Australian Government
Department of Health

PBS Post-market Review Framework - Revised October 2022

Information for Stakeholders

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Abbreviations

Abbreviation	Full Name / Wording
COIs	Conflicts of interest
DUSC	Drug Utilisation Sub-Committee
ESC	Economics Sub-Committee
GP	General practitioner
HTA	Health technology assessment
MA	Medicines Australia
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PMR	Post-market Review
PSCR	Pre-sub-committee response
ToRs	Terms of Reference

Background

In 2015, the Australian Government introduced Pharmaceutical Benefits Scheme (PBS) Post-market Reviews (PMRs) as a systematic approach to monitoring medicines following PBS listing, to inform decision making relating to ongoing access and subsidy. PMRs provide evidence and options to the Pharmaceutical Benefits Advisory Committee (PBAC) on continued access, investment, or disinvestment in PBS-listed medicines.

PMRs fall under the quality use of medicines objective of the National Medicines Policy framework. This includes promoting the safe and effective use of medicines, with the aim to improve health outcomes for all Australians.

PMRs were established under the 2011-12 Budget measure *Improving sustainability of the PBS through enhanced post-market surveillance*.

The PMR program was established to contribute to:

- Ensuring the ongoing viability of the PBS through targeted medicines usage and avoiding preventable wastage or inappropriate prescribing.
- A better understanding of medicines utilisation, to review intended clinical benefit and inform medicines evaluation processes.
- Ongoing cost-effectiveness, including through better management of clinical and economic uncertainty.
- Overall improvements to the quality use of medicines and education for patients and health professionals.

Details of current and completed PMRs are available on the PBS website. A recent example is the PMR of medicines for smoking cessation. Following consideration of the evidence and consumer input, the PBAC recommended changes to the PBS restrictions for nicotine replacement products, including subsidised access to concurrent use of two forms of nicotine replacement therapy (See the outcome statement for more information).

In 2022, the PMR framework was reconsidered in the context of the new Strategic Agreements between the Commonwealth, Medicines Australia (MA) and the Generic and Biosimilar Medicines Association (GBMA).

Under the new Strategic Agreements, the Commonwealth and MA agreed to:

> "*Work together with other relevant stakeholders to improve the current PMR framework with the goal of reducing the timeframe from PBAC recommendation of the commencement of a Review, to completion of the Review, to a timeframe of within 12 months, subject always to the framework not limiting PBAC independence*."

Introduction

When a medicine is recommended for PBS listing, the PBAC's advice is made in the context of the treatments and evidence available at that point in time. Over time, new medicines may be developed and subsidised, more data on safety and efficacy may become available and treatment guidelines may change. As a result, the actual use and/or benefits of a medicine may change and may no longer reflect the evidence considered by the PBAC at the time of recommendation for listing.

The PMR framework provides a mechanism for medicines to be re-considered in the current treatment context. It provides a transparent and formal approach to the ongoing evaluation of medicines subsidised by the Australian Government through the PBS. This includes consideration of actual utilisation, comparative efficacy, cost-effectiveness, treatment guidelines, health benefits and consumer experiences. As a result, the PMR framework allows for measures to be implemented to address concerns around how a medicine is used that may have arisen since the time of listing such as, improving education around medicines and their use, or revising subsidy arrangements.

PMRs are overseen by the PBAC and its sub-committees. Further information regarding the PBAC and its sub-committees is provided below.

Pharmaceutical Benefits Advisory Committee (PBAC)

The PBAC has a broad statutory function under the *National Health Act 1953*, to advise the Minister for Health and Aged Care on any matters concerning the operation of the PBS, which includes making further recommendations regarding the safety, effectiveness, and cost-effectiveness of medicines after they have been listed. Therefore, the PBAC also considers the need for, and provides recommendations on PMRs.

The PBAC is an independent expert body appointed by the Australian Government and is comprised of doctors, health professionals, health economists and consumer representatives. The PBAC meets regularly throughout the year, per the PBS calendar, to consider applications for funding new medicines. The PBAC Executive is comprised of the Chair and Deputy Chair of the PBAC, the Chair of the Drug Utilisation Sub-Committee, the Chair of the Economics Sub-Committee, and a consumer nominee from the PBAC. The PBAC Executive meets in the lead up to each regular PBAC meeting to review less complex submissions such as category 3, category 4 and committee secretariat submissions, and to consider other matters.

The PBAC is responsible for evaluating the clinical and cost-effectiveness of medicines in order to make recommendations relating to listing on the PBS. Recommendations for new listings are informed by evidence of a medicine's clinical effectiveness (how well it works), safety, and cost-effectiveness ('value for money') compared with other treatments.

The PBAC has two sub-committees to assist with analysis and advice in these areas: The Drug Utilisation Sub-Committee (DUSC) and the Economics Sub-Committee (ESC).

Additional information relating to the PBS, PBAC meeting dates, agendas and outcomes is available on the PBS website.

Drug Utilisation Sub-Committee

The DUSC assesses estimates on projected usage and the financial cost of medicines to be considered for listing on the PBS. It also collects and analyses data on actual use of PBS-listed medicines (including in comparison with other countries).

New medicines on the PBS are routinely monitored by the DUSC 24 months after listing. Monitoring may include analyses to examine the actual use of a medicine and medicine utilisation trends in comparison to the predicted usage when recommended by the PBAC and listed on the PBS. The DUSC can also analyse the utilisation of a class or category of medicine, or a group of medicines that are used to treat a particular condition and compares these with the basis of PBS listings. These analyses can highlight medicines use issues that need to be considered by the PBAC, which may result in a recommendation for further research and consultation according to the PMR framework.

The DUSC meets three times a year, in February, June and October, and is constituted by a broad range of experts, such as clinicians, academics, a consumer representative and an industry representative from MA.

Additional information relating to the DUSC is available on the PBS website.

Economics Sub-Committee

The ESC of the PBAC assesses clinical and economic evaluations of medicines submitted to the PBAC for listing and advises the PBAC on the technical aspects of these evaluations.

Clinicians and academics with relevant expertise, and an industry representative from MA, are members of the ESC. The ESC meets the week following the DUSC, three times a year.

Additional information relating to the ESC is available on the PBS website.

Additional Information

Public announcements and general PMR framework information for each PMR will be communicated on the Post-market Review webpage and via PBS News Updates.

Stakeholders are encouraged to subscribe to PBS News Updates for the latest information and to be advised of the timing and processes for each PMR.

Information on consultation processes for medicines and vaccines can be viewed at Office of Health Technology Assessment (OHTA) consultation hub.

Revised Pharmaceutical Benefits Scheme Post-market Review Framework

The draft framework described in this document relates to PMRs for medicines listed on the PBS. However, PMRs can be conducted for a range of other health technologies and health-related initiatives, policies, and programs.

The framework described in this document (illustrated at Figure 1 and Figure 2), outlines the revised approach to PMRs and estimated time frames.

Figure 1 illustrates the activities preceding a PMR. This includes compilation and consideration of potential PMRs through to ministerial approval of the commencement of a PMR.

Figure 2 illustrates the PMR process. This includes the steps from when the Review Terms of Reference (ToRs) are approved by the PBAC, through to PBAC consideration of the draft PMR Report and the post-review process.

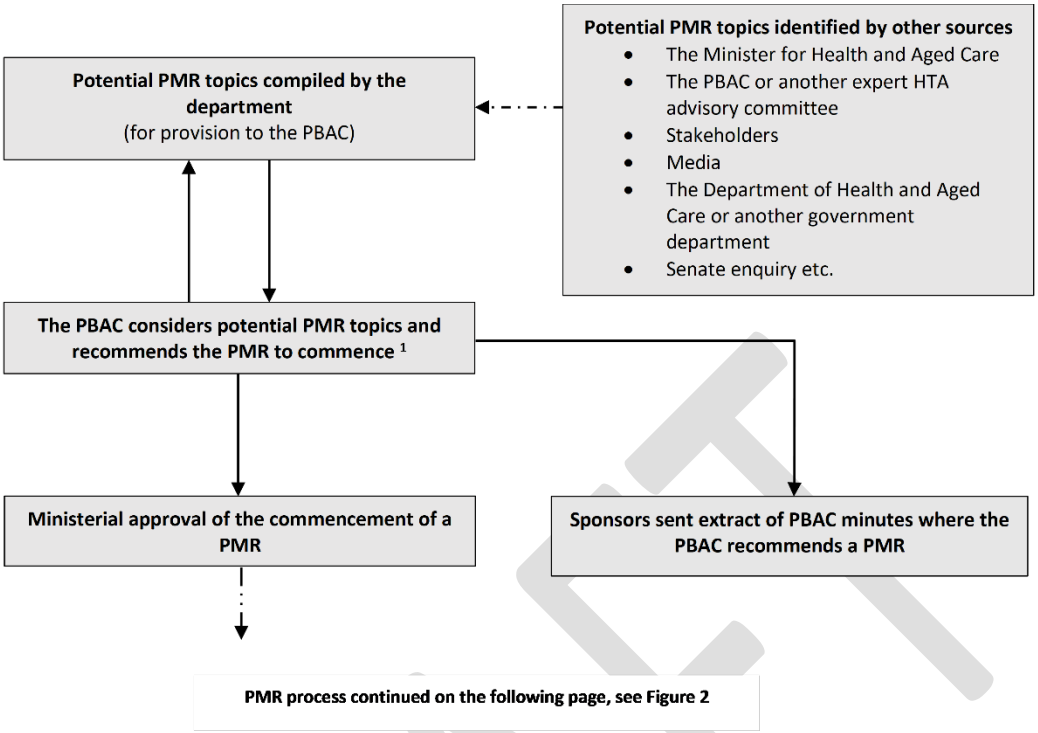
According to the framework outlined in this document, a PMR is considered to have commenced when the PBAC approves the Review ToRs.

The PMR framework is not intended to be prescriptive, as PMRs will differ in their complexity and focus. The framework promotes consistency in approach, while providing the flexibility necessary to accommodate the different requirements of each Review.

The estimated time for completion of key PMR milestones, from approval of the Review's ToRs to PBAC consideration of the draft PMR Report, is 52 weeks (Figure 2). Information on timeframes for each PMR will be communicated via PBS News Update and published on the Post-market Review webpage as it becomes available. Consumers, health practitioners and any other interested groups or organisations can provide input to PMRs by visiting the Office of Health Technology Assessment (OHTA) consultation hub.

An ongoing PMR does not interrupt or prevent the submission processes for seeking subsidy of new or amended listings of medicines on the PBS. However, new medicines that are recommended for PBS listing during the course of a PMR may be affected by any subsequent recommendations arising from the Review.

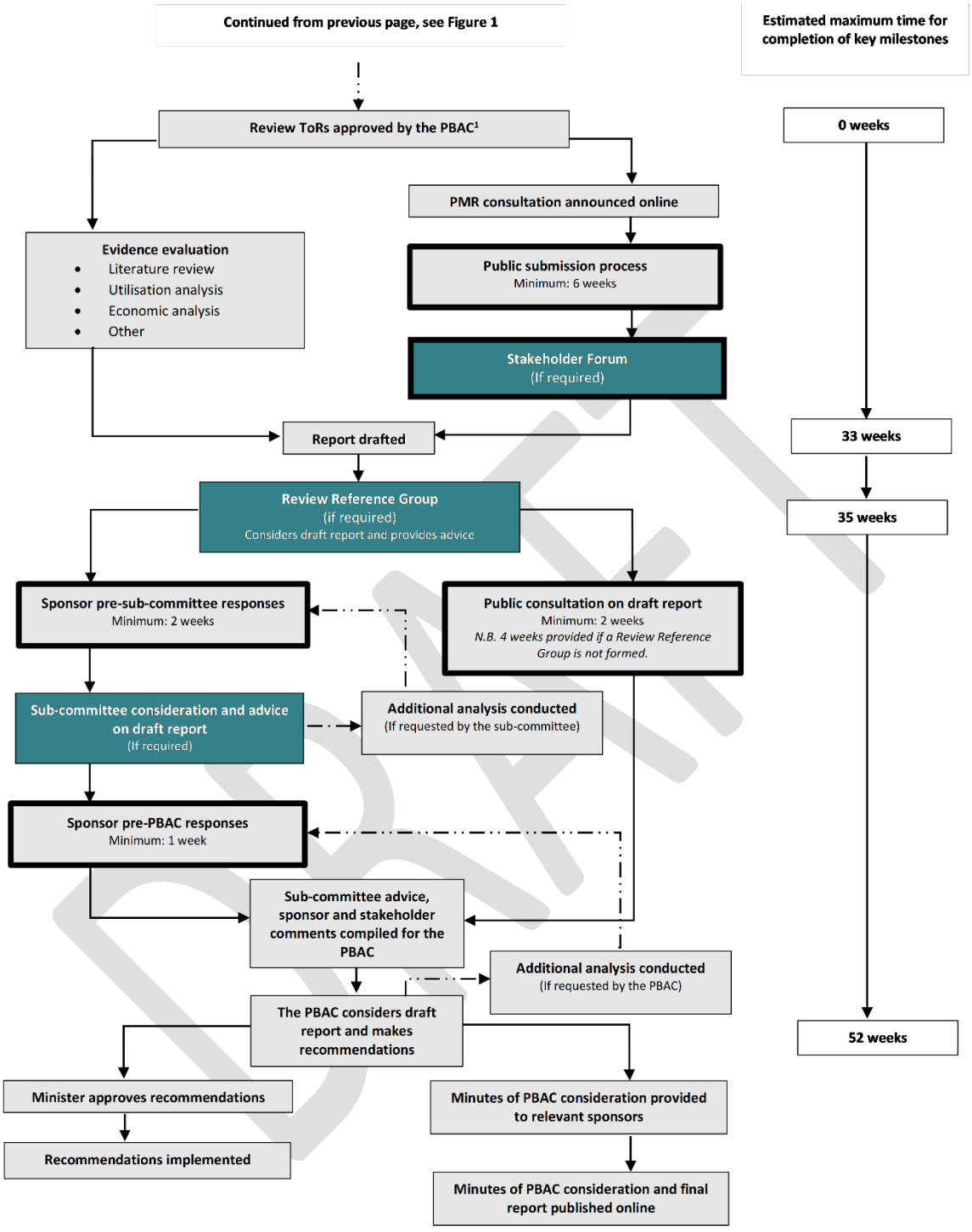
Figure 1. Activities preceding a Post-market Review



Abbreviations: HTA = health technology assessment; PBAC = Pharmaceutical Benefits Advisory Committee; PMR = Post-market Review

[1] At this stage, the PBAC will also be asked to advise on the Review's Terms of Reference (ToRs) as prepared by the department.

Figure 2. Post-market Review Process



Abbreviations: PBAC = Pharmaceutical Benefits Advisory Committee; PMR = Post-market Review; ToRs = Terms of Reference

[1] At this stage, the PBAC will also advise on whether a stakeholder forum should be held and whether a Review Reference Group should be formed as part of the PMR.

Notes:
1. A box with a thick border indicates an opportunity for stakeholder and/or sponsor input into the PMR process.
2. A blue/green coloured box indicates an optional step in the PMR process that will only proceed if required.

Activities Preceding a PBS Post-market Review

Sources of Potential Post-market Reviews

A PMR may involve a single medicine, a class or category of medicines, or multiple classes of medicines that are used to treat a particular condition. PMRs may be initiated at any time, and be triggered by a number of issues including, but not limited to:

- clinical efficacy and safety
- use that is inconsistent with treatment guidelines and emerging clinical data
- use outside of listing restrictions/subsidy arrangements
- cost-effectiveness.

These issues can be identified through a number of sources, including:

- stakeholders such as clinicians, patients, and industry
- the PBAC (or a PBAC sub-committee)
- a request by the Minister for Health and Aged Care
- an academic publication or media release
- a health technology assessment (HTA) evaluation group
- another area of the department such as the Therapeutic Goods Administration (TGA), Services Australia, or another government department/agency
- a Senate Inquiry.

Recommendation for a Post-market Review by the PBAC

The department will provide information on potential PMR topics to the PBAC. This may include information regarding data sources following consultation with data stewards and/or experts in observational research.

The PBAC considers the potential PMR topics and is responsible for:

- making a recommendation to the Minister to commence a PMR
- providing advice on a Review's ToRs.

In response to potential PMR topics raised by other sources, the department may conduct or contract preliminary research, such as a literature review or an analysis of utilisation, to be provided to the PBAC (or sub-committee) to support the PBAC's (or its sub-committee's) consideration of potential PMRs. Alternatively, the PBAC may itself identify a potential issue that could lead to a PMR and request further research or evidence on an issue prior to making a recommendation to commence a PMR.

The committee will prioritise PMR topics and make a recommendation on the PMRs to be progressed based on a range of factors including, but not limited to:

- urgency relating to a safety concern
- urgency relating to a quality use of medicines concern

- urgency relating to a gap in service provision, e.g., where there is new evidence which could lead to an expansion of a service or funding (or the converse)
- potential impact to the health budget
- data availability to investigate identified issues
- the ability of the department and the PBAC to resolve identified issues
- the priorities of the Australian Government and the department.

The PBAC will provide advice to the department on the content of the Review ToRs and the research questions to be associated with each ToR at this stage.

An extract of the minutes that includes the PBAC's consideration of the PMR topic and any resulting recommendation to undertake a PMR, will be provided to relevant medicine sponsors. This will serve as an early notification that a PMR has been recommended by the PBAC and will commence when, and if, the Minister agrees.

Ministerial Approval of the Review's Commencement

Following a PBAC recommendation for a PMR to commence, the Minister will be asked to consider the commencement of the Review. Relevant sponsors will be advised of the Minister's decision.

PBS Post-market Review Process

Approval of the Review Terms of Reference by the PBAC

The ToRs for each PMR outline the key issues and guide the focus of the Review and the research questions to be addressed in collating the evidence.

The department will further develop the Review's ToRs by providing supporting information such as potential research questions, sources of evidence and previous consideration of the medicine/s by the PBAC (or sub-committee). The Review ToRs will be provided to the PBAC for consideration and final approval. The PBAC will also be requested to advise on whether a Stakeholder Forum should be held and/or a Review Reference Group formed as part of the PMR.

A PMR is considered to have commenced upon PBAC approval of the ToRs.

Minister informed of the Review's Terms of Reference

Once the ToRs for the PMR have been approved by the PBAC, the Minister will be informed.

Stakeholder Communication

There are usually up to three key opportunities for stakeholders to provide input during the PMR process:

- the Public Submission Process addressing the PMR
- a Stakeholder Forum (if required)
- comments on the draft PMR Report (see Stakeholder Consultation on the Draft Report for further details).

In addition to this:

- Where the draft PMR Report is to be provided to a PBAC sub-committee for advice, relevant sponsors are able to provide a Pre-Sub-Committee Response (PSCR) (see Sub-Committee Consideration of the Draft Report for further details) to be considered by the sub-committee alongside the draft Report.
- Relevant sponsors are also given the opportunity to respond to sub-committee advice prior to PBAC Consideration of the Draft Report in the form of a pre-PBAC response.

Role of the Department of Health and Aged Care

The Technology Assessment and Access Division in the department is responsible for the management of PMRs. This includes, but is not limited to:

- managing the process for identifying reviews, either through PBAC or other processes

- providing background information on potential PMRs to the PBAC (and/or its sub-committees)
- drafting ToRs for PBAC consideration
- establishing a Reference Group (if required)
- sourcing and managing contracts for research conducted by external parties
- organising the Public Submission Process and Stakeholder Forum (if required)
- drafting and editing the Report to be presented to the PBAC
- orchestration and management of PSCRs and pre-PBAC responses by sponsors.

Evidence Collation and Evaluation

PMRs consider the most recent, relevant evidence available on the clinical safety, efficacy, and utilisation of the medicine/s of interest, as guided by the ToRs.

During the Public Submission Process of the PMR, stakeholders may provide information on what should be the most appropriate information and evidence considered as part of the Review. It is not necessary for all evidence to be in the same form as that provided as part of initial PBAC listing applications, although it must be robust and defensible. In particular, evidence on the safety and quality use of the medicine/s outside the clinical trial setting is valuable.

Research for a PMR is typically contracted to independent external providers with demonstrated subject matter and technical expertise, selected from a panel of experts maintained by the department. Most PMRs will involve a literature review and/or utilisation analysis. Additional evaluations may involve a systematic literature review, an economic analysis, further utilisation analysis, or other sources of evidence relevant to the Review (see the Appendix for further details).

Public Submission Process

A call for public submissions addressing the PMR is posted on the Post-market Review webpage and communicated via PBS News Update. All interested parties are welcome to make a submission to the Review. The standard submission period is a minimum of six weeks. This is an opportunity for stakeholders to identify additional areas for evaluation, particularly those issues related to how medicines are accessed and used by patients and their clinicians. It also provides an opportunity to present any evidence or data that may inform the PMR, particularly evidence that the PBAC may not have previously considered.

All submissions received are published on the Post-market Review webpage at the conclusion of the public submission period, unless otherwise requested. Where submissions indicate commercial-in-confidence or sensitive personal information, this is redacted before publication.

All stakeholder submissions are made available to the PBAC (and its sub-committees) for consideration with the draft PMR Report.

Stakeholder Forum

Following the public submission process, a stakeholder forum may be held to offer interested parties an additional opportunity to provide input to the PMR. This would particularly be the case in Reviews that are of significant public/consumer interest or complexity.

While the PBAC will initially advise whether a stakeholder forum should be held during the development of the ToRs, stakeholders may also request that a stakeholder forum be held during consultation on the TORs. A stakeholder forum may not be warranted due to the size or scope of the PMR, or because alternative consultation processes are considered more appropriate.

Forums will usually be held via webinar. Discussion is based on focus questions developed around the key points raised during the public submission process or evidence analyses. The forum is an opportunity for stakeholders to provide further comment on and to propose options to address these issues. The department requires all participants of a stakeholder forum to declare any conflicts of interest (COIs) and to sign confidentiality agreements prior to attending the forum.

A summary of the forum is published on the Post-market Review webpage and included in the PMR Report.

Reference Group

A Reference Group may be formed for a PMR to provide independent, expert advice on the draft Report prior to consideration by the PBAC (and its sub-committees). A Reference Group may not be considered necessary if there is sufficient expertise in the membership of the PBAC and its sub-committees to guide the Review in terms of sources of evidence. Where the proposed PMR requires considerable stakeholder input and where there is little trial evidence to answer the ToRs, a Reference Group may be deemed necessary.

The decision to form a Reference Group will be at the department's discretion based on advice received from the PBAC. If a Reference Group is formed for a Review, the number of meetings held will be at the discretion of the Chair of the Reference Group.

The Reference Group consists of members who have expertise in HTA, drug utilisation, health economics, as well as consumer and stakeholder representatives. Reference Group members are also selected for each PMR on the basis of demonstrated relevant expertise. Members of a Reference Group may also include:

- independent specialist clinicians and/or nurse practitioners
- researchers and representatives of peak healthcare professional organisations related to the medicine/s under review
- health educators
- representatives of relevant consumer advocacy organisations

- representatives of industry groups.

The department requires all Reference Group members to declare any COIs and to sign confidentiality agreements prior to joining the Reference Group. As a result of feedback received since the initial framework was established in 2015, information on the membership of the Reference Group for each PMR will be published on the Post-market Review webpage at the beginning of the Review and also included in the final PMR Report.

Stakeholder Consultation on the Draft Report

The draft Report is provided to key stakeholders, including clinicians and consumer groups, and made publicly available on the Post-market Review webpage for comment. The framework provides at least ten working days for stakeholders to submit up to four pages of comments and two pages of tables to the department consistent with the initial PMR framework.

All stakeholder comments on the draft Report are made available to the PBAC for consideration alongside the draft PMR Report. The draft Report may also be revised based on stakeholder feedback where there is an error of fact identified during the consultation process and prior to consideration by the PBAC.

Sub-Committee Consideration of the Draft Report

The draft report will be provided to one or both sub-committees of the PBAC when it contains new evidence relevant to their area of expertise. Sponsors of the medicines included in the PMR will be provided with a copy of the draft Report and given at least ten working days to provide a PSCR. The PSCR is limited to four pages of text and two pages of graphs and tables consistent with the initial PMR framework and PBAC processes for assessing new submissions.

Following the sub-committee meetings, their advice to the PBAC will be provided to relevant sponsor companies to prepare a pre-PBAC response. Consistent with the initial PMR Framework, at least five working days are provided for sponsors to submit up to three pages of text, in response to the sub-committee advice, to the department prior to the PBAC meeting.

The draft Report may also be revised to address certain sub-committee advice.

A PBAC sub-committee may request that additional information or analyses be provided, such as an economic evaluation. The sub-committee may request that the additional information is resubmitted to the same sub-committee for consideration at a later date, a different PBAC sub-committee, or provided directly to the PBAC. Relevant sponsors will be provided with any additional information/analyses once completed and will be invited to submit a PSCR and/or pre-PBAC response.

PBAC Consideration of the Draft Report

The PBAC considers the draft PMR Report, including stakeholder comments, sub-committee advice, sponsor pre-PBAC responses and any Reference Group comments, before making recommendations.

In some cases, the PBAC may request additional work be carried out.

Sponsors of the medicine/s involved in the PMR are contacted after the PBAC meeting and provided with the minutes ahead of the PBAC meeting outcomes being published (six weeks post-meeting).

PBAC recommendations and options for implementation are provided to the Minister for consideration, where they impact on the PBS. The final PMR Report and PBAC minutes are published on the Post-market Review webpage at the conclusion of the PMR.

The PBAC may make a range of recommendations, including:

- taking no action
- changes to PBS restrictions
- measures to improve the cost-effective use of the medicine/s under review
- referral to relevant clinical organisations to update clinical guidelines
- education for health professionals or consumers to improve the quality use of the medicine/s
- a recommendation for a review of other related medicines or issues
- a request for additional information/analyses to be provided
- measures to support deprescribing or delisting from the PBS.

Where the PBAC requests that additional information/analyses be provided to the committee at a later date, relevant sponsors and stakeholders will be provided with the additional information once completed along with an invitation to submit a pre-PBAC response.

Implementation of Recommendations

Recommendations Relating to the PBS

Recommendations relating to the listing of the medicine/s under review are implemented according to standard post-PBAC processes. Under these processes, sponsors are advised of a recommendation following the PBAC meeting and will be followed up by relevant areas of the department.

Other Recommendations

Recommendations made by the PBAC that do not relate directly to the PBS will be referred on for implementation through existing, applicable programs, including through collaboration with state and territory health departments.

Recommendations to improve prescriber and/or clinical provider education may be implemented through relevant professional organisations or other areas of government.

Recommendations for changes to treatment or management guidelines may be implemented through the National Health and Medical Research Council (NHMRC) or in consultation with the external developer of the relevant guidelines.

Recommendations for future research may be referred to the area of the department responsible for administering the Medical Research Future Fund for consideration in future grant rounds.

Appendix

Literature Review

The scope of each literature review is dependent on the requirements of the PMR. However, there is usually a focus on the most recent clinical evidence that the PBAC has not previously considered. The literature review may focus on one, or a combination, of the following areas:

- efficacy of the medicine/s
- comparative efficacy between medicines used to treat the condition of interest
- safety of the medicine/s
- comparative safety between medicines
- clinical guidelines for prescribing/recommending the medicine/s under review or treating the condition of interest
- economic utility or cost-effectiveness.

An initial literature review of previously conducted meta-analyses and additional clinical trials may be conducted by the department or an independent external contractor to provide an overview of the subject area and identify any potential issues. A systematic review may be conducted where a specific research question has been identified.

Utilisation Analysis

Analysis of medicine utilisation provides information on how the medicine/s of interest are being used in practice. Specifically, these analyses can provide information relating to:

- patterns of use (including adherence, persistence, prevalence, incidence, co-prescribing/combination use, switching between alternative therapies, and use of other medicines prior to or following initiation)
- adherence to treatment guidelines and PBS restrictions
- patient access across geographical regions
- other outcomes associated with use of the medicine/s, such as use of other medicines as a proxy for adverse events
- the conditions medicines are being prescribed/recommended to treat.

The most commonly used source of data for analyses of medicine utilisation in Australia is the PBS data set. However, additional data sources may also be used to establish a more complete picture of prescribing and use in Australian clinical practice. These include, but are not limited to:

- Veterans' Medicines Advice and Therapeutic Education Services (MATES)
- Australian Bureau of Statistics (ABS) National Health Survey
- Medicare Benefits Schedule (MBS) data

- MedicineInsight general practitioner (GP) prescriber data
- samples of GP activity
- disease registries
- Australian Institute of Health and Welfare (AIHW) linked datasets.

Economic Analysis

An economic analysis may be conducted as appropriate. This analysis may assess the impact of actual use, or the impact of a Review's proposed changes to actual use, on the cost-effectiveness of the medicine/s under review.

Revised or new economic modelling may be required if there is new evidence available that would change previous assumptions used in the cost-effectiveness model considered by the PBAC. A summary of this analysis is included in the PMR Report.

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All information in this publication is correct as of October 2022.