Submission by AbbVie on the draft revised PBAC Guidelines (V5.0)

AbbVie welcomes the opportunity to make this submission on the Draft of Version 5.0 of the PBAC Guidelines.

As noted in the first meeting of the Guidelines Review Steering Committee (GRSC), the first two aims of this current review of the PBAC Guidelines are to be consistent with international standards (UK, CAN, EU); and to create guidelines that are world's best practice. AbbVie welcomes a number of elements of the draft guidelines including: the addition of a disease overview in section 1, particularly important for rare or little known diseases; and the incorporation of translational issues into the appropriate clinical and economic sections. It is AbbVie's opinion, however, that there are two important issues to be raised, those being Section 1.1 on the choice of comparator and consideration on whether the draft guidelines represent international best practice. Other issues with draft guidelines include a lack of guidance for other methodologies for indirect comparisons and whether the de-cluttering of the guidelines, an aim specified by the GRSC, has been met.

Choice of Comparator

The draft PBAC Guidelines at paragraphs 1 and 2 under the heading "Justification for the selection of the main comparator" in Section 1.1 focus on whether a proposed medicine is "substantially more costly than an *alternative therapy*" and indicate that "where multiple alternative therapies could be used for the *majority of patients*" the PBAC "cannot recommend a new medicine at a price that is substantially higher than the least expensive alternative medicine". This suggests that greater emphasis is given to the cost of possible comparators rather than the likely magnitude of substitution.

This section makes reference to Sections 101(3A) and 101(3B) of the National Health Act 1953. These sections do not require the PBAC to adopt the "least expensive alternative medicine" as the sole alternative therapy against which the proposed medicine is assessed, nor does it make reference to the "majority of patients". This section of the draft Guidelines is unclear in that it suggests that the starting point for the PBAC's consideration of effectiveness and cost of therapy should involve identifying the least expensive alternative medicine as the main comparator, whilst at the same time acknowledging that the main comparator is the therapy that prescribers would most likely replace with the proposed medicine in practice. It is also unclear whether this interpretation of the Act will relate to the choice of comparator for both cost-minimisation and cost-effectiveness submissions. AbbVie believes that choice of the least cost (price) comparator without consideration of degree of utilisation (and substitution) is

flawed from a ‘good practice’ economic evaluation perspective. The Act requires that the PBAC consider clinical and cost effectiveness and cost. As the assessment of clinical and cost effectiveness is by definition a comparative exercise the most relevant comparator will always be the one that is replaced most in practice.

Choosing a ‘minor’ comparator based on low unit cost (price) is problematic for economic evaluation if the intention is to make efficient health care decisions to direct the allocation of scarce resources:

- Low cost per unit comparators tend to be older therapies, many of which have been superseded in clinical practice for good reasons. An economic evaluation based on such comparison is not efficient as it will not represent the type of substitution that will happen in real life when the new medicine is PBS listed;
- Often the older low cost per unit medication has a sparse, out of date evidence base that does not reflect standard of care. Generally the new medication seeking PBS listing will have a stronger evidence base against contemporary/relevant comparators. Such comparisons present comparability issues in economic evaluation that lead to increased uncertainty. The additional uncertainty caused may lead to more PBAC rejections and effectively make the reimbursement hurdle for new medications higher than at present. AbbVie believes that this provides a disincentive for listing newer more innovative medicines on the PBS.

In terms of the PBAC’s requirement to consider ‘cost’ as distinct from cost effectiveness, the minor comparator with the least cost per unit will not be a major driver in determining ‘cost’ to the PBS when deciding whether to list a new medication or not. The most relevant comparator with respect to understanding the overall financial impact on the PBS will be the comparator that will be replaced most in clinical practice.

In terms of standard best practice in other relevant HTA markets, the UK NICE Guidelines state that “the Committee will normally be guided by established practice in the NHS when identifying the appropriate comparator” (https://www.nice.org.uk/article/pmg9/ chapter/). The Canadian CADTH Guidelines state that “in the Reference Case, use “usual care” (i.e., the most common or frequently used care) which the intervention is intended to replace (https://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf).

AbbVie believes that the preferable approach for the choice of comparator in Australia be consistent with that taken in England and Canada, that being a comparator that reflects standard of care at the time. This will be the comparator that is replaced the most in clinical practice. This is consistent with the requirements of the National Health Act. Given this AbbVie proposes that paragraph 1 (second sentence) and paragraph 2, should be amended or removed.

Are the proposed guidelines international best practice?

The aim of the Review was to be comparative in terms of world's best practice. Information relating to what other countries are doing that Australia is not and vice versa could be helpful in terms of ratifying the document as world's best practice. Based on the current information provided, it is difficult to determine whether this version of the Guidelines meets its objective to be consistent with best practice.

One area of international best practice relates to patient/consumer needs that could be enhanced in the Guidelines.eg technical methods used to gather patient information (such as Delphi) are used in other HTA jurisdictions. The PBAC Guidelines, if they are to be consistent with international best practice, should have a role in discussing these techniques and the importance given to such information in the PBAC decision-making process.

Other issues

Indirect comparison methods

In terms of best practice, an obvious omission from the current draft of the guidelines is clearer acceptance and guidance on appropriate methods for performing indirect comparisons. The guidelines still state that the preferred methodology for performing indirect comparisons is the Bucher methodology. While this may be appropriate for comparisons of a new medicine with only one comparison, international standards would suggest that for comparisons with multiple comparators other methodologies such as network meta-analyses and Bayesian methodology may be more appropriate. While the guidelines do not exclude these types of analyses from being presented within a submission to PBAC, it is important that guidance on how these analyses should be performed be added to the guidelines.

De-cluttering of the guidelines

As noted in the first meeting of the GRSC, one of the aims of the Review was to de-clutter the Guidelines, in line with the Government's deregulation policy. AbbVie acknowledges that Version 5.0 of the Guidelines better articulate real PBAC decision making (and precedence). However, AbbVie believes that the draft Version 5.0 Guidelines are too prescriptive and this appears contradictory to this aim of the Review.

For example: the requirement to provide a cohort-based model in addition to an individual-level simulation model (page 101 of draft Version 5.0) not only increases uncertainty but, in some cases, is methodologically inappropriate. In most cases, an individual-level simulation model would only be used when a cohort-based model is insensitive or inappropriate, and thus

the results from the inadequate cohort-based model will be misleading. The requirement to provide such a model adds to the complexity of submissions and to the complexity of reviewing submissions.

Summary

As technologies and HTA methodologies continue to change, periodic evaluation of the PBAC guidelines is important to keep Australia up to date with best practice. AbbVie welcomes this new version of the guidelines, however have identified some issues that need addressing. AbbVie believes that the new text inserted in Section 1 under the justification of the comparator regarding the lowest cost comparator, creates confusion and is not based on best practice economic evaluation principles. AbbVie recommends that the choice of comparator be based on that which will most likely be replaced in clinical practice which is in line with other HTA evaluation agencies around the world. In terms of making the guidelines best practice, it is unclear from the information provided to date, whether this aim has been achieved. While AbbVie welcomes the inclusion in the guidelines of acknowledgement of alternative methodologies for indirect comparisons, we believe that the guidelines are still lacking in terms of the PBAC's acceptance of these methodologies and on guidance on how best to carry out and present these analyses. Further, there are aspects of the new guidelines that appear to be overly prescriptive adding to the complexity of the guidelines rather than a de-cluttering as was the aim.