The Access to Medicines Working Group

Interim Report to Government

July 2008

Access to Medicines Working Group

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Table of Contents

Introduction 3
Membership 3
Executive Summary 4
The Effects of Statutory Price Reductions on the listing of New Medicines 4
Managing Uncertainty in the Assessment of Medicines for listing on the Pharmaceutical Benefits Scheme 4
Streamlining the listing of New Medicines 5
Transparency in the Pharmaceutical Benefits Advisory Committees (PBAC) decision making processes – Publication of PBAC submissions 5
Future Work for the Access to Medicines Working Group 6

List of Attachments

A. The Effects of Statutory Price Reductions on the listing of New Medicines.

B. Managing Uncertainty in the Assessment of Medicines for listing on the Pharmaceutical Benefits Scheme.

C. Streamlining the listing of New Medicines.

D. Transparency in the Pharmaceutical Benefits Advisory Committees (PBAC) decision making processes – Publication of PBAC submissions.

E. Future Work for the Access to Medicines Working Group.

F. Access to Medicines Working Group – Terms of Reference.

G. Access to Medicines Working Group – Work Plan.

Introduction

The Access to Medicines Working Group (AMWG) is an ongoing joint Department of Health and Ageing (DoHA) and Medicines Australia (MA) working group established in 2006 as a result of the reforms to the Pharmaceutical Benefits Scheme (PBS).

The purpose of the AMWG is to:

1. Provide strategic oversight of joint activities undertaken by the Department and Medicines Australia to enhance the PBS processes.
2. Consider issues relating to timely and appropriate access to effective new medicines on the PBS following the PBS reforms.

The full terms of reference for the AMWG are at Attachment F and the current full Work Plan is at Attachment G.

The AMWG has met four times, with the last meeting held on 18 April 2008. The next meeting is scheduled for August 2008. A communiqué from each of the meetings is available on the Department's website.

The AMWG Work Plan identifies 15 projects, grouped under six areas specified in the Terms of Reference. Three current priority areas for consideration have been agreed:

- The effects of statutory price reductions on medicines in Formulary 2 (F2) on the listing of new Formulary 1 (F1) medicines;
- Managing uncertainty of evidence in the Pharmaceutical Benefits Advisory Committee (PBAC); and
- Streamlining the registration process for new medicines.

Membership

The AMWG is composed of the following members

Department of Health and Ageing

- Mr David Learmonth
  AMWG Co-Chair
  Deputy Secretary
- Mr Stephen Dellar
  First Assistant Secretary, Pharmaceutical Benefits Division
- Ms Diana Macdonell
  Assistant Secretary, Pharmaceutical Evaluation Branch
- Mr Andrew Mitchell
  Strategic Advisor, Pharmaceutical Evaluation Branch

Medicines Australia

- Mr Will Delaat
  AMWG Co-Chair
  Chairman of the Board
- Mr David Grainger
  Director, Corporate Affairs and Health Economics, Eli Lilly
- Dr Brendan Shaw
  Executive Director
  Health Policy and Research
  From August 2007
- Mr Ian Noble
  Associate Director, Market Access and Product Support, Merck Sharp & Dohme
  From April 2008

Former Members

- Ms Rosemary Huxtable
  First Assistant Secretary, Pharmaceutical Benefits Division
  From April 2007 to December 2007
- Mr Duncan O'Brien
  Director, Economic Operations
  Medicines Australia
  From April 2007 to August 2007
- Mr Steven Crowley
  Director, Health Economics and Outcomes Research, Janssen-Cilag
  From April 2007 to March 2008

Secretariat support is provided by the Department.

Executive Summary

The major attachments to this report (**Attachment A** and **B)** detail the AWMG's exploration of two areas: the effects of statutory price reductions on the listing of new medicines and managing uncertainty in the assessment of medicines for listing on the PBS. A summary of these papers is provided below.

The Effects of Statutory Price Reductions on the listing of New Medicines

The Department and Medicines Australia, both independently and collaboratively, have examined the possible impacts on the listing process of mandatory price reductions from 1 August 2008 for medicines on the new F2 formulary as part of their discussions through the AMWG. Both parties agree that, in principle, a subset of new medicines seeking listing on the PBS may be impacted in the future as a result of PBS reform.

The AMWG agrees that there should be no departure from the fundamental principle of cost effectiveness in evaluating new medicines. The Department notes that changes that affect cost effectiveness are influenced by many policy changes over time and the price reductions applying from 1 August 2008 are inherently no different from previous policies that lead to pricing changes. These include Therapeutic Goods Premiums, Brand Price Premiums, Weighted Average Monthly Treatment Cost and the 12.5 percent policy, all of which could reduce the price of comparator medicines.

In AMWG discussions, the Department has maintained that any issues that arise will be relatively contained and that the current system of evaluating medicines for listing on the PBS is sufficiently flexible to handle such issues. MA maintains that this is a 'problem', that it will be more widespread and that a way of managing this needs to be agreed now.

Both parties have discussed several options for managing the issue including substituting an F1 comparator for clinical and/or price comparisons where an F2 product would otherwise normally be the comparator.

Managing Uncertainty in the Assessment of Medicines for listing on the Pharmaceutical Benefits Scheme

Uncertainty in the context of Pharmaceutical Benefits Advisory Committee (PBAC) submissions and evaluations refers to areas where the evidence, results or conclusions

provided are unclear, ambiguous or open to various or different interpretations. Uncertainty can impact on four important aspects influencing decision making – clinical, economic, utilisation and financial. As a general rule, the more complex the submission, the higher the likelihood that there will be some areas where there are shortcomings in the available evidence that will need to be considered by PBAC when deciding whether to recommend a medicine be listed on the PBS.

The result of increased uncertainty is an increase in the rate of rejections. This in turn can lead to an increase in the rate of resubmissions, which places a further demand on the resources and analysis required to evaluate the medicine. This in turn can further increase resource demand on industry and the PBAC and can delay the listing of new medicines.

This paper discusses what gaps in the evidence arise in relation to the listing of medicines on the PBS, examines what the PBAC already does to address the gaps and identifies areas where further work may be required. It is accepted that while every effort can be made to minimise uncertainty it cannot be eliminated and therefore the remaining uncertainty needs to be managed. A work plan is being developed around these identified areas for the AMWG to consider at its next meeting in August 2008.

Other papers

The remaining Attachments detail other areas of work of the AWMG.

Streamlining the listing of New Medicines

The AMWG has been examining ways in which the time taken to have new medicines listed on the PBS can be reduced and has received 'in principle' agreement from the TGA on ways to decrease the time to have new medicines registered on the Australian Register of Therapeutic Goods.

The AMWG will also continue to examine ways to both leverage this improvement in regulatory time lines and also build improvements into the PBS process to facilitate earlier times to listing. All parties have agreed this cannot be at expense of rigorous assessment of safety, efficacy and cost-effectiveness.

Increased public input into Pharmaceutical Benefits Advisory Committee Decision making processes: Publication of PBAC agendas

The AMWG has been working on ways to provide better input by interested parties to PBAC deliberations through increasing the transparency in PBS listing processes. To this end agreement in principle has now been reached between DoHA, MA and the PBAC that a version of the PBAC agenda will be made publicly available 4-6 weeks before the relevant meeting. This agenda will be published on the Department's website and will include the generic and trade name of the medicine, the sponsor and the purpose of the submission. No details will be published for submissions intended solely to affect pricing relativities.

This initiative will give interested people and organisations opportunities for direct input into the PBAC, and a better understanding of the decision making process. Discussion is continuing between the Department and MA on the details around implementing this process from mid September for the November 2008 PBAC meeting.

Future Work for the Access to Medicines Working Group

The AWMG has identified two further areas where it would like to direct some future efforts. The first area is developing an improved understanding of the PBAC decision making process. This would help industry by improving its PBAC submissions and would help the PBAC in its decision making.

The second is on gaining a mutual understanding of what innovation means in the drug development process. This would include an examination of the nature of innovation in the pharmaceutical industry and how the incentive of PBS subsidy shapes that innovation.

Attachment A

The Effects of Statutory Price Reductions on the listing of New Medicines

Executive Summary

The Department of Health and Ageing (DoHA) and Medicines Australia (MA) through the Access to Medicines Working Group (AMWG), have examined the possible impacts on the listing process for mandatory price reductions from 1 August 2008 for medicines on the new F2 formulary. Both parties agree that, in principle, a subset of new medicines seeking listing on the Pharmaceutical Benefits Scheme (PBS) may be impacted in the future as a result of PBS reform. In AMWG discussions, DoHA argued the issue will be relatively contained and that the current system of evaluating medicines for listing on the PBS is sufficiently flexible to handle any issues that may arise, while MA suggested that it will be more widespread and argued that changes are needed. Both parties have discussed several options, involving substituting an F1 comparator or F1 price for evaluations where an F2 product is the comparator.

Introduction

This paper presents a discussion by the Access to Medicines Working Group (AMWG) of possible effects of statutory price reductions for Pharmaceutical Benefits Scheme (PBS) Formulary 2 (F2) medicines on the cost effectiveness assessment of new Formulary 1 (F1) medicines seeking PBS listing.

Background

The AMWG, consisting of Department of Health and Ageing (DoHA) and Medicines Australia (MA) members, was established to consider issues relating to timely and appropriate access to effective new medicines on the PBS, and issues resulting from the 2006 PBS reforms.

The AMWG was, amongst other things, tasked with considering "the possible impacts on the listing process for mandatory price reductions from 1 August 2008 for medicines on the new F2 formulary"[1] This paper builds on discussions and analyses on this issue undertaken by MA and DoHA from mid-2006 through to 2008.

Context

PBS Reform

In November 2006, the then Government announced a number of changes to the PBS to protect patients from higher out of pocket costs, get better value from market competition among brands of generic (off-patent) medicines and recognise the importance of world-class life-enhancing drugs to patients. The main change is in the way in which the Government prices medicines that are operating in a competitive market (F2). These medicines will take a series of price drops, and eventually will move to a system where the price they are sold to pharmacists will be the same price paid by the Government.

In its response to Medicines Australia's 2007 election document prior to last year's federal election, the then Federal Opposition signalled what would become the new Government's support for PBS reform and commitment to ensuring patients have timely access to new medicines:

> *"A Rudd Labor Government will implement the program of PBS reform legislated in June 2007. However, in doing so, we will continue to monitor both the effectiveness of the reforms and their impact on consumers, the generic medicines sector and other stakeholders … Federal Labor is committed to ensuring timely access to PBS medicines for the Australian public"*[2].

The Basis for PBS listing

Proposals for listing new medicines or medicinal products on the PBS, or making changes to existing listings, must be considered by the Pharmaceutical Benefits Advisory Committee

[1] The Australian Government, Department of Health and Ageing and Medicines Australia. *Access to Medicines Working Group, Communiqué July 2007.* http://www.health.gov.au/internet/main/publishing.nsf/Content/853C29FD6750F74ECA2573D1001EFA17/$File/AMWG%20-%20July%202007%20communique.pdf

[2] Federal Labor Response to Medicines Australia Election Statement *Medicines Matter to Australians*, Office of Nicola Roxon MP, Shadow Minister for Health, Canberra, 22 November 2007.

(PBAC), which is required to take into account the effectiveness and cost of a medicine compared with other drug or non-drug therapies when reaching a decision. The *National Health Act 1953* Section 101(4) stipulates that a positive recommendation by PBAC is required before any new medicine can be listed.
The economic basis of a PBAC recommendation usually follows one of two approaches:

- A *cost-effectiveness* analysis allows a proposed new drug to be listed with a price advantage over its comparator, provided the extent of this price advantage can be justified by improved health outcomes, efficacy or safety.
- A sub-set of cost-effectiveness analysis, a *cost-minimisation* approach applies where there are insufficient gains in health outcomes to justify a higher price for the proposed drug over currently listed alternatives.

The statutory price cuts resulting from PBS Reform may impact on the listing of new medicines where the listing has been on the basis of either cost-effectiveness or cost-minimisation analysis.

Assessment of potential impact

What is the issue?

As a result of PBS reform, some new innovative medicines will be compared to F2 medicines for pricing comparator purposes. This is likely to lead to some new medicines being offered a lower listing price in F1. On the basis of consultations with its membership, MA believes that there is a possibility that Australians' future access to some new innovative medicines may be delayed or compromised as a result of PBS Reform.

As the economic evaluation of a new medicine is assessed by comparison with an existing treatment, it follows that from time to time a new medicine will be compared with an existing F2 medicine. Normally, if the claim is that it is "no worse than" an existing PBS-listed medicine (ie cost-minimised), it would be expected to match the total cost of treatment using the existing medicine. If the claim is that the new medicine is better (ie cost-effective), then it would be expected that extra expenditure through the PBS would reflect the value of that measurable health improvement.

The issue arises because F2 medicines will experience statutory price reductions from 1 August 2008, and may experience further reductions from 1 August 2009 due to the new price disclosure pricing policy. This may impact on the listing of new F1 medicines where the comparator is a F2 medicine that has experienced a price reduction due to the reforms.

Analysis (what are the facts)

MA and DoHA have undertaken retrospective analyses to measure the likely proportion of comparators which will be listed in F2 by profiling recent PBAC outcomes (refer Appendix D and Appendix E).

This analysis has identified that between 15% and 21% of new PBS applications in recent years were evaluated against medicines that are now listed in F2. Seven to eight per cent of successful applications used comparators that are now listed on the F2T formulary, where a 25% price reduction will occur on 1 August 2008. A further 8% to 14% of successful applications have a comparator in F2A where there is a possibility of significant price

reductions from 1 August 2009 as a result of price disclosure. This might also affect the listing of a new drug. A greater proportion of new drugs will be compared against medicines listed on F1, a smaller proportion of which will experience price reductions under the PBS Reforms compared to the previous situation.

An examination of 113 PBAC decisions from November 2005 to November 2006 was carried out through information available in public summary documents (PSDs). The analysis indicated that for cost effectiveness submissions:

- the comparator was a F1 medicine or placebo in approximately 85% of cases; and
- the comparator was a F2 medicine in approximately 15% of cases.

As part of AMWG's work, MA also undertook a prospective survey of its member companies to understand the extent to which new medicines seeking PBS listing in the future would have an F2 comparator. From responses from 16 MA member companies, a total of 37 new chemical entities and indications for which a company had expected to seek a PBS listing in the next five years were identified as expected to have an F2 comparator. To put this is perspective, given that there will be at least 15 PBAC meetings over this time, this means, on average between 2 and 3 submissions per PBAC meeting may have an F2 comparator. It is worth noting that the MA survey most likely underestimates the actual extent of the problem as the absolute numbers provided are derived from a small sample size of the membership (16 out of 50 member companies).

Perspectives on likely potential impact

Both DoHA and MA agree, in principle, that the evaluation of some new medicines will be against comparators that are in the F2 formulary. However, DoHA and MA have differing views on the extent to which this is likely to be an issue for the availability of new medicines in the future. The extent to which comparator price reductions will affect the listing of new medicines is dependent on a number of factors. These include: the number of new medicines that will have an F2 comparator; the ultimate success of the price disclosure policy in delivering ongoing savings in the F2 market; and the combined impact of all price reductions in establishing the relative cost-effectiveness of new medicines.

MA view

During AMWG discussions, MA suggested that this change has created a problem. This is due to the number of medicines that may have an F2 comparator in the future, the number of medicines experiencing patent expiry in the next few years, and the fact that several categories of new medicines may be adversely affected and the likelihood of larger than expected price reductions in F2 as a result of the Government's policy of price disclosure. MA's view is that it is preferable to pre-empt any potential unintended consequence of PBS reform and introduce sufficient flexibility in the listing process to ensure that 'at-risk' medicines can be dealt with on a case by case basis, particularly because PBS Reform was not intended to negatively impact on *any* important medicine. MA argues that the two formularies are separate, with prices in F1 determined by evidence-based medicine and cost-effectiveness analysis, while in F2 market competition determines price and that given the different markets, there should be no price linkage between F1 and F2 medicines at the time of price setting as well as price maintenance after listing.

DoHA view

In discussion at AMWG, DoHA suggested that given the apparent small numbers of PBAC submissions in the past that have had an F2T comparator, and the uncertain likelihood of further price reductions in F2, the issue is likely to be confined to a subset of medicines and that the current system of evaluating medicines for listing on the PBS is sufficiently flexible to handle issues that may arise. DoHA therefore does not agree there is a problem.

DoHA notes that many policies that affect pricing and therefore comparator pricing and cost effectiveness have been introduced over time. The price reductions applying from 1 August 2008 are inherently no different to previous pricing reductions. The fundamental application of cost-effectiveness when considering new medicines does not alter with the introduction of price reductions flowing from PBS Reform, nor will the existing flexibility of the PBAC be altered by the pricing reductions. Constraining cost effectiveness comparators to within the F1 and F2 formularies is an artificial construct, as comparators can be drawn from any formulary or from outside the PBS for the purposes of price setting. DoHA suggests that on average the size of the price reduction required to significantly impact on the cost-effectiveness equation is larger than the size of the mandatory price reductions being implemented as part of PBS reform, although this varies with different medicines. DoHA agrees that there will be some applications using a F2 comparator which will experience these impacts, and believes that perhaps in some circumstances PBAC will need to take that into consideration.

Options for managing impact of F2 comparator price reductions

The AMWG discussed a range of possible approaches for ensuring that price reductions that occur as a result of PBS reform, do not unintentionally affect the listing of new medicines on the PBS. Some of the options initially proposed by Medicines Australia in the discussions, such as CPI adjustment of F1 medicine prices and adjusting the PBAC's incremental cost-effectiveness ratio (ICER) were deferred for later discussion under other AMWG terms of reference.

Discussion then focussed on three options, with some variations, to address the situation where a new single brand medicine is seeking listing on the PBS but its clinical comparator (the medicine most likely to be replaced in clinical practice) is an F2 medicine, and therefore may be more difficult to gain a higher price than the comparator medicine as a result of the Government's PBS reform policy. In the discussion of each option below, a summary of the strengths and weaknesses of the options discussed during AMWG deliberations is provided. Examples of how the options might work are described in Appendix G.

All the following options will increase the cost to Government of PBS medicines more than would be the case if new F1 medicines were evaluated against the appropriate F2 comparator.

a) Use of F1 comparator

When a company submits a new medicine for listing on the PBS which would otherwise be compared against an F2 medicine, the comparator against which it will be considered will automatically be another F1 product. Where a relevant F1 product does not exist the comparator is placebo for standard management. Note that the new medicine will only achieve a higher price than currently listed F1 medicines if it demonstrates superior outcomes

supporting acceptable cost-effectiveness, the same as the current situation. Thus the principle of the need to establish cost effectiveness is unchanged by this option. A variant to this is that the company may choose whether it would exercise its option to have an F1 comparator.

Strengths: Simple and easy to understand and achieves the quarantining of any changes in the pricing of medicines on the F2 formulary affecting the determination of the cost effectiveness of a new medicine. Sponsors will still need to satisfy that medicines are effective and safe but the cost-effectiveness of the medicine will not be influenced by the impact of changed pricing arrangements for existing generic medicines as a result of the Government's PBS reform policy. Can be implemented within the boundaries of the current F1/F2 split in PBS reform.

Weaknesses: Such an approach is at odds with current practice of comparator choice and cost-effectiveness analysis. Excluding as potential comparators all products listed in F2, regardless of their appropriateness as defined by current clinical practice, compromises the principles of cost-effectiveness analysis as defined by the current PBAC guidelines. This option may also give rise to undue incentives to bring non-innovative products to market. There may also be situations where a company would prefer to have an F2 comparator and this option would prevent them from doing so, even if that might be most appropriate.

b) Use of F1 price for pricing purposes only

Under this option, where a company is seeking the listing of a new medicine and its clinical comparator (the medicine most likely to be replaced in practice) is in F2, that comparator is used for clinical evaluation, but an equivalent F1 price is substituted in the economic evaluation. Sponsors would need to establish relative clinical effectiveness against the relevant comparator product regardless of whether that medicine is listed on F1 or F2. For the purposes of establishing cost-effectiveness and price setting, however, the comparator would be adjusted to reflect equivalent F1 pricing, either by reference to an equivalent F1 comparator or re-calibrating the F2 comparator's price to its pre-F2 level.

An example of how this might work in practice would mean that when evaluating the cost-effectiveness of a new medicine the PBAC would be required to take into account the following for pricing purposes where nominated by the sponsor:

- an F1 medicine previously linked to the F2 clinical comparator, for example if the F2 comparator was part of an F1 price reference group prior to moving to F2, the price of another product in that F1 price reference group would be used in the evaluation; or
- where there is no equivalent F1 comparator, the price of the F2 comparator prior to its exposure to the mandatory and disclosure-based F2 price cuts resulting from the introduction of the two formularies and the price disclosure policy; or
- a current F1 medicine that is likely to become the market leader in clinical practice in the future, instead of the current F2 comparator, and thus can be used for pricing purposes in the evaluation.

It should be noted that this option would apply to both cost-minimisation and cost-effectiveness analysis.

Strengths: This option quarantines F2 pricing effects like Option (a) but in addition allows the PBAC to establish the relative clinical effectiveness of a medicine against all currently listed medicines regardless of their F1 or F2 status, consistent with current guidelines. This option also allows companies the flexibility to propose an equivalent F1 price if they so choose, rather than it being an automatic requirement.

***Weaknesses*:** This option and may increase the administrative complexity of any solution, as more than one comparator may be involved, including the establishment of guidelines around which F1 comparator should be used in pricing. The PBAC will be required to make its decision based on a secondary analysis for pricing scenarios, possibly increasing the administrative workload. The separation of the F1 and F2 formularies is compromised at the pricing level, but not clinical level.

c) Use of F1 comparator for pricing purposes in certain circumstances

A variant to b) is to allow the use of an F1 price for pricing purposes, but for only some new medicines based on a list of criteria. This would permit the Government to exclude some new medicines with an F2 comparator having an F1 price adjustment on the basis that they provide no additional benefit to the Australian community over and above those products already listed in F2. A series of exclusion criteria could be developed by the Government in consultation with industry. Variants to this option include developing such criteria for *including* such medicines for F1 price adjustment, rather than the basis of *exclusion* from F1 price adjustment.

These criteria, whether used to exclude or include medicines for F1 price treatment, could include a range of factors designed to ensure that patients did not miss out on a range of new medicines in the future. As already flagged, F1 price treatment occurs when a new medicine with an F2 comparator on clinical grounds is compared against an equivalent F1 price for pricing purposes. When deciding whether to exclude/include a medicine for such treatment, the Government may seek PBAC advice on the relevant new medicine. Factors the PBAC might be required to consider, on a case by case basis, in providing advice to the Government include:

- Whether the medicine is cost-effective – a medicine that PBAC has agreed is cost-effective at the F2 comparator price suggests the medicine has some significant improvement in patient outcomes over its comparator
- Even where a company is making a cost-minimisation submission for a new medicine (ie. 'no worse than' an F2 comparator), factors that should be considered include:
    - The range and choice of alternative treatment options available to patients and health professionals for the disease area and whether the listing of the new medicine enhances that choice that results in an improved outcome for all or some patients
    - Whether the medicine is a new mechanism of action, introduces a novel delivery action, a new pharmacological class or provides some other innovation of benefit that improves the outcome for the patient
    - Whether there are other medicines already available that are interchangeable at the patient level with the proposed new medicine
    - The extent to which the medicine provides a unique treatment, safety advantage or effectiveness advantage at least in some patients

  - The extent to which formulations of the medicine can be uniquely used where other formulations cannot be used to benefit a sub-population of patients

- The extent to which patients, or a sub-group of patients, will be disadvantaged if the new medicine is not listed on the PBS

These criteria might be conveyed to the PBAC by the Minister in writing, as part of a statement of intent confirming that the purpose of PBS reform is not to make it more difficult for new medicines to be listed on the PBS in the future.

Strengths: As in b), but limits the use of F1 pricing of F2 comparators to medicines that provide improvement in patient treatment. Does not provide higher pricing to medicines with no additional benefit to patients or sub-groups of patients. While still at odds with current cost-effectiveness practice it seeks to regularise the flexibility that is inherent in the current PBAC decision making process, where PBAC consider it appropriate.

***Weaknesses*:** While less at odds with cost-effectiveness processes than options a) or b), option c) this is still at odds with cost-effectiveness analysis. Criteria need to be developed not only of which F1 comparator should be used in pricing, but which new medicine submissions with an F2 comparator should be given this treatment. The more prescriptive the list of considerations, the more likely existing PBAC flexibility will be restricted.

Implementation aspects (DoHA & MA)

There are a range of issues that need to be considered should any one of the above options be implemented:

- *Mandatory/discretionary consideration by PBAC of a new F1 medicine application*

The extent to which PBAC's ability to use its existing flexibility when considering the appropriate comparator will be constrained if mandatory requirements are imposed under options (a) or (b). PBAC currently has some flexibility in decision making which provides it and companies with a degree of room to move. A mandatory approach, namely that PBAC is required to use an F1 comparator or price, while providing additional certainty to companies in putting their new medicines forward for listing would limit this flexibility.

- *Timing issues*

Ideally, if a decision were made to adopt one of the options above as a solution for managing any potential impact of comparator price reductions, it would need to be put into effect as soon as practicable. Although it is conceivable that some F2 price reductions may have already influenced the comparator price for new medicine applications (eg. 12.5% cuts when a medicine moves from F1 to F2 prior to August 2008), in all likelihood the impact will not start to become apparent until after 1 August. The ability to have a solution in place in time is influenced by the extent to which that solution needs to be considered by Government and its administrative complexity.

- *Cost*

Each of these options may cause the PBS to cost more than would otherwise be the case if the impact of F2 comparator price reductions were allowed to flow fully on to the setting of the initial list price for new F1 medicines. However, this will need to be balanced against the possibility that there may be some new F1 medicines that may not be listed on the PBS or whose listing on the PBS may be somewhat delayed (if a company also has a price at which the new medicine would not be cost effective).

- *How to effect any change*

Implementing any-of these options could be achieved through administrative process, following a Government decision about any policy change and resultant cost impact. While PBAC already has the flexibility to use alternate comparators at its discretion, mandating or restricting the type of comparator that can be used will require the development of clear administrative guidelines. A legislative approach may provide greater certainty to companies and PBAC on how medicines will be assessed, but requires lead time, is subject to Parliamentary approval and importantly compromises flexibility for both the PBAC and for companies. It is also likely that a non-legislative route will facilitate quicker implementation and while it could present problems of interpretation allows for flexibility and ease of updating as changes are required.

- *Consultation with other stakeholders*

The Government has made clear that it expects any initiatives emerging out of AMWG will require consultations with affected stakeholders before implementation. MA agrees with and supports this approach.

Conclusion

Through its examination of the comparators issue, the AMWG has confirmed that, in the future, there will be new drugs considered for listing in F1 which have an F2 comparator which has had a statutory price reduction. There is disagreement within the AMWG, however, as to the impact of this comparison.

MA believes that this is an issue which should be addressed by the application of one of the options discussed in the paper, with a preference for option *a) Use of an F1 comparator*. DoHA believes that the flexibility in the consideration of applications by PBAC is sufficient to handle any situations that may arise, including F2 comparators which have had a statutory price reduction.[3]

Next steps

DoHA and MA have agreed that each will separately brief the Minister for Health and Ageing on the likely impact of F2 comparator price reductions on new medicines seeking PBS listing and management options.

If the Minister requires further work DoHA and MA will work together, in consultation with any other parties the Minister indicates, to respond to the request.

3 It should be noted that while the two parties comprising the AMWG disagree on this point, this is not a reflection on the joint work conducted on this issue, which has been undertaken cooperatively and in the spirit in which the AWMG was formed.

References

1. AMWG, Agenda Paper 3.1, 18 December 2007. *Comparator price reductions issues paper.*
2. Medicines Australia, Agenda Paper 3.2, 18 December 2007. *PBS Reform: Choice of Comparator – Summary of Medicines Australia Position*.
3. AMWG, Agenda Paper 3.3, 18 December 2007. *Impacts of F2 on new F1 medicine pricing – Meeting notes re preliminary options.*
4. Medicines Australia, November 2007, *MA member company survey – examples of future F2 comparators for yet-to-be-considered F1 medicines – next five years*.

Appendices

Appendix A – PBS Reform

In November 2006, the Government announced a number of changes to the PBS to protect patients from higher out of pocket costs, get better value from market competition among brands of generic (off-patent) medicines and recognise the importance of world-class life-enhancing drugs to patients. The main change is in the way that the Government prices medicines that are operating in a competitive market. These medicines will take a series of price drops, and eventually will move to a system where the price they are being sold for will reflect the price that the Government pays.

The New Formularies

From 1 August 2007, PBS medicines have been divided into two separate groups ('formularies'), each subject to different pricing arrangements:

- ***F1*** for medicines where there is only a single brand listed. F1 contains both on patent and off patent medicines that are not substitutable with other brands or medicines.
- ***F2*** for multiple brand medicines, and single brand medicines interchangeable with a multiple brand medicine.

F2 is further divided into:

- ***F2A*** for multiple brand medicines with low levels of price competition; and
- ***F2T*** for multiple brand medicines with high levels of price competition.

Reference pricing

Reference pricing links the price of a medicine to the price of other medicines that provide a similar health outcome. It will continue for F1 medicines in reference price groups and for F2 medicines that belong to groups of medicines that are interchangeable between patients. If a price change occurs for one of these medicines, this will flow to the others.

Statutory Price Reductions

The requirement for a 12.5% price reduction when the first new brand of a medicine is listed on the PBS is continuing. There are no statutory price reductions for F1 medicines and existing price linkages are retained within F1.

F2 medicines will experience statutory price reductions from 1 August 2008 as follows:

- F2A medicines will begin a series of three annual price reductions of 2%;
- F2T medicines will have a single 25% price reduction (phased over the remaining patent life for interchangeable patented medicines in therapeutic groups).

Price reductions no longer flow between medicines listed on different formularies. This represents a significant benefit for sponsors of many F1 drugs, which will no longer experience price reductions as a result of generic competition for medicines in the same reference priced group. In addition, Government and taxpayers will benefit from lower prices for multiple brand medicines in F2. Such price reductions may provide headroom for the listing of cost-effective new medicines.

Appendix B – Description of Price Disclosure

Under the 2006 PBS Reforms, the Government will over time move to a system of price disclosure, where the price that the Government pays will reflect the actual price at which the medicine is being sold.

Price disclosure will be phased in for medicines that operate in a competitive market:

- For medicines where price competition is low (F2A), suppliers of any new brand listing from 1 August 2007 will agree to disclose its price as a condition of listing. Price changes based on disclosure will commence for these medicines from 1 August 2009.
- For those medicines where price competition is high (F2T), suppliers of any new brand listing from 1 January 2011 will agree to disclose its price as a condition of listing. Price changes based on disclosure will commence for these medicines from 1 August 2012.

When the first new brand of a single brand medicine is listed on the PBS that medicine will become subject to regular price reductions and price disclosure.

Appendix C – Cost effectiveness and the incremental cost effectiveness ratio (ICER)

Cost effectiveness assessment compares the price advantage sought by a sponsor to the net additional health gains conferred by the new drug over its main comparator, together with any cost implications arising from changes in the provision of health care resources. The main comparator is the current therapy that prescribers would most replace with the new drug in practice. The main comparator can be another PBS-listed drug or, where there is no existing effective drug therapy, placebo for standard medical management of the condition. The preferred metric for describing the overall changes in health outcomes is the number of Quality Adjusted Life Years (QALYs) gained. This summarises the effects of a health intervention on both survival and quality of life.

In calculating the costs associated with listing a drug on a cost-effectiveness basis, a wide range of costs (and cost offsets) can be taken into account beyond drug costs. These can include diagnostic, medical, hospital, residential age care and allied health services costs. For the sake of simplicity, the discussion and examples below focus on the drug costs of the new drug and its main comparator only and not any other sources of costs and cost offsets.

The ratio of additional costs to additional health gains is known as the Incremental Cost Effectiveness Ratio (ICER), which is simplified below as:

$$\text{ICER} = \frac{\text{price advantage requested}}{\text{additional QALY gained}}$$

The ICER presents the extra cost for each additional QALY gained offered by the new drug therapy. The larger the ICER, the more "expensive" is the additional health gain and the less favourable the economic credentials are for a PBAC recommendation to list. Increasing the price advantage requested over the comparator increases the value of the ICER. Increasing the additional QALY gained decreases the value of the ICER.

While there is no single maximum ICER value set by PBAC – no "cost effectiveness threshold" – there is evidence that medicines are more likely to be recommended for listing with an ICER around $30,000 than with an ICER above $70,000.

Table 1 provides an example of a new drug with an ICER of $30,000. A $1,500 price advantage is requested for the new drug, and there is an additional health gain of 0.05 QALYs. In this simple example there are no non-drug costs or cost offsets to take into account.

Table 1

Comparator cost/year	$500
New drug cost/year	$2,000
Price advantage requested	$1,500
Additional QALY gain/year	0.05
ICER	$30,000

Appendix D – Comparator Analysis (Medicines Australia)

MA provided a report on a review of 113 PBAC decisions from November 2005 to November 2006 through information available in public summary documents (PSDs). The analysis indicated that for cost effectiveness submissions:

– the comparator was a F1 medicine or placebo in approximately 85% of cases; and

– the comparator was a F2 medicine in approximately 15% of cases.

In commissioning this analysis, the MA representatives advised that they anticipated the impact of price reductions could be greatest for:

- The case of a new high cost medicine with a good QALY gain (eg. >0.1) where the comparator is also high cost but has moved to F2. In this case, the ICER may move from what is acceptable to one that exceeds what PBAC considers acceptable value for money.
- The situation where a modest price advantage is requested over a moderate to low priced comparator but the new drug's QALY gain is low (eg chronic therapy in therapeutic areas such as the current TGP groups)
- A product of modest price that attempts to cost-minimise against a low priced comparator which has been subject to a 25% price cut.

By way of example, a range of scenarios presenting increases in the cost/QALY ratio as a result of a 25% price reduction are presented below. In this example, new high cost medicines that have a relatively high cost comparator (eg. some of the treatments for cancer) experience a significant increase in the cost/QALY ratio as a result of a 25% price reduction in their comparator (noting MA's view that some F2 comparators are likely to see a greater than 25% price reduction as a result of PBS reform). MA notes previous DoHA analysis showing that a 50% reduction in the price of a comparator for a sample of existing medicines on the PBS shows an increase in the incremental cost-effectiveness ratio of between 0% and over 70% depending on the medicine, raising the possibility that some new medicines on the PBS now would not have been listed if their comparators had undergone PBS reform price reductions at the time.

Pre-PBAC Reform

Price Adv of drug	Price of comparator	QALY gain	
		Large 0.15	Small 0.04
Large	Large $10,000	$33,333	$125,000
$15,000	Small $1,000	$93,333	$350,000
Small	Large $1,000	$3,333	$12,500
$1,500	Small $500	$6,667	$25,000

Post-PBAC Reform (25% price reduction)

Price Adv of drug	Price of comparator	QALY gain	
		Large 0.15	Small 0.04
Large	Large $7,500	$50,000	$187,500
$15,000	Small $750	$95,000	$356,250
Small	Large $750	$5,000	$18,750
$1,500	Small $375	$7,500	$28,125

Appendix E – Comparator Analysis (Department of Health and Ageing)

DoHA looked at the comparator used for each major drug submission recommended for listing by PBAC between March 2004 and August 2006. This focus on the subset of all submissions which were recommended by PBAC was justified because it excluded submissions rejected by PBAC for reasons which would not be affected by statutory price reductions.

During that period PBAC gave positive recommendations for 106 major submissions:

- 44 (42%) listed on a cost effectiveness basis; and
- 62 (58%) listed on a cost minimisation basis.

Diagram 1 shows what proportion of submissions recommended by PBAC on a cost-effectiveness basis used another medicine as the comparator (55%) in their economic analysis, and what proportion used placebo/standard medical care (45%). It further breaks down the PBS-listed comparators into the formularies that those drugs have since been assigned. Seven per cent (n=3) of the total sample used drugs now listed on the F2T formulary as comparators.

Diagram 1

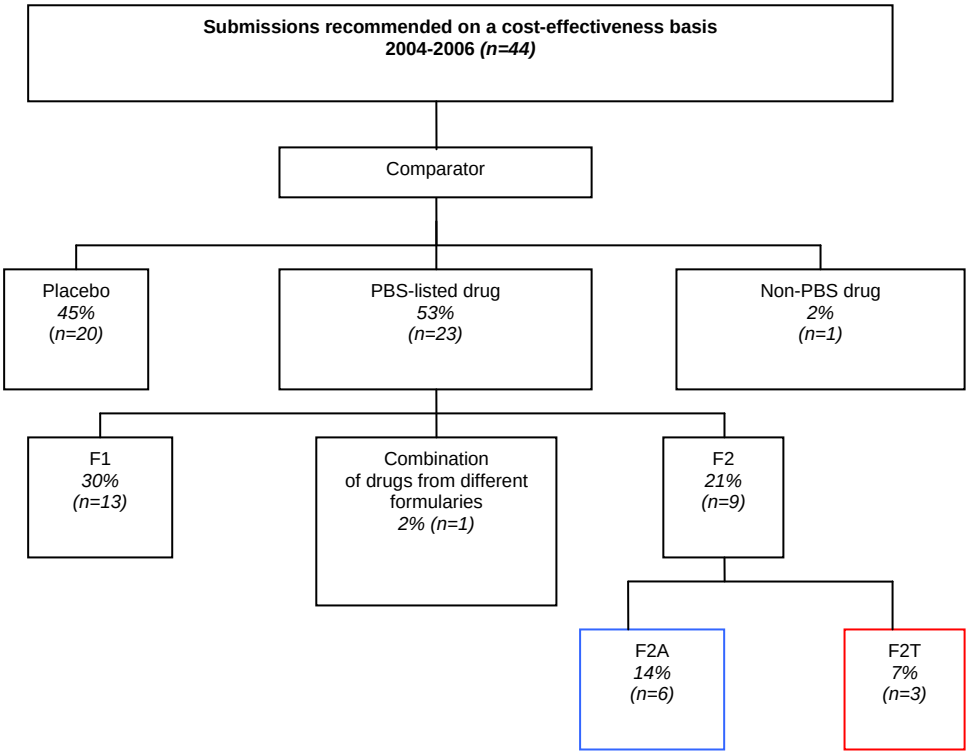
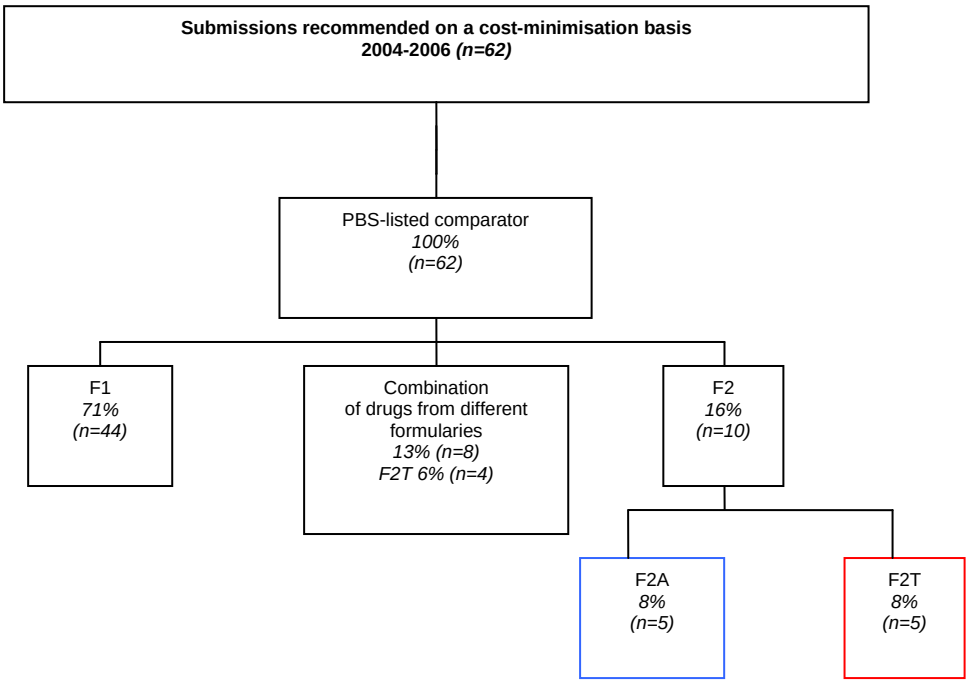


Diagram 2 shows what proportion of submissions recommended by PBAC on a cost-minimisation basis used comparators on each formulary. All cost minimised drugs have PBS-listed comparators. Eight per cent (n=5) of the total sample used comparators now listed on the F2T formulary.

Diagram 2



Effect of a price reduction for a F2T comparator on cost minimised drugs

Cost minimised drugs list at the same price as the comparator. However, the creation of the formularies prevents a new single brand drug from having its price linked to the comparator over time. As a result of the PBS reforms, for products that seek listing on the basis of cost-minimisation analysis where the comparator is a F2 product, it may be problematic for a company to list the product (given global floor price issues) at the reduced price of the F2 comparator. In order minimise the impact of a statutory price reduction, a sponsor may attempt to support listing on a cost effectiveness basis by seeking a tighter restriction to a subgroup of patients unable to benefit from the comparator for sound clinical reasons.

Effect of a price reduction for a F2T comparator on the ICER

The simplified and illustrative analysis below attempts to isolate the difference in the ICER before and after a 25% price reduction is applied to the comparator drug. The analysis is qualified by the following assumptions, which limit the generality of the results.

Simplifying assumptions for analysis

1. All other factors relevant to cost effectiveness assessment, including health and safety benefits (QALY gain), and the price sought by the sponsor of the new drug, are held constant before and after the statutory price reduction is applied. In practice a number of options will be available for the sponsor after a comparator price reduction, including reducing the price sought or attempting to identify a subgroup of the patient population for which acceptable cost effectiveness may be achievable at a larger price advantage.

2. The full costs of both the comparator and the new drug are due to the medicines only with no non-drug costs or cost offsets. A more complex and realistic analysis would take these additional cost factors into account. For example, if half the cost of treatment with the comparator is due to necessary tests and procedures (which will be unaffected by statutory price reductions) then, in effect, a 25% reduction in the comparator drug price

will result in only a 12.5% reduction in the overall cost of therapy involving the comparator.

Summary conclusions from analysis

- The change in the ICER following a reduction in the price of the comparator is determined by the size of the price advantage requested for a new drug. The smallest changes occur when the price advantage requested is large (multiples of the comparator price). Larger changes occur when the price advantage requested is small (some fraction of the comparator price).
- The dollar amount by which the ICER increases as a result of a reduction in the comparator price is less when the additional health gain offered by a new drug is large.

Analysis

On the assumption that the sponsor would seek the same price for its new drug before and after a reduction in the price of the comparator, the price reduction impacts the ICER by increasing the extent of the price advantage requested.
Tables 1 and 2 illustrate this below. In each case, the sponsor seeks a price of $2,000 per year, with an additional QALY benefit of 0.05. In Table 1, this represents a 300% increase over the comparator's price of $500 before the statutory reduction. The ICER increases by 8% from $30,000 to $32,500 after the comparator's price is reduced.
In Table 2, the new drug's price is only 33% higher than the $1,200 price of the comparator before the statutory reduction. This means that, at a value of $16,000, the resulting ICER is less than in Table 2 before a reduction in the price of the comparator. After the comparator's price is reduced, this ICER increases by 38% to $22,000.

Table 1

Large price advantage requested	**Pre-25%**	**Post-25%**
Comparator cost/year	$500	$375
New drug cost/year	$2,000	$2,000
Price advantage requested	$1,500	$1,625
Price increase (%)	300%	433%
Additional QALY gain/year	0.05	0.05
ICER	$30,000	$32,500
Increase in ICER (%)		8%

Table 2

Small price advantage requested	**Pre-25%**	**Post-25%**
Comparator cost/year	$1,200	$900
New drug cost/year	$2,000	$2,000
Price advantage requested	$800	$1,100
Price increase (%)	33%	122%
Additional QALY gain/year	0.05	0.05
ICER	$16,000	$22,000
Increase in ICER (%)		38%

Within the limitations of the analysis identified above, the extent of the additional QALY gain offered by a new drug plays no role in determining the *percentage* change in the ICER resulting from a comparator price reduction. However, a larger QALY gain will mean that the dollar value of the ICER increase is smaller. This can be seen in Tables 3 and 4 below, which show examples differing only in the additional QALY gain offered by the new drug. In each case, the sponsor seeks a price for the new drug of $5,000 per year, which is a 400% increase over the comparator's price of $1,000 before the statutory reduction.

In Table 3, the additional QALY gain is 0.05, resulting in an ICER before the comparator price reduction of $80,000. In Table 5, the additional QALY gain is 0.1, giving an ICER before the comparator price reduction of $40,000. In each case the ICER increases by 6% after the comparator price is reduced.

However, although the percentage increases in the ICER are the same, the dollar value increases by $5,000 for the drug with the lower QALY gain (Table 3) and only $2,500 for the drug with the higher QALY gain (Table 4).

As ultimately it is the dollar increase in the ICER that is most relevant to assessing incremental cost effectiveness, this analysis shows that the advantage that a new drug offering large additional health gains has in achieving acceptable cost effectiveness is maintained in an environment where comparator prices are reduced.

Table 3

Large price advantage requested	**Pre-25%**	**Post-25%**
Comparator cost/year	$1,000	$750
New drug cost/year	$5,000	$5,000
Price advantage requested	$4,000	$4,250
Price increase (%)	400%	567%
Additional QALY gain/year	0.05	0.05
ICER	$80,000	$85,000
Increase in ICER (%)		6%

Table 4

Small price advantage requested	**Pre-25%**	**Post-25%**
Comparator cost/year	$1,000	$750
New drug cost/year	$5,000	$5,000
Price advantage requested	$4,000	$4,250
Price increase (%)	400%	567%
Additional QALY gain/year	0.1	0.1
ICER	$40,000	$42,500
Increase in ICER (%)		6%

Table 5 below shows the percentage increase in the ICER resulting from a 25% comparator price reduction for a selection of annual costs for new drugs and for comparators (listed at their prices before this statutory reduction is applied).[4] Note that the current average cost of PBS items on the F2T formulary is approximately $270 per annum.

[4] The percentage increase in the value of the ICER following a 25% comparator price reduction can be determined quickly by dividing 25% by the percentage price increase requested (before the comparator price reduction and for equal durations of therapy). For example, if the new drug price sought is 400% of the comparator price, the ICER increases by 6.25% - this corresponds to the examples in Tables 3 and 4.

Table 5

% increase in ICER		New drug price sought							
		$200	*$300*	*$500*	*$1,000*	*$2,000*	*$5,000*	*$10,000*	*$15,000*
Comparator price (before-reduction)	*$100*	25%	13%	6%	3%	1%	1%	0%	0%
	$200		50%	17%	6%	3%	1%	1%	0%
	$300			38%	11%	4%	2%	1%	1%
	$500				25%	8%	3%	1%	1%
	$1,000					25%	6%	3%	2%
	$2,000						17%	6%	4%
	$5,000							25%	13%
	$10,000								50%

Appendix F – Further Comparator Analysis November 2007 – March 2008

Diagram 1

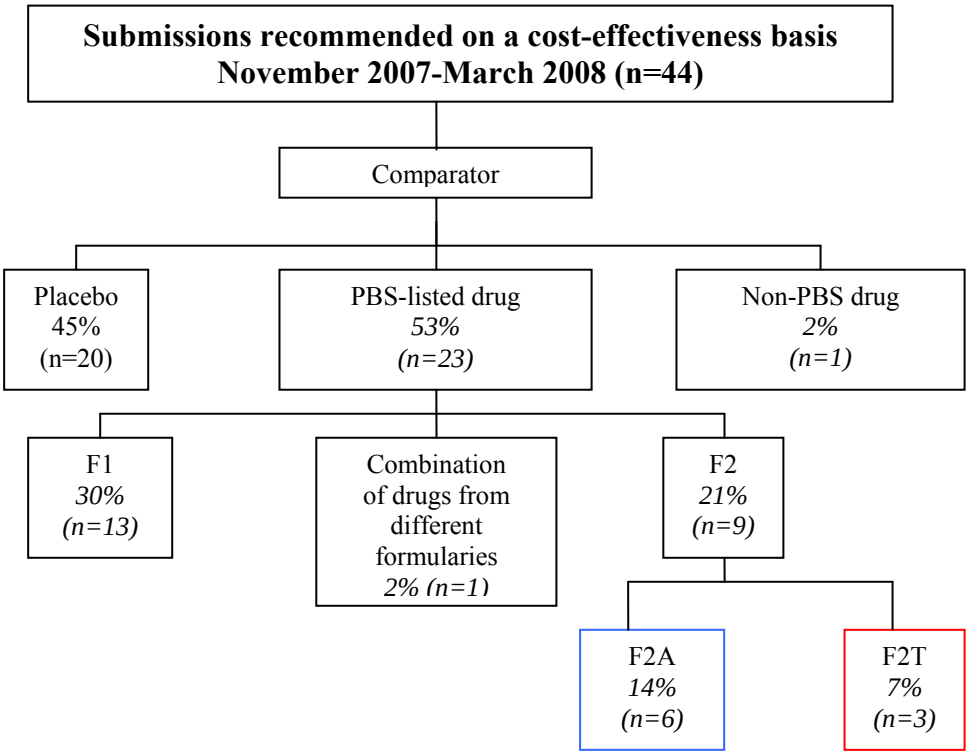


Diagram 2

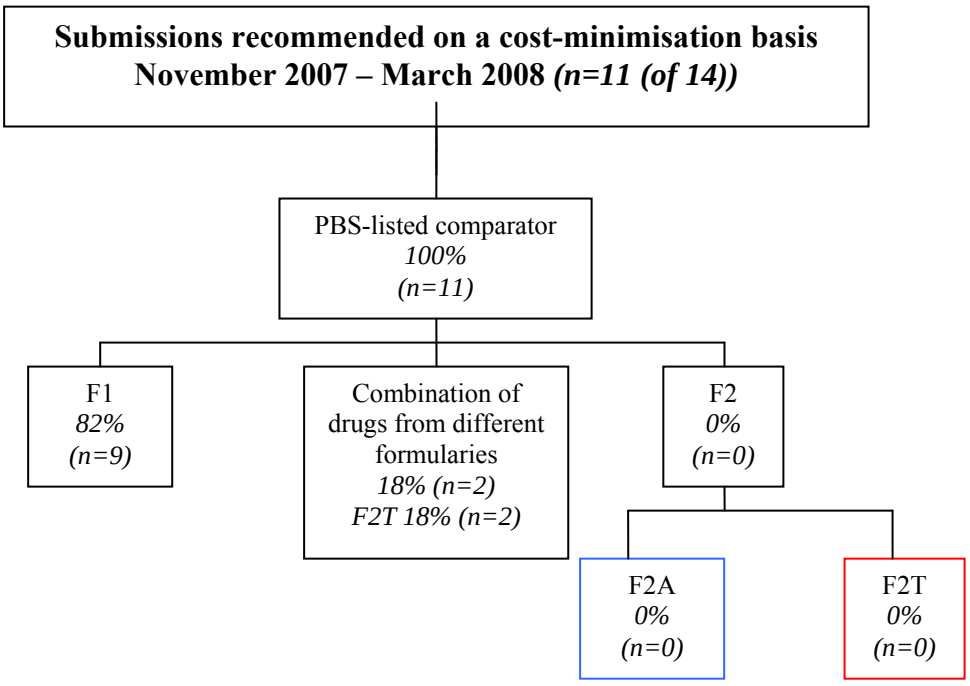


Diagram 3

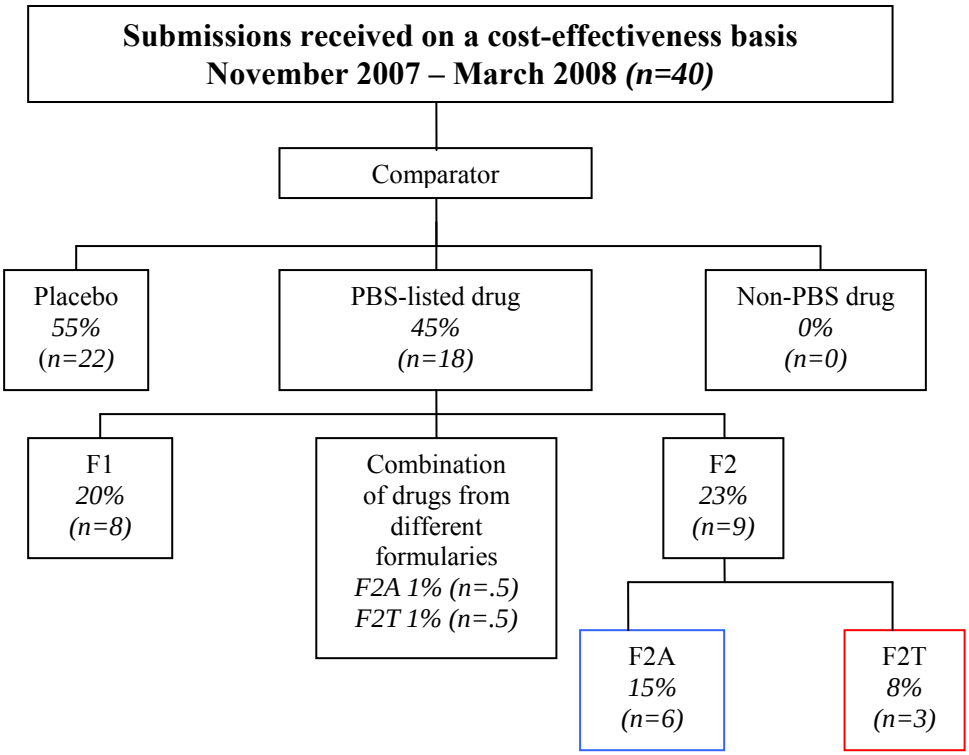
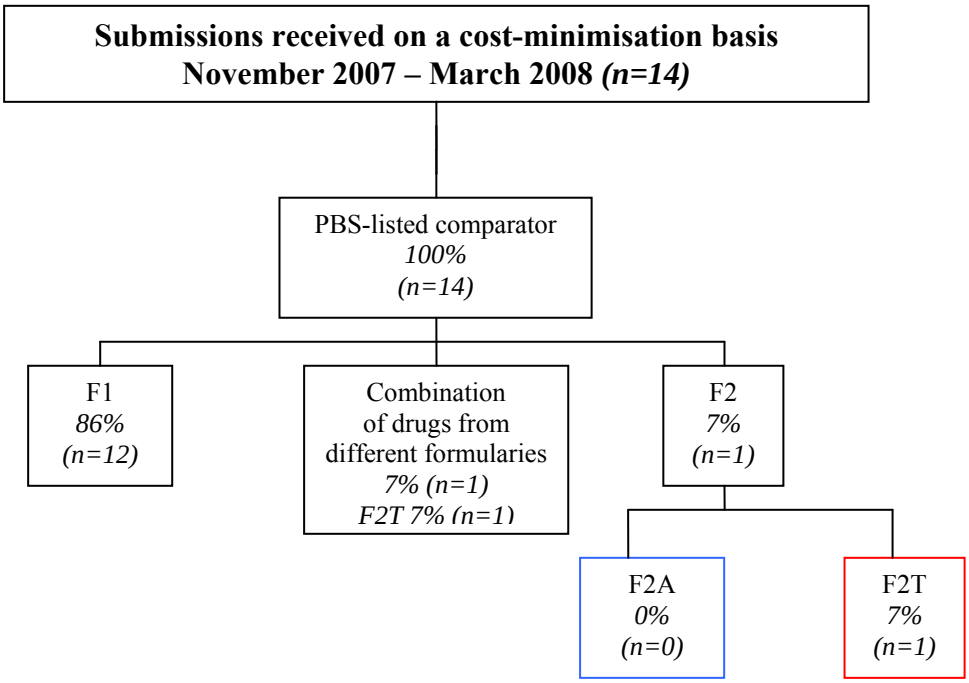


Diagram 4



Appendix G – PBAC evaluation of new listings

The economic basis of a PBAC recommendation usually follows one of two approaches.

- A *cost-minimisation* approach applies where there are insufficient gains in health outcomes to justify a higher price for the proposed drug over currently listed alternatives. Drugs seeking listing on a cost-minimisation basis simply need to demonstrate that, therapeutically, they are at least as effective and safe as ("no worse than") a comparator drug already listed on the PBS. Cost-minimisation results in listing at the same price as the comparator based on equi-effective doses.
- In contrast, a *cost-effectiveness* approach allows a proposed new drug to be listed with a price advantage over its comparator, provided the extent of this price advantage can be justified by improved health outcomes (often summarised as an additional Quality Adjusted Life Years (QALY) gain) and/or cost offsets resulting from changes in the provision of other health care resources. The ratio of additional costs to additional health gains is known as the Incremental Cost Effectiveness Ratio (see Appendix C).

In addition to the results of economic analysis, PBAC takes other relevant factors into account in the process of deciding whether to recommend that a drug be listed. These include:

- the extent of uncertainty relating to the claims made about cost and heath outcomes;
- the total annual costs to the PBS of implementing the listing;
- the extent to which a restriction can be constructed which satisfactorily distinguishes uses which are acceptably cost-effective to justify subsidy from uses which are not cost-effective;
- the scope for usage of the drug beyond any restriction for subsidy;
- the severity of the condition being treated;
- the affordability of the medicine to the patient in the absence of a subsidy; and
- the availability of other effective interventions for the condition.

The decision whether or not to recommend listing requires an overall assessment of all relevant factors – combining a consideration of the results of the economic analysis and other relevant factors such as those listed above.

Appendix H - Examples of how options a) to c) might work in listing new medicines on the PBS

a) Automatic use of F1 comparator

A company submits new anti-depressant therapy for listing on the PBS. While its clinical comparator might be an existing anti-depressant treatment in F2, the new therapy is required to have a similar or alternative anti-depressant therapy in F1 for clinical and economic evaluation and all evaluation is done against this alternative F1 comparator. Where there is no alternative F1 anti-depressant treatment, the new anti-depressant is evaluated for cost-effectiveness against placebo for standard medical management.

b) Use of F1 price for pricing purposes only

A company makes a submission to list a next generation diabetes medicine, but its clinical comparator is in F2. While the medicine is a significant incremental improvement over existing therapies, given the price reductions of the F2 comparator, the medicine is unable to demonstrate cost-effectiveness at the F2 comparator's reduced price – given the new differential between the new diabetes medicine and the older one in F2, the medicine is now not cost-effective in spite of being a clinical improvement. When the F2 comparator's older F1 price is used, however, the new diabetes treatment is cost-effective. In this case, the company may elect to submit the F2 comparator's pre-PBS reform price for pricing purposes and cost-effectiveness calculations.

In another example, a new treatment for prostate cancer is cost-effective over an older F2 comparator at the F2 comparator price; that is, the treatment is an improvement for prostate cancer patients. The F2 comparator may recently have moved into F2 and undergone price reductions as a result of PBS reform, leaving behind one or more other prostate cancer treatments in a reference pricing group in F1 which, although other treatments for prostate cancer, are not the clinical comparator. Prior to entry into F2, the comparator may have been priced at the same level as other prostate cancer treatments in F1. In this case, the equivalent F1 price of another prostate cancer medicine will be substituted in the place of the F2 comparator's price for pricing purposes.

c) Use of F1 comparator for pricing purposes in certain circumstances

A company is seeking listing for a new treatment for psoriasis against an F2 comparator. While cost-minimised for clinical purposes, PBAC may agree that the treatment does provide a benefit in terms of patient choice or an additional treatment option, and therefore should have an equivalent F1 price for pricing purposes. In this example, no equivalent F1 reference pricing group may exist, hence the price of the F2 comparator prior to its move into F2 is used for pricing purposes.

In a further example, a company is seeking to list a new ACE inhibitor medicine. The submission is a cost-minimisation submission against an existing ACE inhibitor in F2, offers no additional patient benefit than existing treatments and is considered interchangeable with several other existing ACE inhibitors, all in F2. In this circumstance, the PBAC may recommend that the new ACE inhibitor not be given an equivalent F1 price.

Attachment B

MANAGING UNCERTAINTY IN THE ASSESSMENT OF MEDICINES FOR LISTING ON THE PHARMACEUTICAL BENEFITS SCHEME

A paper prepared for the Access to Medicines Working Group

Executive Summary

The Access to Medicines Working Group (AMWG), under its terms of reference, is charged with considering issues relating to timely and appropriate access to effective new medicines on the Pharmaceutical Benefits Scheme (PBS), including exploring:

> "the practical limitations to the evidence available to the Pharmaceutical Benefits Advisory Committee (PBAC) to facilitate decision making around access to new medicines and the development of options to manage uncertainty in such situations."

This paper is the result of work conducted by the AMWG under this term of reference.

Uncertainty in the context of Pharmaceutical Benefits Advisory Committee (PBAC) submissions and evaluations refers to areas where the evidence, results or conclusions provided are unclear, ambiguous or open to various or different interpretations. Uncertainty can impact on four important aspects influencing decision making – clinical, economic, utilisation and financial. As a general rule, the more complex the submission, the higher the likelihood that there will be some areas where there are shortcomings in the available evidence that will need to be considered by PBAC when deciding whether to recommend that a medicines be listed on the PBS.

The result of uncertainty is an increase in the rate of rejections. This in turn can lead to an increase in the rate of resubmissions, which places a further demand on the resources and analysis required to evaluate the medicine, which further increases resource demand on Industry and the PBAC and can delay the listing of new medicines.

This paper discusses what gaps in the evidence arise in relation to the listing of medicines on the PBS; examines what the PBAC already does to address these gaps and identifies areas where further work may be required. It is accepted that while every effort can be made to minimise uncertainty it cannot be eliminated and therefore the remaining uncertainty needs to be managed.

Background

The Pharmaceutical Benefits Scheme (PBS), along with Medicare, is a key component of Australia's health system.

The PBS aims to provide timely, reliable and affordable access to effective and necessary medicines and vaccines for all Australians. Under the PBS the Australian Government subsidises medicine costs to help people pay for prescription medicines for most medical conditions.

The Government subsidises medicines and vaccines that meet its criteria. In the context of the ongoing development and release of new medicines which are often relatively expensive, it can be difficult to meet the community's expectations regarding subsidised access to all available medicines. Both the effectiveness and cost effectiveness of the treatments need to be considered in making decisions about subsidisation.

A number of strategies are used to ensure that medicines listed on the PBS and National Immunisation Program (NIP) provide the best 'value for money'. Broadly the Government only subsidises medicines that cost-effectively maintain the health of the community. This is achieved by carefully assessing the therapeutic benefits and costs of medicines, including comparisons with other treatments, where appropriate. If a medicine is found to be cost-effective, then the Government negotiates the price for it with its sponsor.

A medicine proposed for listing is considered acceptably cost-effective by the Pharmaceutical Benefits Advisory Committee (PBAC) if, for significant medical conditions, the improvement in health outcomes justify the additional costs (and any additional harms) compared with its main alternate therapy.

An acceptably cost-effective new medicine can be recommended for listing if:

- It treats or prevents significant medical conditions that are not covered, or only partially covered, by currently listed medicines;
- It is more effective and/or less harmful than a currently listed medicine; or
- It is as effective and safe as an existing listed medication.

In relation to the third option, such a medicine would be recommended for listing on a cost-minimisation basis, which is a sub-set of a cost-effectiveness analysis. This approach applies where there are insufficient gains in health outcomes to justify a higher price for the proposed drug over currently listed alternatives.

Overview of the Listing Process

The PBS listing process, which is managed by Department of Health and Ageing (DoHA) determines which, and under what circumstances, medicines are eligible for subsidy by the Government. Medicines, prices and other terms and conditions are set out in the *Schedule of Pharmaceutical Benefits*. The schedule is updated monthly, being primarily used by prescribers and dispensers, but also available to the general public.

A submission for PBS listing can be made for any medicine for any use for which it is registered (or in the process of being registered) by the Therapeutic Goods Administration (TGA). A sponsor is required to agree to list a medicine.

A medicine can only be listed by the Government on the PBS following a positive recommendation to do so by PBAC.

Pharmaceutical Benefits Advisory Committee

PBAC is an independent statutory body which makes recommendations and provides advice to the Minister for Health and Ageing about which drugs and medicinal preparations should be made available as pharmaceutical benefits. It assesses the clinical benefit and cost effectiveness compared with other treatments or products for the same medical condition or use.

PBAC has two sub-committees that provide expert advice and comments on the medicines: the Economics Sub Committee (ESC); and the Drug Utilisation Sub Committee (DUSC). PBAC may refer submissions to one or both of these committees. PBAC is also assisted by the PBAC secretariat and expert medicine evaluators.

If PBAC decides to recommend that a medicines be listed, it usually also makes recommendations on any conditions or restrictions in the listing arrangements.

PBAC also provides advice to the Pharmaceutical Benefits Pricing Authority (PBPA) about comparators, the therapeutic relativity and cost effectiveness of recommended or listed medicines and related pricing matters from a clinical perspective.

Pharmaceutical Benefits Pricing Authority

When a medicine is recommended for listing by PBAC, the sponsor makes a pricing application to the PBPA.

The PBPA then negotiates the initial price with the sponsor of the medicine, taking into account the PBAC's recommendations about the cost effectiveness of the medicine. The recommendations of PBAC and PBPA are then considered by Government. If the increased net cost to the Government is projected to be greater than $10 million per annum in any of the first four years of listing, the proposed medicine is considered by Cabinet before the Minister may declare a listing on the PBS.

The advice of PBAC, particularly in relation to clinical and cost effectiveness of proposed items, is a significant factor in determining initial prices. However other considerations include the sponsor's proposed price, prices in comparable countries, the price of alternatives listed on the PBS, manufacturing and supply costs, prescription volumes, cost of the goods and margins and price calculation.

Types of Uncertainty in the PBS listing process

There are several stages and processes involved in listing a new medicine on the PBS. As a general rule, the more complex the submission (and evidence) provided to PBAC the higher

the likelihood that there will be some areas where there are shortcomings in the available evidence that will need to be dealt with by PBAC before it makes its recommendation. This need for decision making in the absence of complete information is a characteristic of the environment, and is called uncertainty.

Uncertainty may impact several aspects of the evaluation and decision making process:

- Clinical uncertainty – there may be uncertainty about whether a new medicine proposed for listing will effectively meet the clinical need it is proposed to treat. There may be uncertainty about the claims related to the long-term extent and nature of the comparative effectiveness of the medicine, its side effects, interaction with other medicines, which therapies it might replace, or its general place in clinical practice.
- Economic uncertainty – while there might be certainty around a medicine's clinical impact, there may still be uncertainties around its value. For example, the utility or value that patients place on the extra health outcomes to be gained may be uncertain, there may be uncertainty around the costs of administration, the wider impacts of the medicine on the use of other health care resources, or perhaps the assumptions and techniques used to model the economic evaluation of the medicine may be under question. Economic uncertainty inevitably increases with increasing clinical uncertainty.
- Utilisation uncertainty – the extent to which the medicine will be used in practice in the Australian community may be unclear. Even in examples where there is a clinical and an economic benefit to eligible patients and the community to subsidise a new medicine, there may be uncertainty around exactly how many eligible patients there are in the community, the extent of substitution for other medicines, the rate of uptake and the doses used in practice.
- Financial uncertainty – in some ways linked to utilisation uncertainty, uncertainty may exist around the overall cost of the medicine to the PBS and perhaps even greater uncertainty about the overall impact of the medicine on other areas of the Government's health budget.

Uncertainty has been demonstrated to have an impact on PBAC's view of the acceptability of the incremental cost effectiveness ratio (ICER, see Appendix A) associated with specific products. In their presentation *Appraising the quality and other dimensions of clinical evidence in health technology assessments,* Harris et al have argued that the greater the degree of certainty, the greater the chance of listing (Harris et al. 2006). These authors argued that where certainty was more evident, the probability of receiving a positive recommendation was approximately 60% at a threshold of $55,000/ extra Quality Adjusted Life Year (QALY, see Appendix A) gained. However if the data were uncertain, the probability of receiving a positive recommendation at a threshold of $55,000/ extra QALY gained was only 15%. Similarly, the National Health and Medical Research Council (NHMRC) published guidelines in its handbook series on preparing clinical practice guidelines (*How to compare the costs and benefits: evaluation of the economic evidence*, July 2001) which recommended that where there was uncertainty, the ICER should only be $30,000/ extra QALY gained. Where there was certainty, the ICER should be elevated to $70,000/ extra QALY gained.

Experiences of PBAC with uncertainty

PBAC is required to determine whether or not a medicine is cost effective, and as part of that process is required to consider the clinical effectiveness of a medicine, taking into account the comparator (the therapy that prescribers would most replace with the medicine in practice if the PBS subsidises it as requested) and the risks of harm associated with the new medicine.

From a PBAC perspective, clinical uncertainties stem from deficiencies in the primary clinical data and the need to translate from such data to address the question of whether the new medicine is cost-effective in the PBS listing as requested. A particular issue is the design of the trial. Ideally PBAC would like to see, wherever possible, direct "head-to-head" randomised trials against the prevailing medicine or treatment. It is acknowledged however that this can be difficult at times because the comparator in Australia may not be the same as it is in other countries, because of the changing nature of listings on the PBS, because of trial design issues or because of ethical considerations. It can be that the comparator changes in the years between the commencement of a trial and the eventual consideration of a submission by PBAC, which also makes direct comparisons more difficult.

In the absence of direct randomised trials, indirect comparisons are often provided as the primary source of clinical evidence. This matter was substantially addressed in the 2006 revision of the PBAC Guidelines, with a separate Section B(i) on presenting such evidence. The Economics Sub-Committee of PBAC has also established an Indirect Comparisons Working Group involving independent experts and representatives of both the committees and the industry, to look at this matter, which first met on 11 April 2008.

Another major source of clinical uncertainty is the reliance on translating surrogate measures reported in trials to final outcomes presented in modelled economic evaluations, and it needs to be noted that this issue has been identified both nationally (including at the 2006 Joint Policy Conference) and internationally. This issue was partially addressed in the 2006 revision of the PBAC Guidelines. The Economics Sub-Committee of PBAC has also similarly established a Surrogate to Final Outcomes Working Group to look at this matter, which also met on 11 April 2008.

PBAC experience indicates that companies could do more to tailor their clinical trials to meet the needs of the health technology assessment step which is necessary for listing a medicine for public subsidy. PBAC encourages companies to take advantage of the pre-submission meetings with the PBAC secretariat to identify issues of predictable uncertainty earlier in the process. Open and early dialogue can provide the company with feedback to take into account when finalising its trial design. Increasing the number of pre-submission meetings may have resource implications for DoHA.

How Government entities deal with uncertainty

PBAC and DoHA therefore and on balance prefer to deal with uncertainty by adopting a flexible approach to each situation within the constraints of the legislative framework within which they operate. Each submission is different and where uncertainties exist, the PBAC response is tailored to address each specific issue. A rigid 'tick box' set of criteria that passes

or fails an application is not the best way to deal with uncertainty that arises in assessing a complex pharmaceutical listing submission. In fact while a "tick box" approach could enable **some** companies on **some** occasions to tailor their submission to meet the criteria, the degree of variation is such that DoHA and PBAC believe that such an approach will likely limit PBAC in finding pathways to list an expensive new medicine associated with elements of uncertainty.

Assessing the clinical benefit and cost effectiveness of a medicine on evidence supplied by an applicant is often not straight forward. The data presented may differ in quality between applications, there may be queries on the accuracy or relevance of data presented or on restrictions requested by the applicant, or further information may be required to support the request.

The existing flexible arrangements to deal with uncertainty permit PBAC to:

- recommend (or not) PBS listings on the information provided;
- defer a decision subject to further information from the applicant company;
- based on input from the Restrictions Working Group, recommend variations to restrictions sought by the applicant company; or
- provide additional advice alongside a recommendation to list, for example on pricing.

Examples of ways to address uncertainty, by using the existing flexibility in assessment include:

- **Restrictions** - such as restricting to closely defined populations within the TGA approved indications or, less frequently, continuation rules where there is uncertainty over who will benefit sufficiently from the medicine to justify continuing subsidy on a cost effectiveness basis. DoHA has evolved a restriction taxonomy which allows quite fine adjustments to the level of restriction assurance required. This ranges from unrestricted benefits through to complex requirements requiring prescribers to supply written requests to Medicare Australia for authorisation to prescribe. These restrictions are primarily designed to ensure that only the right patient is treated under the right circumstances, but they can also have the effect of ensuring that very expensive medicines are used wisely and carefully and are only substituted for less expensive treatments where there is a clear clinical need to do so.
- **Deeds of Agreement** – such as recommending a weighted average price across subgroups of a PBS eligible population that account for differing prices 'justified' by differing levels of clinical benefit and hence differing cost effectiveness. Deeds are also used to give Government greater certainty around projected expenditure for some listings by establishing usage thresholds over which payment of a rebate may be required. This type of risk-sharing arrangement is aimed at encouraging each sponsor to ensure its medicine is being prescribed appropriately. For example, rebate payments have been required for 'leakage' of the medicine beyond the PBS restriction into uses which have not been accepted as cost effective at the listed price, including uses for indications which have not been approved by the TGA. They have also been used to address financial uncertainties about the extent of use consistent with the restriction, for example where the extent of prescribing exceeds predicted behaviour.

- **Relevant randomised trials which measure more patient-relevant health outcomes** – such as on-going trials conducted elsewhere which are reported to PBAC when updated and/or completed. For example, ongoing follow-up from Phase III trials designed for regulatory purposes or new trials, including Phase IV trials from the drug company, designed to address questions relevant to decisions for listing a medicine for public subsidy.
- The inclusion of **Quality Use of Medicines** (QUM) programs and cooperation with other QUM partners with the view that, for some medicines, such programs may reduce uncertainty related to utilisation and clinical outcomes.
- **Consumer Impact Statements** – PBAC is currently trialling Consumer Impact Statements, which allow patients to present in their own words, details about how a condition affects their daily life and the impact on carers. Initial feedback from the PBAC about the usefulness of the information provided has been positive.

It is important when dealing with uncertainty to acknowledge that uncertainty is not simply resolved by agreeing to list an item. Populations, treatment algorithms and the emergence of new medicines and technologies can cause changes over time and create new uncertainties around the clinical effectiveness of a medicine, or exacerbate existing uncertainties. PBAC has dealt with this in part through "predicted versus actual" utilisation reviews conducted by its Drug Utilisation Sub-Committee.

Another post-listing action has been to meet with treating clinicians and affected companies to consider how the treatment algorithm is changing. For example at the present time, PBAC is concerned about a rare condition for which there were no effective medicines 2 or 3 years ago, but for which there are now 5 or 6. PBAC has therefore initiated a meeting with clinicians to look at how each of the medicines is being used in practice, the evidence for that use, and the extent to which current restriction arrangements help or hinder best quality cost effective medication use.

A summary of international examples of dealing with uncertainty is contained at Appendix B.

Principles around managing uncertainty in the PBS listing process

It is acknowledged that uncertainty in the PBS listing process cannot be eliminated, but it can be minimised and/or managed. Guiding principles in managing uncertainty include:

- Uncertainty should be accepted and managed, and where possible minimised;
- Stakeholders should recognise that a flexible approach acknowledges that there are many different types of uncertainty and its management requires a suite of options to draw from, tailored to the specific issue;
- Stakeholders in the Australian system can learn from and contribute to global developments in dealing with uncertainty;
- Patient access, benefit and safety and the viability of the PBS should be foremost in efforts to manage uncertainty.

Possible future options for dealing with uncertainty

As noted above, PBAC adopts a flexible approach when dealing with uncertainty to enable it to respond to individual situations in the most constructive manner within the legislative framework governing its operation. The nature of particular uncertainties will vary from submission to submission and will require ongoing flexibility and responsiveness from PBAC.

However, the following activities not already explicitly undertaken by PBAC, might be worthy of further examination and discussion about any possible practical application in the PBS listing process. This list is not arranged in priority order.

- The encouragement of more detailed and extensive pre-submission meetings between the sponsor and DoHA. In these meetings key areas of uncertainty would be more clearly identified and discussions held relating to how these may be addressed either prior to or during the assessment period. (NB this project would have significant overlap with elements of the AMWG's work on streamlining the registration and reimbursement processes).
- The examination of a case-manager role who would liaise between the sponsor and the PBAC (its sub-committees) and Departmental officers. The case-manager would assist in finding solutions to problems as they emerge during the assessment process, with a particular focus on addressing areas of uncertainty. It is not expected that every submission would need a case-manager, but only those that have been identified at the pre-submission meeting as being sufficiently complex that it would benefit from such an intervention.
- Further exploration of the use of Coverage with Evidence Development (CED, see Appendix B) as a tool for managing uncertainty under pre-defined circumstances. Significant theoretical work and debate has already been undertaken in this area, and it is proposed that the AMWG work towards examining its possible application to the PBS.

Conclusion

This paper has identified three options for managing uncertainty in the PBAC decision making process that merit further consideration. The AMWG will develop a work plan of projects to explore the management of uncertainty in greater detail and will keep the Minister informed in a future report.

Appendix A – Cost effectiveness and the incremental cost effectiveness ratio (ICER)

Cost effectiveness assessment compares the price advantage sought by a sponsor to the net additional health gains conferred by the new drug over its main comparator, together with any cost implications arising from changes in the provision of health care resources. The main comparator is the current therapy that prescribers would most replace with the new drug in practice. The main comparator can be another PBS-listed drug or, where there is no existing effective drug therapy, placebo for standard medical management of the condition.

The preferred metric for describing the overall changes in health outcomes is the number of Quality Adjusted Life Years (QALYs) gained. This summarises the effects of a health intervention on both survival and quality of life.

In calculating the costs associated with listing a drug on a cost effectiveness basis, a wide range of costs (and cost offsets) can be taken into account beyond drug costs. These can include diagnostic, medical, hospital, residential age care and allied health services costs. For the sake of simplicity, the discussion and examples below focus on the drug costs of the new drug and its main comparator only and not any other sources of costs and cost offsets.

The ratio of additional costs to additional health gains is known as the Incremental Cost Effectiveness Ratio (ICER), which is simplified below as:

$$\text{ICER} = \frac{\text{price advantage requested}}{\text{additional QALY gained}}$$

The ICER presents the extra cost for each additional QALY gained offered by the new drug therapy. The larger the ICER, the more "expensive" is the additional health gain and the less favourable the economic credentials are for a PBAC recommendation to list. Increasing the price advantage requested over the comparator increases the value of the ICER. Increasing the additional QALY gained decreases the value of the ICER.

While there is no single maximum ICER value set by PBAC – no "cost effectiveness threshold" – there is evidence that medicines are more likely to be recommended for listing with an ICER around $30,000 than with an ICER above $70,000.

Table 1 provides an example of a new drug with an ICER of $30,000. A $1,500 price advantage is requested for the new drug, and there is an additional health gain of 0.05 QALYs. In this simple example there are no non-drug costs or cost offsets to take into account.

Table 1

Comparator cost/year	$500
New drug cost/year	$2,000
Price advantage requested	$1,500
Additional QALY gain/year	0.05
ICER	$30,000

Appendix B Some International examples for handling uncertainty

An analysis conducted of published internationa l initiatives aim ed at handling uncertainty identified a num ber of s olutions which to vary ing degrees have been applied in Au stralia. These initiatives from the EU, USA and Canada are categorised below:

- Risk sharing linked to clinical outcomes (UK, Canada, EU)
  - Reimbursement is agreed on the basis that additional data is forthcoming from studies th at will f urther clar ify or stre ngthen th e claim in r egard to clinical outcomes. Studies must be of appropriate quality and size to address the area/s of uncertainty.

- Coverage with Evidence Development (Mostly USA)
  - As f or risk sharing lin ked to clini cal outcom es. Coverag e with Evidence Development (CED) is a term used m ainly in the United S tates, and implies Medicare coverage (reimbursem ent) w ith the condition that additional data (evidence) is being developed. This ev idence development may be via various methods, again with consideration of size and quality of the research. The reimbursement during this period of fu rther developm ent of evidence m ay occur v ia lim ited and f ormal tria l part icipation, or on a wider bas is with separate evidence developm ent on an ongoing basis. The form er may al so be termed Coverage with Study Participation.

- Price Volume/dosage Arrangements (USA Managed Care)
  - Where the uncertainty is related to the daily cost of the m edication and where that m ay vary significantly, reim bursement decisions m ay be m ade on the assumption of a certain daily cost of m edication. This m ay be based on the average d aily dose (and cost) and the risk sharing arrangem ent m ay r equire some change to the price or coverage decision if actual daily doses vary fro m that average.

Streamlining the Listing of New Medicines on the Pharmaceutical Benefits Scheme

The Access to Medicines Working Group has been exploring the capacity to further streamline and coordinate processes to reduce the time it takes to list a medicine on the Pharmaceutical Benefits Scheme (PBS).

As part of this exploration, the AMWG has met with the Therapeutic Goods Administration (TGA) to discuss the various ways in which the TGA and the Pharmaceutical Benefits Advisory Committee can increase the efficiency of their processes. These discussions included examining the possibility of aligning the medicine registration and PBS listing processes to allow parts of these areas to run concurrently.

During these discussions a number of areas have been identified where efficiencies in the registration of new medicines by the TGA can be made, while maintaining the integrity of the regulatory process. The AMWG has received 'in principle' agreement from the TGA on ways to decrease the time to have new medicines registered on the Australian Register of Therapeutic Goods.

The AMWG will work closely with the TGA on these identified areas, as there is agreement that this is the area where the greatest gains can initially be made.

AMWG will continue to examine ways to both leverage this improvement in regulatory time lines and also build improvements into the PBS process to facilitate earlier times to listing. Possible improvements in the PBS process that might be explored include the use of pre-submission meetings, improvements to the post-PBAC processes, and, possibly, earlier commencement of PBAC evaluation whilst TGA assessment is under way.

It should be noted that while every effort will be made to streamline the areas identified, all parties involved stress that this work will be conducted with absolute regard to maintaining high standards in relation to the assessment of efficacy, safety and cost-effectiveness in the processes of the registration and PBS listing of new medicines.

A working group consisting of AMWG members, the Pharmaceutical Evaluation Branch and the TGA will be convened to further discuss work in these areas. It is expected this group will provide a report to the Minister on its findings at a later date. As well as identifying areas where the time to listing could be improved, the AWMG will continue to receive updates on the streamlining work of the TGA, offering support as needed.

Increased public input into PBAC Decision making processes - Publication of PBAC Agendas

Under its terms of reference the AMWG, in collaboration with the PBAC, is charged with improving the transparency of the decision making processes around the assessment of medicines for subsidy through the Pharmaceutical Benefits Scheme.

To this aim, agreement has now been reached between the Department, Medicines Australia (MA) and the PBAC that a version of the PBAC agenda will be made publicly available 4 - 6 weeks before the relevant meeting. This will facilitate members of the public, including consumers and medical practitioners, to submit their views on the medicines being considered by the PBAC.

This agenda will be published on the Department's website and will include the generic and trade name of the medicine, the sponsor and the purpose of the submission. No details will be published for submissions intended solely to affect pricing relativities.

The website with this information will allow members of the public to provide comments on the medicines being considered by the PBAC.

The AMWG believes that the publishing of a list of PBAC agenda items will allow consumers and others to provide input on the medicines being considered. A summary of this input will be made available to the PBAC and the sponsors and can be considered by the PBAC when assessing each medicine. This will give interested people and organisations more direct input into, and a better understanding of, the PBAC decision making process.

Discussion is continuing between the Department and MA on the detail of implementing this process from mid September in time for the November 2008 PBAC meeting.

Future Work of the Access to Medicines Working Group

The Access to Medicines Working Group has highlighted the following areas in which the future work of the group may be directed, once the projects currently underway are complete.

While the subjects listed below are areas where work may be carried out, the group has given priority to streamlining the registration of new medicines and managing uncertainty in PBAC submissions. These projects will continue to be the focus of the group's endeavours in the immediate future.

Two identified areas of future work are:

Understanding the Pharmaceutical Benefits Advisory Committee decision making process

Notwithstanding the extensively documented processes and criteria described in a set of guidelines issued by the PBAC, sponsors advise that the factors influencing decision making in the medicine evaluation process are not always well understood.

This work will therefore examine how to achieve a better understanding to assist companies preparing submissions, and potentially reduce the number of resubmissions required. Better prepared submissions are also less burdensome on the PBAC and facilitate more informed decision making.

Understanding innovation in the drug development process

Innovation is considered to be essential to the business of the pharmaceutical industry.

This work would be to develop a shared understanding of the nature and dimensions of innovation that underpin the drug development process. This would include examining how the PBS listing process shapes incentives towards innovation.

Access to Medicines Working Group – Terms of Reference

1. Providing strategic oversight of joint activities undertaken by the Department and Medicines Australia to enhance the Pharmaceutical Benefits Scheme (PBS) processes; and
2. As a result of reforms to the PBS announced in 2006, considering issues relating to timely and appropriate access to effective new medicines on the PBS, including:
   - the capacity to further streamline and coordinate processes to reduce the time it takes to list a medicine on the PBS;
   - possible impacts on the listing process of mandatory price reductions from 1 August 2008 for medicines on the new F2 formulary;
   - the potential for improving clinical trial, economic and financial data to inform Pharmaceutical Benefits Advisory Committee (PBAC) and Pharmaceutical Benefits Pricing Authority (PBPA) decision making processes;
   - in collaboration with the PBAC, developing and articulating a set of principles for assessing evidence and information relating to new medicines and for improving the transparency of the decision making process;
   - the practical limitations to the evidence available to the PBAC to facilitate decision making around access to new medicines and the development of options to manage uncertainty in such situations;
   - opportunities for informing and learning from the broader international debate about evidentiary requirements and trends in drug development to support the economic evaluation of new medicines.

Access to Medicines Working Group - Work Plan

This work plan identifies three streams of work:

1. Current AMWG projects being undertaken directly by the AMWG.
2. Potential AMWG projects to be undertaken directly by the AMWG.
3. Other current MA-DHA activities of interest to AMWG.

Items are listed under the most relevant of the AMWG terms of reference.

a) the capacity to further streamline and coordinate processes to reduce the time it takes to list a medicine on the PBS

Current AMWG projects

1. Understand and map current processes up to PBS listing (from both government and industry perspectives) and identify key issues that impact on timeliness/efficiency.
2. Articulate options to improve these processes, taking into account cost recovery interaction and key performance indicators (KPIs) where necessary. Options include:
   a) Starting the listing process at an earlier point in the corresponding TGA process (noting potential for increased financial risk associated with increased PBAC deferrals and rejections, cost recovery issues, and possible increased workloads for contingency planning)
   b) Exploring opportunities for investment in earlier pre-submission dialogue, including to identify and seek to resolve technical and evidentiary issues about medicines under development to help influence design of trials which will eventually form the evidence base of PBAC submissions.
   c) Exploring streamlining options for the current PBS listing process, such as tiering of submissions with explicit criteria such as evidentiary requirements, cost to Government etc.

Other current MA-DHA activities

3. Development of key performance indicators for the PBS listing process, including further development to describe impact of serial submissions for a medicine on listing times.
4. Risk-sharing arrangements

b) possible impacts on the listing process of mandatory price reductions from 1 August 2008 for medicines on the new F2 formulary

Current AMWG projects

5. Identify and agree on possible impacts on the listing of new medicines.
   a) Report on outcomes of joint MA-DoHA workshops held in 2006 about the possible effects of price reductions for comparators on cost-effectiveness assessment of new medicines.
   b) Report on further work undertaken on possible effects of comparator price reductions.

c) Quantify the proportion of submissions in recent years where the comparator would be an F1 or F2 product.

d) Analyse data from PBAC evaluations in the period after the August 2008 price reductions take effect to determine any impacts on the listing of cost-effective new medicines.

6. Production of a joint MA – DoHA paper on the comparators issue.

a) Issues; and

b) Discussions of different options for their management if necessary.

c) the potential for improving clinical trial, economic and financial data to inform Pharmaceutical Benefits Advisory Committee (PBAC) and Pharmaceutical Benefits Pricing Authority (PBPA) decision making processes

Current AMWG projects

7. Issues paper on identifying uncertainty in the assessment of medicines for listing on the pharmaceutical benefits scheme - *Identifying the Issues and Gaps in current practices*

Other current MA-DHA activities

8. Evaluation of the impact of the 2006 PBAC Guidelines on PBAC submissions from both government and industry perspectives, including interaction with:

– Joint Policy Conference issues and outcomes (refer to Joint Policy Conference outcomes, Item 2: Standards of evidence and transparency);

– Coordination of and with Guidelines steering group activities;

– Workload from both government and industry perspective;

– Assessments of the extended use of both clinical and non-clinical data.

d) in collaboration with the PBAC, developing and articulating a set of principles for assessing evidence and information relating to new medicines and for improving the transparency of the decision making process

Potential AMWG projects

9. Identify what additional considerations are taken into account other than cost-effectiveness to improve understanding and transparency of decision making processes.

10. Develop protocols which enable the PBAC to explain publicly its controversial decisions ahead of the timeframes agreed for the standard processes for publishing PBAC outcomes.

Other current MA-DHA activities

11. Coordinate with ESC/MA's PBAC Guidelines revision steering group to examine risks and benefits of more timely public feedback from PBAC.

12. Report from Joint Policy Conference (JPC) oversight management committee on outcomes and work plan with respect to standards of assessing evidence relating to new medicines, including:

– Publishing a list of items for each PBAC agenda once these are accepted for evaluation.

– Enabling independent clinician and consumer input into PBAC considerations of submissions.

– Including the outcomes of "Item 8" PBAC agenda items as part of the processes to publish PBAC outcomes and PSDs (Item 8 consists of submissions to PBAC to request a change in price relativity).

e) the practical limitations to the evidence available to the PBAC to facilitate decision making around access to new m edicines and the developm ent of options to m anage unc ertainty in such situations

Current AMWG projects

13. Identify where the uncertainties are that hinder decision making, and identify potential solutions.

– For example, exploration of how "coverage with evidence development" might assist with the collection of additional post-listing data in order to enable a more confident PBAC recommendation to list in the future.

f) opportunities for informing and learning from the broader international debate about evidentiary requirements and trends in drug development to support the economic evaluation of new medicines

Potential AMWG projects

14. Identify framework and objectives for international engagement.

15. Assess opportunities at international forums to discuss health technology assessment consistent with this framework and where appropriate incorporate lessons into the Australian system.

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