



## **An open letter to pharmaceutical companies**

We are pleased to advise you of recent developments improving the transparency of decisions taken by the Pharmaceutical Benefits Advisory Committee (PBAC). Work has been underway between the Pharmaceutical Benefits Branch (PBB) of the Department of Health and Ageing and Medicines Australia (MA) since it was announced by the Government last year that it wished to improve the reporting of PBAC decisions.

Decisions of PBAC have long been reported on the PBAC website if they are recommendations for listing. We have been much less informative when a decision has been taken to either defer or reject an application for PBS subsidy from a sponsor. The decision by Government of last year on transparency of PBAC processes requires us to report on all decisions from the meeting of PBAC being held in June 2003 onward. A code of conduct governing the implementation of this Government decision is at Attachment 1.

It has been agreed that the information provided relating to PBAC's recommendations will be structured. It will be a process that is refined over the next year or so as we work out improved ways to make the reporting most useful, constructive and reasonable from the point of view of all stakeholders.

The information released provides the outcome of each application to the PBAC and a summary of the reasons for each outcome. Details of the process and timing for making public the outcomes of the June 2003 PBAC meeting are at Attachment 2. Agreement has been reached that each sponsor will receive a draft of the proposed publication of the outcome of its application, with an opportunity to comment on the content, before finalisation. On this first occasion, 15 working days will be allowed to enable agreement but, in future, 10 working days will be allowed. At Attachment 3 are the formats and wording for this process developed to date.

Agreement has also been reached that the each sponsor will have the opportunity to provide a summary comment in response to each outcome (pertaining to each submission), on the PBS website. If a sponsor wants to link the reader to its own website where further information is available, this will also be permitted. Each sponsor will have discretion about whether to include a comment or not and whether or not to provide a website link.

Transparency in the PBAC processes is a high priority issue for the Department, for Medicines Australia and for Government. There have been reasonable concerns that greater explanation could be provided on how decisions are come to relating to the PBS subsidy and it is time that we made new efforts to ensure a good understanding of our system. The PBS system is one to be proud of. It is evidence-based, it is informed by the work of many experts

and it is a growing and important priority within the government's commitment to the health and care of the Australian community.

It is agreed between PBB and MA that we will continue to work together through the implementation of these new arrangements and make changes as required. The rules are not hard and fast at this stage but rather a good operationalised form of guidelines for us to adopt.

We trust that you will welcome this development and assist us with its implementation over the coming months.

Joan Corbett  
Assistant Secretary  
Pharmaceutical Benefits Branch  
20 June 2003

Kieran Schneemann  
Chief Executive Officer  
Medicines Australia  
20 June 2003

**CODE OF CONDUCT – A GUIDE FOR THE RELEASE OF THE OUTCOMES OF  
CONSIDERATIONS BY THE PHARMACEUTICAL BENEFITS ADVISORY  
COMMITTEE (PBAC)**

**Purpose of Code:**

The purpose of this code is to provide guidance to officers of the Department of Health and Ageing on the principles to be followed in the publication of the outcomes of PBAC meetings.

**Background:**

The PBAC is established under the *National Health Act 1953* to advise the Commonwealth Government on the listing of medications on the Pharmaceutical Benefits Scheme (PBS). There is a public interest in the applications for listing considered by the PBAC, and the outcomes of those considerations.

The Government supports the need to make these outcomes publicly available to promote the transparency of the decision making process on the availability of subsidised medication to the Australian community.

Commencing with the June 2003 PBAC meeting, the outcomes of all listing applications or changes to current listings, are made available via the Department of Health and Ageing's PBS website.

**Guiding Principles:**

The information released provides the outcome of each application to the PBAC and a summary of the reasons for each outcome. The emphasis is on the views of the PBAC rather than the facts of the submission.

Information relating to the PBAC recommendations which should be kept confidential are those which are clearly:

- trade secrets;
- any other information having a commercial value that would be, or could reasonably be expected to be, destroyed or diminished if the information were disclosed; or
- information concerning the business, commercial or financial affairs of an organisation, being information the disclosure of which would, or could reasonably be expected to, unreasonably affect that organisation in respect of its lawful business or financial affairs.

Examples of commercial information that should not be disclosed include that information which is clearly:

- of a proprietary nature;
- in relation to prices which are still in negotiation; and
- data from studies, trials and models which are not yet published.

## Process and timing for making public the outcomes of the June 2003 PBAC meeting

### Information to sponsors about PBAC outcomes

- By Friday 27 June 2003: PBAC 'Short Minutes' to each sponsor.
- By Friday 4 July 2003: Proposed draft publication of outcome for consideration by sponsor, which indicates those matters which are at the discretion of the sponsor (for example, sponsor's comment). *Following future PBAC meetings, it is expected that this draft publication will accompany the PBAC 'Short Minutes'.*

### Dialogue between sponsors and PBB about publication of PBAC outcomes

- By Friday 11 July 2003: An indication from sponsors about whether or not there are any concerns with the draft publication, preferably with suggestions for changes. This should be conveyed to Diana MacDonell, PBAC Secretary.
- Monday 14 July 2003: PBB and MA officials meet to discuss particular concerns, where the sponsor has authorised MA involvement, and to review progress of this process to date.
- By Friday 25 July 2003: Finalisation of publication of PBAC outcomes. *Following future PBAC meetings, it is agreed that this period for dialogue between the sponsor and PBB will reduce to 10 working days. An extra 5 days was agreed for dialogue for the initial process following the June 2003 PBAC meeting. It is preferred that individual items be finalised sooner rather than later within this period.*

### Publication

- By Friday 1 August 2003: PBAC outcomes published on PBS website. *Following future PBAC meetings, it is expected that this publication will occur sooner after finalisation.*

### Dispute resolution

It is expected that the extensive negotiations between PBB and MA have minimised the likelihood that there will be outstanding issues requiring resolution following this process. In this unlikely event, the following process is proposed.

- By Friday 1 August 2003: As necessary, discussion between the sponsor and Joan Corbett, Assistant Secretary, PBB to address the impasse between the PBAC Secretariat and the sponsor. In the meantime, an agreed minimal set of facts of the submission will be included on the PBS website alongside the other PBAC outcomes, with the statement that 'The PBAC deferred/rejected the application (wording to be finalised).'
- By Friday 8 August 2003: As necessary, discussion between the sponsor, Philip Davies, Deputy Secretary, Department of Health and Ageing, and Kieran Schneemann, Chief Executive Officer, Medicines Australia, to resolve any remaining impasse. *The need for and operation of a second consideration of such a dispute following discussion with the Assistant Secretary, PBB, will be kept under active review by PBB and MA.*

## Formats and wording to be used in making additional types of PBAC outcomes public

### Format for deferrals (with examples)

DRUG and FORM	DRUG USE and TYPE	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Generic name, formulation type, strength, brand name Company name	An antibiotic	Authority required listing [for <i>wording of the restriction (optional, by consent of sponsor)</i> ]	The PBAC deferred consideration pending advice from EAGAR on the appropriateness of the restriction requested.
			Sponsor's comments [as per possible wording below] Sponsor's web link (if provided by sponsor)
Generic name, formulation type, strength, brand name Company name	An anti-cancer agent	Authority required listing [for <i>-wording of the restriction (optional, by consent of sponsor)</i> ]	The PBAC deferred consideration pending the receipt of further information from the sponsor.
			Sponsor's comments [as per possible wording below] Sponsor's web link (if provided by sponsor)

### Notes

#### Column 3

- Will be drafted by PBAC at the time of its decision.
- Will comprise structured wording consisting of up to two parts:
  1. Wording that specifies the type of listing requested by the sponsor, for example, 'Authority Required/Restricted Benefit/Unrestricted/Section 100'.
  2. The PBAC has the opportunity to propose additional wording setting out the specific nature of the restriction. The draft publication provided to sponsors will show this wording in different type (for example, *italics*). It will indicate clearly that **inclusion, amendment or deletion of these words is at the discretion of the relevant applicant.**

#### Column 4

- Will be drafted by PBAC at the time of its decision.
- Will comprise structured wording setting out in a sentence the general reason for PBAC's deferral decision, summarising the matters to be addressed in a re-consideration, including who will address these matters. The following table provides an example and other suitable examples can be found in the Attachment.
- There will be an opportunity for **sponsors' comments** and sponsor's web links as follows:
  - comments will be at the discretion of individual sponsors;
  - sponsors may select from a menu of generic words (cf Attachment); and

- inclusion of links to sponsors' websites will be possible at the discretion of individual sponsors (with the default being no link to a website unless specifically provided for by the sponsor in its communications to the PBB on the proposed publication).

**Format for 'first-time' rejections (with examples)**

DRUG and FORM	DRUG USE and TYPE	LISTING REQUESTED BY SPONSOR	PBAC OUTCOME AND COMMENTS
Generic name, formulation type, strength, brand name Company name	An antibiotic	Authority required listing [for – <i>wording of the restriction (optional, by consent of sponsor)</i> ]	The PBAC rejected the application due to concerns with cost-effectiveness.
			Sponsor's comments [as per possible wording below] Sponsor's web link (if provided by sponsor)
Generic name, formulation type, strength, brand name Company name	An anti-cancer agent	Authority required listing [for – <i>wording of the restriction (optional, by consent of sponsor)</i> ]	The PBAC rejected the application on the grounds of issues with the clinical and economic claims.
			Sponsor's comments [as per possible wording below] Sponsor's web link (if provided by sponsor)

**Notes**

Column 3

As for deferrals (see page 1).

Column 4

- Will be drafted by PBAC at the time of its decision.
- Will comprise structured wording that:
  - provides in a sentence a general and simple indication of the PBAC outcome (the following table and the Attachment include suitable examples);
  - does not contain qualifying words that could be considered emotive or value laden to the average person;
  - addresses one or more of the four major areas considered by the PBAC, that is:
    - the requested restriction
    - the nominated comparator
    - the clinical claims
    - the economic claims.
- There will be an opportunity for **sponsors' comments** and sponsor's web links, as for deferrals (see page 1).

**Format for ‘subsequent’ rejections (with examples)**

Drug and Form	TGA approved indication	Current PBS listing	Listing requested by Sponsor	PBAC outcome and comments
Generic name, formulation type, strength, brand name Company name	[As per latest PI] <sup>1</sup>	[Nil] or [as per current PB Schedule]	Restricted benefit for [wording as requested]	Accepted
			<i>Comparator</i> [name of comparator]	Accepted
			<i>Clinical Claim</i> [The proposed drug] is at least as effective and safe as [the main comparator]	Accepted – The PBAC accepted the claim, but, due to the small size of the trials, considerable uncertainty remained.
			<i>Economic Claim</i> A [cost analysis] approach was adopted.	Rejected - The PBAC had concerns with the modelled economic evaluation.  The PBAC rejected the application because of issues with the modelled economic evaluation and the cost-minimisation basis for listing.
				Sponsor's comments: [as per possible wording below] Sponsor's web link (if provided by sponsor)

<sup>1</sup> Provided to TGA by sponsor

**Notes**

**Column 2**

The TGA registered indication will be extracted from the latest Product Information provided by the sponsor at the time of PBAC consideration. Any as yet unregistered indication published will be footnoted to this effect (see table above).

**Column 3**

The current PBS listed restrictions will be published, as per the schedule.

**Column 4**

- Will be drafted by PBAC at the time of its decision from the re-submission and will contain:
  - wording that specifies the type of listing requested by the sponsor, for example, ‘Authority Required/Restricted Benefit/Unrestricted/Section 100’;

- the specific requested wording of the restriction, in keeping with the proposal to compare the requested restriction with the TGA-approved indication; and
- a summary of the nominated comparator, the clinical claim and the economic claim (the latter two from agreed lists, see Attachment).

#### Column 5

- Will be drafted by PBAC at the time of its decision.
- Will comprise structured wording that:
  - (i) provides consistency across companies and products, and (ii) ensures information made public is consistent with the PBAC decision provided to the applicant;
  - does not contain qualifying words that could be considered emotive or value laden to the average person (see Attachment for suggested wording);
  - includes a statement of ‘accepted’ or ‘rejected’ next to each of the four major areas considered by PBAC:
    - the requested restriction
    - the nominated comparator
    - the clinical claims
    - the economic claims; and
  - in the PBAC commentary, will outline areas of uncertainty or reasons for ‘acceptance’ or ‘rejection’ of what the sponsor has put forward, as appropriate.
- The length of total PBAC commentary to aim for no more than 100 words maximum.
- There will be an opportunity for **sponsors’ comments** and sponsor’s web link as for deferrals (see page 1).

## **Possible wording for making PBAC outcomes public**

*The following is an indicative, but not exhaustive set of possible words.*

### **For deferrals**

#### *Possible words for PBAC comment*

The PBAC deferred the application due to issues with regard to the requested restriction.

The PBAC deferred the application due to issues with regard to the nominated comparator.

The PBAC deferred the application due to issues with regard to the clinical evidence.

The PBAC deferred the application due to issues with regard to the economic evidence.

The PBAC deferred the application due to issues with regard to the cost effectiveness claim.

In view of uncertain cost-effectiveness, the PBAC deferred the application so that the applicant can further clarify and elucidate the model.

The PBAC deferred the application to seek advice from .... on the appropriateness of the requested restriction.

### **For ‘first-time’ rejections**

#### *Possible words for PBAC comment*

The PBAC rejected listing due to issues with regard to the requested restriction.

The PBAC rejected listing due to issues with regard to the nominated comparator.

The PBAC rejected listing due to issues with regard to the clinical evidence.

The PBAC rejected listing due to issues with regard to the economic evidence.

The PBAC rejected listing due to issues with regard to the cost effectiveness claim

### **Proposed listing or request by sponsor (for ‘subsequent’ rejections)**

#### *Possible words for PBAC comment*

The PBAC considered that the evidence does not provide a direct basis for the requested restriction.

The PBAC noted that the trials included patients who were not representative of those for whom PBS listing is sought.

The PBAC considered that a listing as a restricted benefit would lead to widespread use outside the intended population.

The principle area of clinical uncertainty was that none of the trials available in the submission present data specific to the effectiveness of the drug in the requested restriction, and therefore they do not allow a direct comparison with the comparator.

### **Comparator (for ‘subsequent’ rejections)**

#### *Possible words for PBAC comment*

The PBAC considered that the comparator inappropriate because the proposed drug belongs to a new class of ..... drugs, and has recommended the use of XXX as the main comparator in any re-submission.

### **Options for clinical claims of the submission (for ‘subsequent’ rejections)**

- [The proposed drug] is significantly more effective than [the main comparator] and has similar or less toxicity.
- [The proposed drug] is has similar effectiveness to [the main comparator], but has less toxicity.
- [The proposed drug] is significantly more effective than [the main comparator], but has more toxicity.
- [The proposed drug] is at least as effective and safe as [the main comparator] in terms of effectiveness and toxicity.
- [The proposed drug] is less effective than [the main comparator], but has less toxicity.

#### *Possible words for PBAC comment*

The PBAC considered that there was uncertainty with respect to the choice and interpretation of the outcome measure. The PBAC concluded that it is difficult to interpret the clinical importance of a .... reduction in the ..... score as an outcome measure.

The comparative effectiveness and safety between the drugs remains uncertain and the PBAC did not consider that the submission had clarified the patient relevance and the magnitude of the clinical benefit of ..... Thus the clinical importance of each outcome measure remains unclear and it is difficult to extrapolate from the surrogate outcomes to clinically important endpoints.

The PBAC identified several clinical uncertainties in the trials that formed the basis of the submission. These related to deficiencies in the measures taken to minimise bias, particularly potential problems relating to temporal factors, such as regression to the mean.

The PBAC considered that the estimate of effectiveness may be greater in the randomised trials than in the regular clinical setting of the requested restriction because the randomised trials were not conducted on patients who had demonstrated failure to respond to other interventions.

### **Options for economic claims of the submission (for ‘subsequent’ rejections)**

- A cost-effectiveness analysis approach was adopted.
- A cost-utility analysis approach was adopted.
- A cost-benefit analysis approach was adopted.
- A cost-minimisation analysis approach was adopted.
- A cost analysis approach was adopted.
- A theoretical cost-effectiveness analysis approach was adopted.

#### *Possible words for PBAC comment*

The PBAC considered that there is uncertainty with the economic claim in the submission as it depends on interpreting the value of a partial response.

In view of the uncertain clinical benefit, there was also uncertainty about the cost-effectiveness analyses.

The PBAC concluded that it would have been more appropriate to conduct a cost-minimisation analysis incorporating cost off-sets for reduced rescue therapy, and the additional costs of managing side-effects in patients receiving .....

The PBAC agreed that the magnitude of the difference in survival (which vary depending on whether medians or truncated means are used to estimate this difference), and the need to adjust the quality of any survival gain to account for the toxicity of the proposed drug, as well as the disease itself, remain the main issues of concern in interpreting the results of the economic evaluations.

The PBAC noted that a number of assumptions made in the economic model were clinically implausible.

The PBAC noted a number of concerns with the modelled economic evaluation. In particular, the model assumes a survival advantage even though no survival advantage was demonstrated in the trial.

The costs to treat adverse events associated with the proposed drug are not incorporated into the calculations for the modelled economic evaluation.

The PBAC concluded that the determination of incremental utility, and thus the QALY denominator in the cost-utility analysis, is questionable. The incremental cost/extra QALY gained result in the submission was therefore considered unreliable.

## **PBAC conclusion and outcome (for ‘subsequent’ rejections)**

### *Possible words*

The application was rejected because of the uncertain clinical benefit and uncertain and unfavourable cost-effectiveness.

The application was therefore rejected because of uncertain clinical benefit, in terms of doubts about the nature and extent of the lower toxicity than the comparator and uncertain and unfavourable cost-effectiveness.

The application was rejected because of the uncertainty with the modelled economic evaluation, which did not allow the PBAC to assess a cost-minimisation basis for listing.

In view of the uncertain clinical benefit and unfavourable cost-effectiveness, the application was rejected.

The application was rejected because of a lack of data and unknown cost-effectiveness in the requested restriction.

The application was therefore rejected primarily because of lack of evidence in the proposed population and uncertain cost-effectiveness in this patient group.

The application was rejected because of insufficient demonstration of effectiveness across the full population of patients for whom listing is requested and unfavourable cost-effectiveness.

## **Options for sponsors’ comments for deferrals and rejections**

*Text in italics to be inserted only at sponsor’s request, with details of website to be provided.*

- The sponsor has no comment, *but refers you to its own website for further information.*
- The sponsor will be considering its position regarding any future course of action, *but refers you to its own website for further information.*
- The sponsor disagrees with the decision, *and refers you to its own website for further information.*
- The sponsor needs to clarify the decision with the PBAC, *but refers you to its own website for further information.*
- The sponsor may be seeking legal opinion regarding the decision of the PBAC, *and refers you to its own website for further information.*
- The sponsor agrees with the decision, *but refers you to its own website for further information.*