$5,602,959	$6,158,215	$21.00	102%
Mark-ups increased by 10%	$4,485,036	$4,734,145	$5,589,633	$6,143,568	$20.95	101%
Mark-ups increased by 25%	$4,569,783	$4,823,598	$5,695,251	$6,259,653	$21.35	103%
Avelumab						
Base case	$0	$0	$15,417,696	$25,768,042	$41.19	100%
No public/private distinction	$0	$0	$15,448,767	$25,819,972	$41.27	100%
Mark-ups increased by 10%	$0	$0	$15,445,975	$25,815,306	$41.26	100%
Mark-ups increased by 25%	$0	$0	$15,488,393	$25,886,200	$41.37	100%
Bortezomib						
Base case	$25,077,466	$24,396,037	$27,211,575	$30,105,403	$106.79	100%
No public/private distinction	$25,782,240	$25,081,660	$27,976,327	$30,951,482	$109.79	103%
Mark-ups increased by 10%	$25,520,287	$24,826,825	$27,692,081	$30,637,008	$108.68	102%
Mark-ups increased by 25%	$26,184,519	$25,473,007	$28,412,839	$31,434,415	$111.50	104%

Source: Developed for this Review using PBS line level data
Abbreviations: PBS, pharmaceutical benefits scheme; RPBS, repatriation pharmaceutical benefits scheme.
Note: [1] This is the percentage change from base case.

Table A66. Net cost PBS/RPBS based on full calendar year, per-mg pricing

Item	*2017*	*2018*	*2019*	*2020*	*Sum at 4 years (million)*	*Change*[1]
Cabazitaxel						
Base case	$4,428,539	$4,674,509	$5,519,221	$6,066,178	$20.69	100%
Per mg pricing	$3,215,319	$3,393,905	$4,007,203	$4,404,318	$15.02	73%
Substitution per mg pricing 95%	$3,275,980	$3,457,935	$4,082,804	$4,487,411	$15.30	74%
Substitution per mg pricing 90%	$3,336,641	$3,521,965	$4,158,405	$4,570,504	$15.59	75%
Substitution per mg pricing 80%	$3,457,963	$3,650,025	$4,309,607	$4,736,690	$16.15	78%
Substitution per mg pricing 70%	$3,579,285	$3,778,086	$4,460,808	$4,902,876	$16.72	81%
No public/private distinction and per mg pricing	$3,277,509	$3,459,548	$4,084,709	$4,489,505	$15.31	74%
Mark-ups increased by 10% and per mg pricing	$3,268,940	$3,450,504	$4,074,031	$4,477,769	$15.27	74%
Mark-ups increased by 25% and per mg pricing	$3,349,372	$3,535,403	$4,174,272	$4,587,944	$15.65	76%
Avelumab						
Base case	-	-	$15,417,696	$25,768,042	$41.19	100%
Price per mg	-	-	$10,661,514	$17,818,899	$28.48	69%
Substitution per mg pricing, 95%	-	-	$10,905,695	$18,227,005	$29.13	71%
Substitution per mg pricing, 90%	-	-	$11,149,876	$18,635,112	$29.78	72%
Substitution per mg pricing, 80%	-	-	$11,638,237	$19,451,324	$31.09	75%
Substitution per mg pricing, 70%	-	-	$12,126,599	$20,267,537	$32.39	79%
No public/private distinction and per mg pricing	-	-	$10,689,509	$17,865,688	$28.56	69%
Mark-ups increased by 10% and per mg pricing	-	-	$10,687,668	$17,862,610	$28.55	69%
Mark-ups increased by 25% and per mg pricing	-	-	$10,726,898	$17,928,176	$28.66	70%
Bortezomib						
Base case	$25,077,466	$24,396,037	$27,211,575	$30,105,403	$106.79	100%
Price per mg	$20,898,296	$20,330,426	$22,676,753	$25,088,324	$88.99	83%
Substitution per mg pricing, 95%	$21,107,254	$20,533,707	$22,903,495	$25,339,178	$89.88	84%
Substitution per mg pricing, 90%	$21,316,213	$20,736,987	$23,130,236	$25,590,032	$90.77	85%
Substitution per mg pricing, 80%	$21,734,130	$21,143,548	$23,583,718	$26,091,739	$92.55	87%
Substitution per mg pricing, 70%	$22,152,047	$21,550,109	$24,037,200	$26,593,447	$94.33	88%
No public/private distinction and per mg pricing	$21,581,751	$20,995,311	$23,418,372	$25,908,810	$91.90	86%
Mark-ups increased by 10% and per mg pricing	$21,340,084	$20,760,210	$23,156,138	$25,618,689	$90.88	85%
Mark-ups increased by 25% and per mg pricing	$22,002,766	$21,404,885	$23,875,215	$26,414,236	$93.70	88%

Source: Developed for this Review using PBS line level data
Abbreviations: PBS, pharmaceutical benefits scheme; RPBS, repatriation pharmaceutical benefits scheme.
Note: [1] This is the percentage change from base case.

Conclusion

By implementing a price per mg method using the average quantity supplied within each medicine there are potentially significant cost reductions available to Government. The base case in the current analysis assumes that there is no wastage of vials, and it does not take into consideration

potential unavoidable loss due to overage. Results from subsequent sensitivity analyses show that there are still cost reductions available from adopting a per mg pricing model, even in the presence of wastage. With respect to changes in mark-ups and fees, an increase in mark-ups by 25% (and to a lesser extent 10%) or the removal of public hospital item codes, erodes some of the cost reduction to Government from moving to per mg pricing.

Sources

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Appendix 10. Consideration of Wastage in PBAC Decision-making

Public summary documents (PSDs) for all medicines considered by the PBAC between March 2017 and November 2020 were searched using an in-house database. Documents were searched for the keyword 'wastage.' Relevant PSDs EFC-listed drugs were extracted and reviewed for product information and the specific contexts in which the PBAC referred to wastage. Findings are summarised in Table A67.

Table A67. PSD extracts referring to wastage

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
CARFILZOMIB	Jul-17	Treatment of relapsed or refractory multiple myeloma (RRMM).	Cost-utility analysis against bortezomib (Bd)	*The resubmission proposed that increased **wastage** could be identified by a review of PBS/Authorities data. It was not clear whether this could be implemented as it would require data at the individual patient level, which may not be feasible given the estimated patient numbers.	Recommended
CARFILZOMIB	Jul-20	Treatment of relapsed or refractory multiple myeloma (RRMM).	Cost-minimisation analysis (CMA) of Cd70 QW compared to Cd56 BIW.	Mentioned as : *Average dose (mg) per infusion, with **wastage**. *Per-protocol use of carfilzomib, with **wastage.**	Recommended
CARFILZOMIB	Mar-18	Relapsed or refractory multiple myeloma (RRMM).	No economic evaluation. The minor submission sought listing of a new strength of the currently listed drug carfilzomib.	*The PBAC noted that the TGA had approved registration of the 10 mg form for the same indications as the currently listed 30 and 60 mg forms at the time of consideration. The PBAC also recalled that they previously accepted that the 10 mg form, once listed, would reduce **wastage.**	Recommended
NIVOLUMAB plus IPILIMUMAB	Jul-18	Treatment of unresectable Stage III or Stage IV malignant melanoma	Cost-analysis	Mentioned in cost calculation: Mean dose/infusion (including **wastage**)	Recommended
NIVOLUMAB plus IPILIMUMAB	Jul-18	First line treatment of Stage IV clear cell variant renal cell carcinoma (RCC)	Cost-utility analysis against sunitinib	Mentioned in intervention costs: Assumes mean weight and dose intensity (+ **wastage**) from CA209214.	Rejected
NIVOLUMAB	Aug-18	Adjuvant treatment for completely resected Stage III or Stage IV melanoma	Cost-utility analysis againt observation	Drug cost/patient/course: *Based on a mean (SD) weight of 81.33 (SD: 19.42) kilograms per person (CA209238), assuming a normal distribution around the mean. The expected number of whole 20 mg dispensing intervals (i.e. incorporating **wastage**, as nivolumab may be dispensed in 20 mg intervals) per dose was calculated to be 12.70, which equated to a mean dose 254 mg per person. This was multiplied by the expected average number of doses of	Rejected

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
				nivolumab ([redacted] doses) as observed in CA209238, assuming 70% will be dispensed for use in a private hospital (based on PBS statistics for ipilimumab, nivolumab and pembrolizumab).	
NIVOLUMAB	Mar-19	Adjuvant treatment for completely resected Stage III or completely resected Stage IV melanoma	Cost-utility analysis againt observation	Drug cost/patient/course: *This cost was based on a recommended dose of 3 mg/kg administered every two weeks and a mean (SD) weight of 81.33 (SD: 19.42) kilograms per person (from CA238), assuming a normal distribution around the mean. The expected number of whole 20 mg dispensing intervals (i.e. incorporating **wastage**, as nivolumab may be dispensed in 20 mg intervals for doses over 80 mg) per dose was calculated to be 12.70, which equated to a mean dose 254 mg per person. This was multiplied by the expected average number of doses of nivolumab (19.6 doses) as observed in CA238 (i.e. 39.2 weeks' total duration) and assuming 70% will be dispensed for use in a private hospital (based on PBS statistics for ipilimumab, nivolumab and pembrolizumab).	Rejected
NIVOLUMAB	Nov-19	Unresectable Stage III or Stage IV malignant melanoma (both as monotherapy and in the maintenance phase following treatment with ipilimumab), second line non-small cell lung cancer (2L NSCLC), second line renal cell carcinoma (2L RCC) and recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN	No economic evaluation. The minor submission requested the addition of two flat dosing regimens to the current 3 mg/kg every two weeks (Q2W) weight based dosing regimen.	*The PBAC noted that the change in dosing has the effect of **wasting** on average 25% of the drug because the flat dosing results in a higher administered dose without any additional patient benefit. For this reason, the PBAC concluded that a change from the weight-based to flat dose regimen would not be cost-effective on a per-patient basis, as currently the mean dose of pembrolizumab is significantly less than 200 mg. *The PBAC noted the Departmental analysis of PBS utilisation indicated that mean doses for some indications were below the proposed 240 mg flat dose. However, the PBAC considered the differences to be small and therefore considered that addition of flat dosing regimens were unlikely to be associated with significant **wastage** or have a significant impact on cost-effectiveness of nivolumab across the	Recommended

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
				different indications.	
OBINUTUZUMAB (RECOMBINANT)	Mar-18	*Previously untreated advanced follicular lymphoma (Stage II bulky or Stage III/IV); and * Rituximab-refractory follicular lymphoma.	CEA/CUA	The resubmission combined the restrictions for induction and re-induction therapy (i.e. in the previously untreated and rituximab-refractory settings, respectively). The PBAC considered this was not appropriate and that separate restrictions would be required given the maximum number of repeats differs between the two settings. The PBAC considered this would reduce **wastage** in the re-induction setting (i.e. rituximab-refractory disease) where fewer repeats are required.	Deferred
PACLITAXEL	Mar-19	Treatment of metastatic (stage IV) adenocarcinoma of the pancreas in combination with gemcitabine	Minor submission requested a Section 100 (Efficient Funding of Chemotherapy) Authority Required listing for an additional 250 mg strength of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) and a price increase for nab-paclitaxel use in pancreatic cancer.	*The PBAC noted at the March 2014 meeting that the 250 mg vial of nab-paclitaxel was not yet TGA registered, and considered that the absence of the 250 mg vial may increase **wastage**. In the March 2019 minor submission, the sponsor requested a price increase based only on the reduction of wastage due to the availability of the 250 mg vial. The sponsor stated that the cost per patient would remain the same. *In this minor submission, the sponsor requested a price increase based only on the reduction of wastage due to the availability of the 250 mg vial. The sponsor stated that the cost per patient would remain the same. *The submission stated that listing of the 250 mg vial would reduce wastage, using the September 2017 DUSC report as evidence presented in Table 1 below. *The Sponsor stated that the current submission did not include wastage due to vial sharing in the scope of the submission however; guidance was requested regarding the Efficient Funding of Chemotherapy process. The Secretariat noted that the process of the Efficient Funding of Chemotherapy is outside of the scope of the PBAC.	Recommended
PEMBROLIZUMAB (RECOMBINANT)	Mar-18	Unresectable Stage III or Stage IV malignant	Minor submission requested amending	*In considering the resubmission for pembrolizumab in NSCLC at its November 2017 meeting, the PBAC noted that	Recommended

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
		melanoma	the dosing regimen of pembrolizumab from a weight-based dosing regimen of 2 mg/kg to a fixed 200 mg per dose regardless of weight	increasing the average per patient cost of pembrolizumab by moving the recommended dose from a 2 mg/kg basis to a fixed 200 mg basis is likely associated with a 25% **wastage** of pembrolizumab because corroborating evidence indicates that this is not also associated with an improvement in patient health outcomes. This conclusion is consistent with that of the "Fixed Dose Clinical Overview" in the minor submission. The PBAC considered that this justified its expectation of a price reduction (paragraph 7.15, [Item 7.07] pembrolizumab November 2017 PBAC PSD). At the same meeting in consideration of the major submission for pembrolizumab for urothelial cancer, the PBAC considered that the request for fixed dosing "results in a considerable proportion of patients with urothelial cancer being given a greater dose, at a greater cost, with no evidence of additional benefit. The PBAC therefore considered that it may be reasonable for the price paid for pembrolizumab in urothelial cancer to reflect the cost if weightbased 2 mg/kg dosing was used rather than fixed 200 mg dosing" (paragraph 7.12, pembrolizumab [Item 6.11] November 2017 PBAC PSD). The PBAC considered that a similar issue of **wastage** applies to the current minor submission. *The PBAC noted that the sponsor's request to change dosing from weight based to fixed dosing [redacted]. The change in dosing has the effect of **wasting** on average 25% of the drug because the fixed dosing results in a higher administered dose without any additional patient benefit. For this reason, the PBAC concluded that a change from the weight-based to fixed dose regimen would not be cost-effective on a per-patient basis, as currently the mean dose of pembrolizumab is significantly less than 200 mg.	
PEMBROLIZUMAB	Mar-18	First-line treatment of	Revised cost utility	At its November 2017 meeting, the PBAC noted that	Deferred

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
(RECOMBINANT)		patients with metastatic (Stage IV) non-small cell lung cancer (NSCLC)	analysis to November 2017 submission	increasing the average per patient cost of pembrolizumab by moving the recommended dose from a 2 mg/kg basis to a fixed 200 mg basis is likely associated with a 25% **wastage** of pembrolizumab because corroborating evidence indicates that fixed dosing does not improve patient health outcomes. The PBAC recalled that this had contributed to its expectation of a price reduction, given that the TGA has accepted the sponsor's submission of fixed dosing in the product information (paragraph 7.15, pembrolizumab November 2017 PBAC PSD). *In a separate minor submission to the March 2018 PBAC meeting, the sponsor has requested changing the PBS listing of pembrolizumab for melanoma from a dose of 2 mg/kg to a fixed dose of 200 mg per dose. This request raised the same issue of **wastage** about which the PBAC had concerns for pembrolizumab for NSCLC. *The PBAC noted that the sponsor moved to a fixed 200 mg dosing regimen for later pembrolizumab trials across multiple indications, which included first-line NSCLC. However the PBAC noted that no clinical rationale was provided for this change in dosing regimen and therefore considered that the issues of **wastage** for pembrolizumab in first-line NSCLC remained relevant.	
PEMBROLIZUMAB (RECOMBINANT)	Nov-17	First-line treatment of patients with metastatic (Stage IV) non-small cell lung cancer (NSCLC)	Cost-utility analysis	*The PBAC also noted that increasing the average per patient cost of pembrolizumab by moving the recommended dose from a 2 mg/kg basis to a fixed 200 mg basis is likely associated with a 25% **wastage** of pembrolizumab because corroborating evidence indicates that this is not also associated with an improvement in patient health outcomes. The PBAC considered that this further justified its expectation of a price reduction, given that the TGA has recommended dosing on a fixed basis.	Deferred

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
PEMBROLIZUMAB (RECOMBINANT)	Mar-20	Treatment of relapsed or refractory primary mediastinal B-Cell lymphoma (R/R PMBCL)	Cost-utility analysis	*The resubmission stated that the difference between the model and the financial estimates in the cost per patient per cycle for the comparator regimens was due to the fact that the model did not explicitly account for **wastage** or for hospital mark-ups at an individual patient level. The difference in the cost for each regimen between the two sections could not be fully reconciled during the evaluation. These differences had minimal impact on the overall outcome of the economic and financial analyses.	Recommended
PEMBROLIZUMAB (RECOMBINANT)	Nov-18	Treatment of unresectable Stage III or Stage IV malignant melanoma.	Minor submission requested removal of the weight-based dosing option for pembrolizumab	*The change in dosing also has the effect of increasing wastage on average by 25% of the drug because the fixed dosing results in a higher administered dose without any additional patient benefit. For this reason, the PBAC concluded that a change from the weight-based to fixed dose regimen would not be cost-effective on a per-patient basis, as currently the mean dose of pembrolizumab is significantly less than 200 mg (Public Summary Document, March 2018 PBAC Meeting).	Recommended
PEMBROLIZUMAB (RECOMBINANT)	Nov-17	Treatment of patients with locally advanced (LA) or metastatic urothelial cancer (mUC) after failure of a platinum-containing regimen	Cost-utility analysis	*The PBAC also noted that this submission presented pembrolizumab as a fixed dosing regimen, whereas pembrolizumab treatment for other PBS-listed indications has used a weight-based dosing regimen. This results in a considerable proportion of patients with urothelial cancer being given a greater dose, at a greater cost, with no evidence of additional benefit. The PBAC therefore considered that it may be reasonable for the price paid for pembrolizumab in urothelial cancer to reflect the cost if weight-based 2 mg/kg dosing was used rather than fixed 200 mg dosing. The PBAC therefore advised that it would be appropriate for the price of pembrolizumab in urothelial cancer to be reduced by a further proportion to account for what could effectively be considered **wastage**.	Rejected
PEMBROLIZUMAB (RECOMBINANT)	Jul-18	Treatment of patients with locally advanced (Stage III)	Cost-minimisation analysis	*The submission's approach to nivolumab costing has incorporated substantial wastage ([redacted] mg of	Rejected

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
		or metastatic (Stage IV) squamous cell carcinoma of the head and neck (SCCHN)		wastage out of the 40mg vial) which is unlikely to occur in clinical practice. A dose of [redacted] mg could also be achieved using 1x100mg vial and 3x40mg vials, resulting in less drug **wastage**. *It is noted that the TGA-approved Product Information recommends a fixed dose (200mg) for treatment of SCCHN, classical Hodgkin lymphoma, urothelial carcinoma or NSCLC and either a fixed dose (200mg) or a weight-based dose (2mg/kg) for treatment of melanoma. Should a weight-based dosing for pembrolizumab (2mg/kg) be used in the proposed R/M SCCHN population in the Australian setting, and when 50mg vials become unavailable, a majority of the proposed target patients would still require 2x100mg vials of pembrolizumab, resulting in considerable **wastage**. *The submission is likely to have overestimated the cost for nivolumab by incorporating substantial **wastage** for nivolumab, and therefore the price of pembrolizumab is likely to have been inflated. The ESC agreed with the evaluation that at the nivolumab vial combination initially proposed by the submission, the price of pembrolizumab was likely inflated.	
PEMBROLIZUMAB (RECOMBINANT)	Jul-18	Treatment of locally advanced (LA) or metastatic urothelial cancer (mUC) patients	Cost-effectiveness analysis (CEA) and cost-utility analysis (CUA)	*The PBAC noted that the November 2017 submission proposed pembrolizumab as a fixed dosing regimen for locally advanced or metastatic urothelial cancer, whereas pembrolizumab treatment for other PBS-listed indications has used a weight-based dosing regimen. The PBAC suggested that the price be reduced to account for what could effectively be **wastage** from the fixed dose regimen. (pembrolizumab PSD, Nov 2017 point 7.12). *The PBAC noted in its previous consideration of	Recommended

Product	*Date of consideration*	*Indication*	*Economic evaluation*	*Wastage/vial sharing context*	*PBAC decision*
				pembrolizumab for urothelial cancer that the fixed dosing regimen proposed results in a considerable proportion of patients with urothelial cancer being given a greater dose, at a greater cost, with no evidence of additional benefit and advised that it would be appropriate for the price of pembrolizumab in urothelial cancer to be reduced by a further proportion to account for what could effectively be considered **wastage** (Paragraph 7.12, 6.11 pembrolizumab PSD, November 2017).	
PRALATREXATE	Jul-17	Treatment of relapsed and refractory peripheral T-cell lymphoma (PTCL).	Structural improvements had been made to the economic model. Cost-utility analysis	Mentioned in the context of March 2016 submission. Paragraph 7.3, March 2016 PSD: Modifications were made to address costs and allowing for **wastage**; however, the technical concerns were not noted.	Rejected

Appendix 11. Impact of CCPS on Fee Distribution

Figure A67. Inclusion of CCPS in EFC cost, (s94) private items (2021)

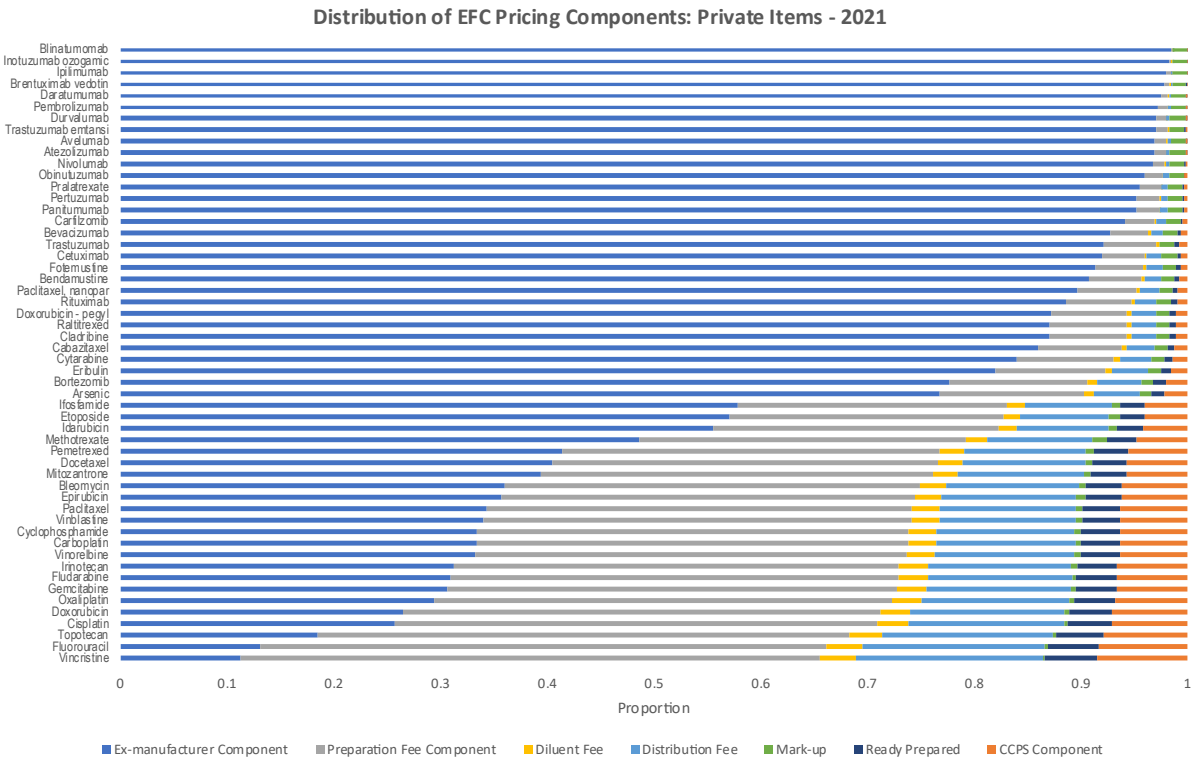


Figure A68. Inclusion of CCPS in EFC cost, (s94) public items (2021)

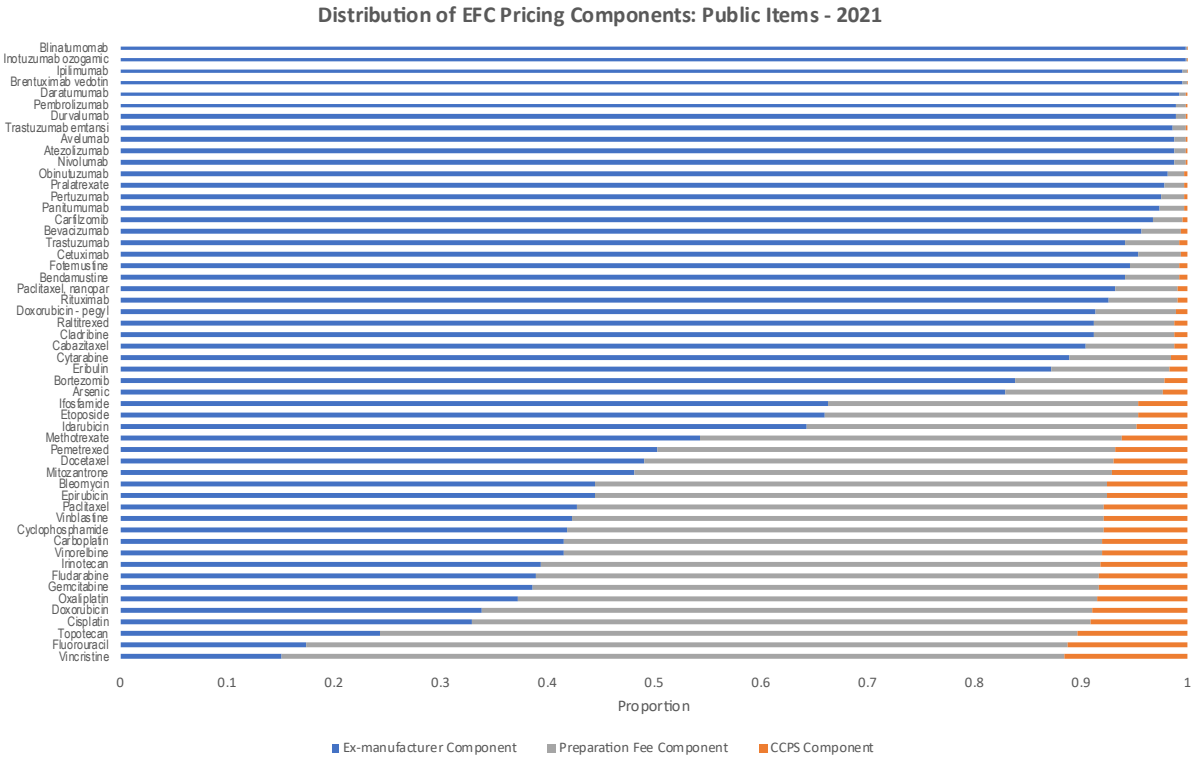
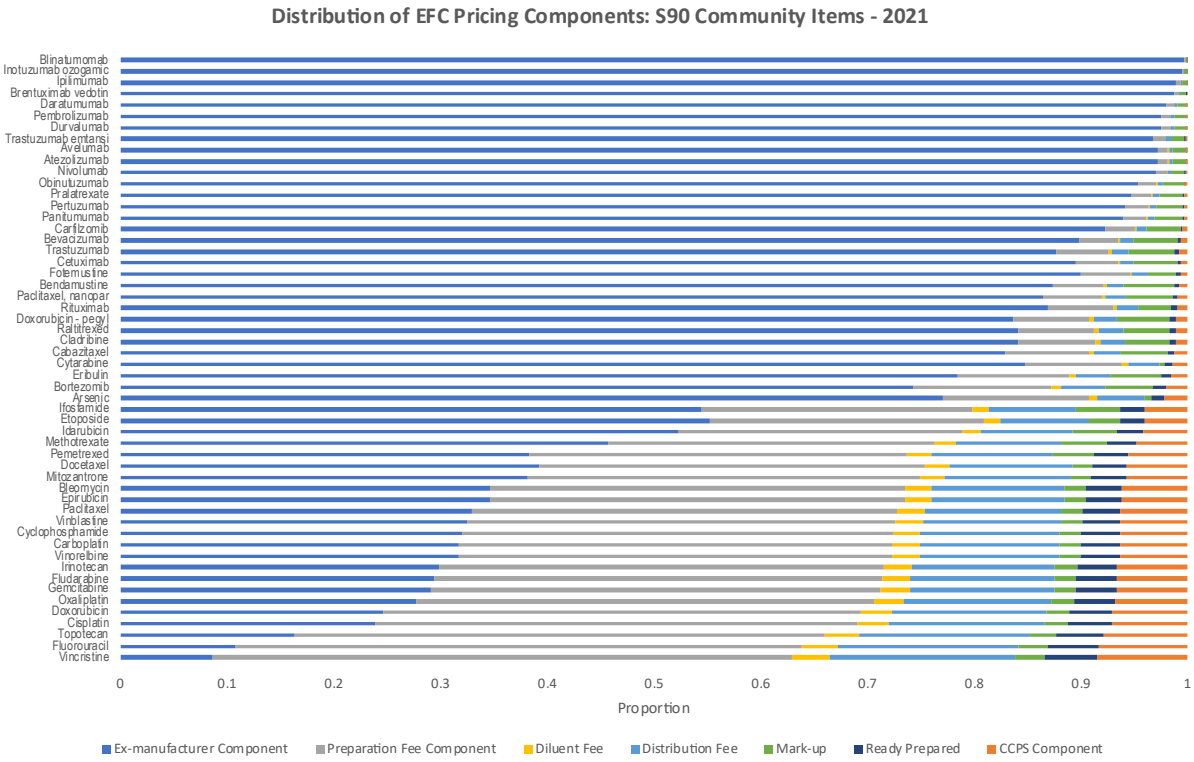


Figure A69. Inclusion of CCPS in EFC cost, (s90) community items (2021)



Appendix 12. Estimating Vial Sharing on the PBS (hypothetical)

Background: Drugs funded via the EFC are reimbursed on the basis of the most efficient combination of vials used in the constitution of the prescribed dose. Efficiency in this instance is based on minimising the quantity of drug funded but not dispensed (wasted) in order to achieve the desired prescribed dose for a given molecule and available vial sizes.

Method: PBS patient-level data for all EFC drugs (and related benefits) were obtained from the Department of Health. This included information on the dose prescribed per service and the vial strength used as the basis to estimate the PBS benefit under the EFC arrangements.

For each service observed, the total number of whole vials required to achieve the requested dose was estimated based on the formulation and strength listed in the database as the basis for payment of the PBS benefit. The difference in the number of whole vials required and the actual number of vials used (given by the dose prescribed divided by the strength in which each vial is supplied) was estimated to derive the proportion of vials funded but not used. The latter provides an estimate of the extent to which existing EFC arrangements pay for wastage.

Results: Data were available for aproximately 6.3 million observations (services) on the PBS for EFC items between June 2016 and July 2021 (1.39 million in the most recent financial year).

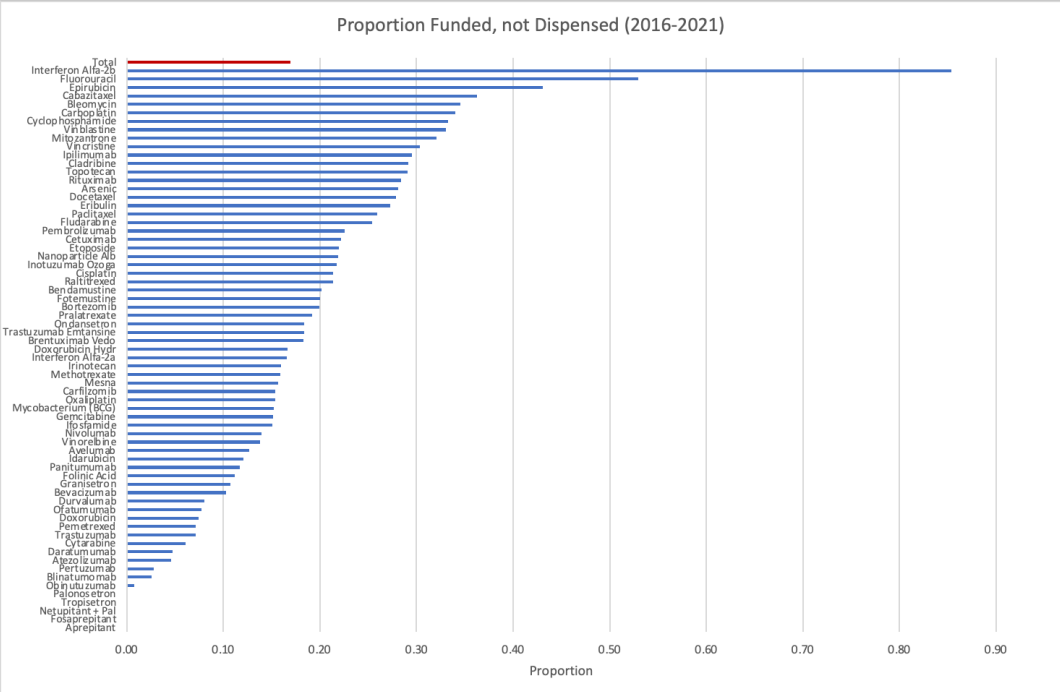
Analysis of total vials funded showed 18.88 million vials of drug were funded over the observation period. Of that supply, 3.19 million (17%) were funded but not dispensed; that is, the total quantity of vials funded exceeded that required to provide the prescribed dose by 17%. This is shown for each molecule available in Figure A70.

Of the molecules with supply funded but unused, Interferon Alfa-2b recorded the highest proportion, but this was based on a low volume of use (and this molecule is no longer PBS listed). Flourouracil was the next highest with 54% of supply funded but unused, followed by epirubicin (43%) and a number of molecules with approximately one third of supply funded but unused (mitozantrone, vinblastine, cyclophosphamide, carboplatin, bleomycin and cabazitaxel). The data also show that for a range of products, there was no supply funded but unused across a range of anti-emetics; this is to be expected as these are supplied as oral products as EFC related benefits. A similar pattern of funded supply with unused drug was observed for the most recent fiscal period (2020-21; see Figure A71).

Discussion: What can be observed from these data is that the basis on which drug is funded via the PBS (the strength used to estimate the most efficient combination of vials) results in a funding of drug in excess of that required to constitute prescribed doses (on average 17%).

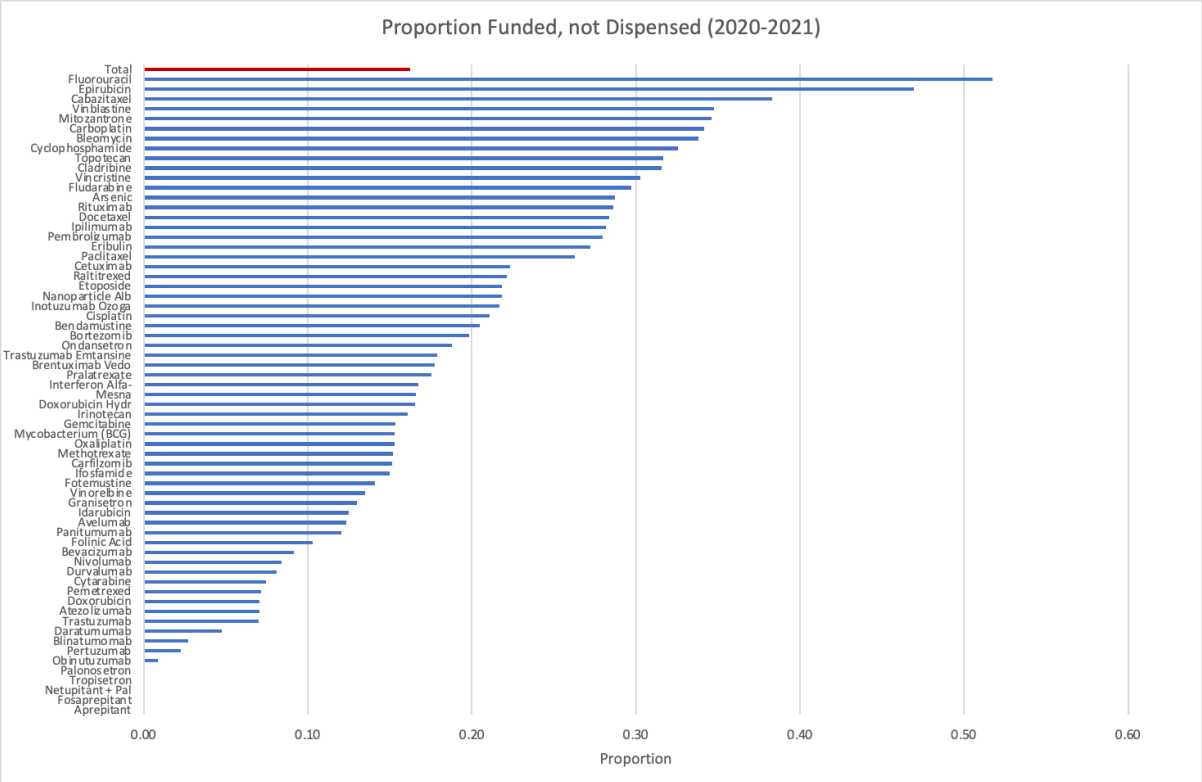
It is not possible from these data to discern the extent to which some of this wastage may be associated with the practice of vial-sharing (potentially resulting in the PBS paying twice for the same volume of drug 'wasted'). Existing data systems do not provide visibility of the extent to which vials claimed have been shared across individual preparations. Although it is possible to identify instances in which vials have been claimed by the same supplier—and even on the same date—it is not possible to infer that co-supply within a day constitutes vial-sharing (or that vial-sharing does not occur across multiple dates, as permitted by molecule stability). Thus, this data cannot be used to estimate the impact of vial-sharing on the funding of waste within the EFC.

Figure A70. Proportion of vials funded but not dispensed (2016 - 2021)



Source: Developed for this Review using PBS line level data.

Figure A71. Proportion of vials funded but not dispensed (fiscal year 2021 - 2021)



Source: Developed for this Review using PBS line level data.

Appendix 13. Comparison of Findings & Recommendations Across Reviews

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
Chemotherapy as a 'specialty service' 1. Short-term: Modify the EFC legislative instrument to recognise that the program funds more than chemotherapy and intravenous cancer medications. Consideration should be given to the following suggestions: (1) 'Efficient Funding of Cancer Medicines'; (2) 'Cancer Medicines Funding Program' 2. System change: Investigate system changes with respect to alternative funding mechanisms for the delivery of cancer medicine services that better integrate all aspects of the care pathway (including assessment for treatment, treatment preparation and delivery, and follow-up care). (see Sections 3.1.1; 3.2.1; 4.1.5)		
Service Viability 3. System change: Consider the potential for the Commonwealth to purchase medicines directly from manufacturers as a means of increasing system efficiency and reducing pharmacy/hospital exposure to cost pressures associated with purchasing and carrying EFC-listed stock. (see Sections 3.2.2; 5.1.1; 6.3.6)	• The excessive margins available on the cost of chemotherapy medicines has provided the capacity for pharmacists to develop and sustain a variety of complex business models, with varying levels of efficiency (Section 12, p. 33)	

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
EFC Fee Remuneration		
4. Short-term: Maintain the EFC's extant fee structure and level as currently legislated, subject to indexing arrangements. 5. Long-term: Consider amending the EFC fee components and levels (subject to an analysis of stakeholders' empirical cost data) to add specific payments with respect to infusion devices, repurposing/reissue of compounded medicines, and the provision of cancer medicines in rural areas. 6. Long-term: Consider amending the EFC distribution fee in lieu of a specific wholesaler payment (potentially as part of future negotiations of the Community Services Obligation). (see Sections 3.2.2; 4.1.6; 4.3.1; 4.3.2; 4.3.3; 5.1.1; 5.1.2; 6.1.1; 6.1.2; 6.3.5)	• Data provided by a small number of dispensing pharmacies (dispensing 35 per cent of all chemotherapy infusions) indicate that the current remuneration for PBS costs (without the interim $60.00 fee) associated with chemotherapy dispensing may be inadequate for some providers (while being sufficient for others). Additionally, the remuneration available underEFC arrangements does not align with the source of costs for chemotherapy infusions. • However, the limited reliability and generalisability of the data means that the quantum ofany required additional fee is uncertain. (Section 14, p. 48) • While the standard device for delivery of chemotherapy infusions is the IV bag, there are also a number of devices which can be used in various situations of the oncologist and patient prefers. • Where a particular device is essential for the delivery of the medicine, this is taken into account by the PBAC in assessing the cost-effectiveness of medicines submitted for listing. However, the cost of these devices is not included in the ex-manufacturer price as the PBS isnot responsible for funding such choices. • As new devices are developed, funding for devices will become more of an issue for hospitals and private health insurers.	• The dispensing fee determined as part of any future negotiations between the Australian Government and the body representing the majority of pharmacy owners (The Pharmacy Guild of Australia), should be based on: (a) an agreed fee that represents the cost of maintaining a viable community pharmacy network in Australia and which meets the requirements of the National Medicines Policy and the expectations of the Australian community and government; and (b) the best available information to both parties at the time of the negotiation and commensurate with the information required of other primary healthcare professionals in determining remuneration levels. (Recommendation 5-2).

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
	(Section 19, p. 64) • Exceptional freight costs can be an issue for facilities providing chemotherapy services in regional centres. This is particularly an issue when short shelf-life medicines require immediate delivery. • Regional public hospitals are provided with additional funding to cover different costs in theIHPA costing models. Private health insurers also consider regionality in determining funding for private hospitals. (Section 20, p. 67)	
EFC Administrative Burden		
7. Short-term: Continue operation of the Medicare Prescribing chart for online prescribing and claiming. 8. Short-term: Expand the medicines covered under the EFC to include all compounded cancer medicines listed for cancer indications on the PBS. 9. Short-term: Develop an education program targeting all system stakeholders to focus on: (1) PBAC cost-effectiveness recommendations, including the setting of PBS restrictions; (2) item coverage under extant EFC arrangements. (see Sections 3.2.2; 3.2.3; 3.2.4; 4.1.3; 5.1.3; 6.1.1)	• There is the capacity to reduce administrative burden, including through the expansion ofthe paperless claiming model and changes to streamlined authorities. (Section 17, p. 59) • Many stakeholders have raised concerns with the way the retail mark-up for pharmacies is calculated for EFC reimbursement, although it is consistent with the remainder of the PBS. • The issue is the difference between the expected retail mark-up and the mark-ups calculatedusing the PBS method. Pharmacies expect that the retail mark-up will be calculated based on the amountdispensed. However, actual retail mark-ups across the PBS are derived using the maximum amount/quantity of the medicine (on a per	

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
	vial/pack basis), then applied according tothe specific vials/packs that are required for the prescription (which can be less than the maximum amount/quantity). (Section 18, p. 62) • Some stakeholders would find value in clarification from DHS on the PBS business rules andin changes to the DHS automatic payment threshold. (Section 21, p. 68)	
Compounding		
10. Short-term: Payment of the CCPS should be: (1) expanded to all (TGA and non-TGA licensed) compounding facilities, subject to annual review of compliance with relevant regulatory guidelines and best practice (Pharmacy Board Guidelines/USP 797); (2) uncoupled from service volume and made on an annual grant basis. 11. Long-term: Investigate the requirements and feasibility of establishing a National Centre for Stability Testing to increase the shelf-life of compounded products under conditions replicable by local compounders. (see Sections 4.1.1; 4.1.5; 4.3.3; 5.1.1; 6.3.4)		• There should be a no difference in the remuneration paid by the Australian Government for the compounding of chemotherapy medicines in any facility that meets the minimum quality and safety standards. In particular, there should be no additional payment for medicines prepared in a facility that meets or exceeds the minimum standards (Recommendation 10-2) • Existing practice models in place in public hospitals for limited trade of medicines prepared onsite should be considered for providing greater access to chemotherapy arrangements. (Recommendation 10-3)

2021 Review - Recommendation | *2013 Review Findings* | *King Review - Recommendations*

Wastage (and vial-sharing)

12. Short-term: Continue the current system of reimbursement based on the most efficient combination of vials.
13. Medium-term: Investigate the introduction of a PBS Dose-Banding chart for cancer medicines to facilitate ease of prescribing within bands (with an aim to reduce wastage on a per-patient basis). Reimbursement would continue based on the most efficient combination of vials (ad-interim).
14. Long-term: Adopt a per-mg reimbursement model as the most efficient use of cancer medicines and to potentially reconcile sales with manufacturers. This is predicated on broader system change with respect to the interface between PBS reimbursement for drug supplied and the flow of funds to states for hospital funding through the Australian Hospital Agreements.
15. Medium-term: Upgrade PBS data collection and reporting systems to ensure information on the form and strength of vials used in estimating the most efficient combination of vials can be readily extracted from the system.
16. Long-term: Serialise vials to facilitate reconciliation of drugs transacted with PBS claims. Feasibility of such an arrangement is subject to requisite infrastructure (e.g., sterility-compliant scanning devices in compounding facilities, pharmacy scanning software) and financial capital investment.
17. System change: Consider the potential for the Commonwealth to purchase medicines directly

- Reimbursement amounts received for discounted brands of chemotherapy medicines havebeen used to fund other non-PBS, non-dispensing activities, including clinical pharmaceutical services, clinical trials and devices.
- Like all PBS medicines, the reimbursement paid for EFC medicines is intended to cover thecost of dispensing the medicine itself. PBS funds are not intended to fund other activities, and any business model that relies on redirecting PBS funds to maintain viability is inherently unsustainable.

(Section 13, p. 35)

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
from manufacturers as a means of increasing system efficiency and more directly align the purchase and reimbursement of PBS medicines. (see Sections 4.1.1; 4.1.2; 4.2.1; 4.2.2; 4.2.3; 5.1.1; 6.1.2; 6.1.5; 6.3.2; 6.3.4; 6.3.5; 6.3.6)		
Patient Access and Safety		
18. Short-term: Remove the distinction between public and private hospital prescribing to rationalise co-payments. 19. Short-term: Expand the availability of Closing the Gap arrangements to all eligible Indigenous peoples accessing cancer medicines. 20. Short-term: Extend the current co-payment arrangements for EFC Schedule I medicines to Schedule II medicines to ensure patients are not differentially affected by co-payments. 21. Medium-term: Conduct a system-wide consultation (State/Territory/Commonwealth Governments and peak cancer care/consumer organisations) to consider initiatives that may improve access to quality cancer care. (see Sections 3.2.1; 5.2-5.4; 6.3.3)	• Key issues for consumers are safety and quality, equity of access and cost to the consumer. • Consumers consider that the funding arrangements could be made more transparent and lesscomplex, with scope for improving accountability and cost-effectiveness. (Section 15, p. 52).	
Standards (Pharmacy)		
22. Short-term: The Review reiterates the findings of the King Review (2017) and recommends the application of a nationally consistent set of standards to the compounding and supply of cancer	• There is an extensive range of guidelines and standards that apply to chemotherapy services, but no existing agreement on a consistent set of standards. • Third-party compounders are licensed by the	• There should be a clear and uniform minimum set of standards for all approved chemotherapy compounding facilities. These minimum standards should: (a) be developed based upon current Good Manufacturing Practice and the

2021 Review - Recommendation	*2013 Review Findings*	*King Review - Recommendations*
medicines. (see Sections 4.1.1; 4.1.4; 4.1.6; 4.3.3; 6.3.4)	TGA however pharmacies that compound in-house are not monitored to the same extent. • Training opportunities vary and there is a recognised need among stakeholders for formalaccreditation. • Any changes to the existing standards, training requirements or licensing requirements could improve the quality and safety of preparation and dispensing in Australia but would also be very costly for the sector. For some providers, particularly smaller ones, these costs may be prohibitive to continued provision of chemotherapy services. • There is a greater role for the sector to play in establishing and enforcing common standards. (Section 16, p. 55)	Pharmacy Board of Australia compounding standards, therefore ensuring all Therapeutic Goods Administration licensed facilities will meet the minimum standards; (b) not require that a compounding facility be Therapeutic Goods Administration licensed to meet minimum requirements; (c)reflect the various settings that are appropriate for the preparation of chemotherapy medicines, including 'urgent' preparations in a hospital or community pharmacy setting; and; (d) detail specific and measurable requirements that will be audited to maintain approval to operate as a chemotherapy compounding facility. • The Pharmacy Board of Australia, or appropriate regulatory authority, should be adequately resourced to monitor compliance with these national standards. (Recommendation 10-1)
Public vs Private Providers 23. Short-term: Remove the distinction between (s94) public and private hospital settings with respect to PBS item codes. 24. Short-term: Remove the distinction between (s94) public and private hospital providers with respect to the EFC fees paid for the supply of cancer medicines. (see Sections 4.1.1; 4.1.5; 5.1.2; 6.3.3)		• The Highly Specialised Drugs Program under section 100 of the National Health Act 1953 (Cth) should be reformed to remove the distinction between section 100 (Community Access) and other medicines listed under section 100 Highly Specialised Drugs arrangements. This should include, for example, harmonising access and fees regardless of where the medicine is dispensed. (Recommendation 7-3)

Appendix 14. Comparison of International Standards for the Compounding of Sterile Preparations

A comparison of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and United States Pharmacopeia (USP) 797 standards as they pertain to the sterile compounding of (cytotoxic) drugs for administration to single patients by injection or infusion is provided in Table A68.

Table A68. Comparison of international compounding standards

	PIC/S Guide to good practices for the preparation of medicinal products in healthcare establishments	*USP <797> Pharmaceutical Compounding—Sterile Preparations*
	General	
Version	PE 010-4	-
Date	1 March 2014	Proposal based on the version of the chapter official as of 1 May 2020
Purpose	Provide guidance on Good Practices on the preparation of medicinal products for human use.	Describe the minimum standards to be followed when preparing compounded sterile preparations (CSPs) for human and animal drugs. Requirements must be met to ensure the sterility of any CSP.
Scope	Applies to the preparation of medicinal products normally performed by healthcare establishments (industrial manufacture) for direct supply to patients	Applies to compounding all categories of CSPs. USP has no role in enforcement.
Hazardous drugs	Not differentiated. Laminar flow cabinets (LFCs) are not suitable for the peraprtion of hazardous drugs. Biohazard safety cabinets (BSCs) should be used instead, with a downward air flow exhausting vertically from the cabinet and not towards to operator.	Handling of sterile hazardous drugs (HDs) must additionally
Definintions	Use of technical terms and their definition were different between the two documents, and thus difficult to compare.	
QA and QC	QA effectiveness and its suitability should be assessed regularly. QA ensures (but not limited to) production and control operations are clearly specified and implemented according to the principles of Good Preparation Practice and documentation systems are in place and maintained.	QA and QC programs must be formally established and documented in SOPs that ensure that all aspects of the preparation of CSPs are conducted in accordance with the requirements in this chapter and laws and regulations of the applicable regulatory jurisdiction.
Personnel—training and continued education	Production should be performed by trained personnel. Personnel should receive initial and continuing training, including necessary hygiene instructions. New personnel should receive training in all areas and continuing education of personnel should be given and documented.	A designated person(s) must oversee the training of personnel and ensure that any person who enters the sterile compounding area and/or handles CSPs completes training and demonstrates competency in maintaining the quality of the environment. All compounding personnel must complete training and be able to demonstrate knowledge of principles and competency every 12 months.
Environment	Clean areas for the preparation of sterile products are classified in 4 grades	Three categories of CSPs: Category 1, 2, and 3, based on the state of

classification	(A, B, C and D) according to the required characteristics of the environment	environmental control under which they are compounded, the probability for microbial growth during the time they will be stored, and the time period within which they must be used. Category 3 CSPs undergo sterility testing.
	Premises	
General requirements	Premises and equipment should be appropriately designed, built, used, maintained and upgraded. The design should enable thorough cleaning. The design should enable thorough cleaning. Dedicated rooms should be provided for hazardous products (e.g., cytostatics, penicillins, biologicals, radiopharmaceuticals, blood products). Weighing and sampling areas should be sufficiently separated from other preparation areas in order to avoid cross-contamination.	Sterile compounding facilities must be designed, outfitted, and properly maintained. The anteroom, buffer room, and SCA must be separated from areas not directly related to compounding. The anteroom and buffer room must be appropriately controlled to achieve and maintain the required air quality classifications.
Airlock	Sterile preparations should be carried out in clean dedicated areas that have airlocks to allow the entry of personnel, materials and equipment. Changing rooms should be designed as airlocks.	Airlocks and interlocking doors may be used to facilitate better control of air balance between areas of differing ISO classification (e.g., between the buffer room and anteroom) or between a classified area and an unclassified area (e.g., between the anteroom and a hallway). If a pass-through is used, both doors must never be opened at the same time, and doors should be interlocking.
	Monitoring	
Classified area tests	Recommended frequencies for classification tests "at rest."[a] Laminar flow cabinets/biohazard safety cabinets: Particle counts: yearly Room air change per hour: yearly Air velocities on workstations: yearly HEPA filter integrity checks: yearly Isolators: Isolator alarm function tests: yearly Isolator leak test: yearly HEPA filter integrity check: yearly	Compounding areas must be certified according to the current Controlled Environment Testing Association (CETA) Certification Guide for Sterile Compounding Facilities or equivalent guidelines. Recertification must be performed at least every 6 months and include: Airflow testing HEPA filter integrity testing Total particle count testing Dynamic airflow smoke pattern test
Microbiological monitoring	Direct working environment (Grade A): Settle plates: every working session Glove finger dabs: at end of each working session Surface samples: weekly Active air samples: quarterly Background environment: Settle plates: weekly	Microbiological air and/or surface monitoring must be conducted in all classified areas during dynamic operating conditions. Frequency (Category 3 CSPs): Air sampling: at least monthly Surface sampling: at least weekly Gloved fingertip and thumb sampling as part of garbing competency: at least every 3 months Media-fill test as part of competency testing in aseptic manipulation: at

	Glove finger dabs: at the end of each working session Surface samples: monthly Active air samples: quarterly	least every 3 months
	Recommended limits b for microbiological monitoring of clean areas (Grade A):[b] Air sample (cfu/m^3): < 1 Settle plates (90 mm; cfu/4 hours)[c]: < 1 Contact plates (55 mm, cfu/plate): < 1 Glove print; 5 fingers (cfu/glove): < 1	The cause must be investigated, and corrective actions must be taken if levels during monitoring exceed (ISO Class 5 criteria)[d]: Air sampling (cfu/m^3 of air/plate): > 1 Surface sampling (cfu/device): 3[e] Gloved fingertip and thumb sampling after garbing (cfu, total from both hands): > 0 Gloved fingertip and thumb sampling after media-fill testing (cfu, total from both hands): 3
Physical monitoring	Limits of controlled areas and devices (Grade A): Maximum permitted number of airborne particles/m^3 (at rest or in operation): ≥ 0.5 µm: 3,520 ≥ 5.0 µm: 20 Air-flow velocity (m/s; +/- 20%): 0.3 for vertical laminar flow	Based on ISO standards for air quality in controlled environments. Limits for number of particles ≥0.5 µm measured under dynamic operating conditions ISO Class 5 (particle/m^3): 3,520 Air-flow velocity: sufficient to sweep particles away from critical sites and maintain unidirectional airflow during operations

Abbreviations: cfu = colony-forming units; CSP = compounded sterile preparation; HD = hazardous drugs; ISO = International Organisation for Standardisation; mm = millimetre; m/s = metre per second; QA = Quality Assurance; QC = Quality Control; USP = United States Pharmacopeia; SCA = segregated compounding area

Notes: [a] At rest conditions defined as complete installation with production equipment but without personnel i.e. unmanned (p30 PE 010-4); [b] Average values; [c] Individual settle plates may be exposed for less than 4 hours in which case the limits should be appropriately reduced; [d] A biological safety cabinet used to prepare a CSP much be capable of providing and ISO Class 5 or better environment for preparation of the CSPs; [e] An attempt must be made to identify any microorganism recovered to the genus level with the assistance of a microbiologist.

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