PBAC Guidelines review

Michael Wonder - Wonder Drug Consulting Pty Ltd

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Thank you for providing me with an opportunity to comment on the draft revised PBAC Guidelines (Version 5.0). As a consultant, I may well provide a different perspective to many other respondents. Whilst I could have commented on many aspects, I have chosen to focus on just a few; other parties will no doubt address the other issues. I hope these comments are helpful.

I note the review has multiple objectives; some are not readily measurable and some may be in conflict with others. One objective is to de-clutter the Guidelines; I assume this means reducing the number of pages in the Guidelines. A possible unintended consequence of seeking to meet this objective is to clutter up the process and/or submissions.

One possible way to de-clutter the Guidelines is to produce a series of documents that address the various elements of the PBS listing process:

- Background document; relevant legislation, Government policy, PBAC decision-making framework and related values, standards and procedures
- Methods document
- Guidance document

These documents would accompany the current supporting publications:

- Glossary of Terms
- Manual of Resource Items

To ensure they remain world's best practice, the Guidelines need to keep abreast with the changes in the types of new technologies (immunotherapies, cellular therapies, etc.) and their suitability for listing on the Pharmaceutical Benefits Scheme. A review of what constitutes a 'pharmaceutical' might be needed. Whilst some of these new technologies will not be suitable for public subsidy via the PBS, others may well. You will be asked by the developers of these new technologies whether or not they are suitable for listing on the PBS so some text on this in the Guidelines may be helpful. Just last month, NICE published a report describing a study exploring the assessment and appraisal of regenerative medicines and cell therapies.

The draft Guidelines uses the terms 'product', 'medicine', 'drug', 'product', 'intervention', 'therapy' and 'treatment' interchangeably. They are not the same and are in need of definition. Additional terms, such as 'pharmacological analogue' are also in need of definition.

The draft revised Guidelines gives a reader the impression that the terms 'indication' and 'patient population' are interchangeable. Insofar as the former is frequently used in the regulatory arena and that the target patient population for a given medicine on the PBS is often described in far greater detail that that in the TGA

approved product information, the use of these terms in version 5.0 of the Guidelines needs to be carefully considered.

The target audience of the Guidelines is the (local) pharmaceutical industry; a more precise target is those who prepare submissions, which in many cases are consultants. Many local consultants have considerable experience in preparing submissions; perhaps more than those who charged with the responsibility of lodging them (e.g. pharmaceutical companies). Whilst most practitioners who compile submissions have considerable experience in their preparation, the Guidelines should be pitched at a level for those with limited knowledge/experience.

The proposed text on the choice of the main comparator in Section 1.1 needs carefully examination. The main comparator should be the **action/intervention/therapy** most likely to be replaced, which may not a **medicine/drug**. The replaced intervention/therapy may not have TGA authorization and/or be listed on the PBS. It does beg the question whether watch and wait/watchful waiting and placebo are interventions/therapies.

Section 2.4 Trial characteristics discuss many aspects, including 'minimal clinically important difference' (MCID) and 'non-inferiority margin'. Whilst they are somewhat related, they are not the same; the latter invariably relates to the primary outcome of the trial, the former relates more to a patient relevant outcome. The two concepts are more closely related if the primary outcome of the trial is a patient relevant one.

For both concepts, the draft revised Guidelines state that the difference/margin should be justified in the submission. The nomination/justification of a MCID for a non-patient relevant outcome may be an unnecessary request. If the primary outcome of the trial was not patient relevant, then the MCID might not have been specified in the protocol.

The draft Guidelines note that the source of the MCID may be "a commonly accepted MCID in the literature for both the trial population and the proposed indication." It is unclear what constitutes 'commonly accepted'. Furthermore, the trial population may be different to other trial populations and the proposed indication/patient population may be different to the trial population.

The issue here is not what the trial investigators thought about the MCID or even what the literature might say, but what the PBAC considers the MCID for a given outcome to be. The PBAC has already determined what is the MCID for many outcome measures. It is unclear whether the PBAC is prepared to accept a lower MCID for a given outcome for patients with more severe disease.

MCIDs accepted by the PBAC are reported in the Public Summary Documents but not on a consistent basis. It is recommended that the PBAC develop and publish a list of MCIDs that it has previously considered/accepted. A similar publication could be developed and published for previously accepted non-inferiority margins.