Input into stakeholder commentary: PBAC Guidelines review

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Amgen Australia would like to add the commentary below for consideration in the stakeholder review of the PBAC Guidelines. Many thanks for the opportunity to comment. Please note the document is in three parts: 1) commentary on presubmission activities, 2) comments on relevant issues within the submission process/ PBAC Guidelines, and 3) commentary on issues post-submission.

1. Pre-work for submissions:

Presubmission meetings: While Sponsors, in general, consider the opportunity to engage in presubmission meetings with the DOH beneficial, the DOH may find differential value depending on the Sponsor's preparation for the meeting and content for discussion. Sponsors do observe that it is difficult to secure presubmission meetings in a timely manner (i.e. close enough to a submission to make the feedback worthwhile, but far enough out to allow for changes to the submission content if required), and should multiple points of feedback be required, somewhat challenging to create a second presubmission meeting. Should there be an opportunity to review the conduct and process for presubmission meetings, it is thought that Industry would genuinely embrace a discussion on how to improve this process.

Early and extended evaluation: For some products/ complex disease areas, the presubmission meetings do not offer sufficient guidance on process or outputs. In such cases, it would be welcomed to have an alternative pathway that allowed for early and extended evaluation prior to submission. While this process may need to be considered in light of cost-recovery, it is thought that Industry would genuinely embrace a discussion on how such a process may be valued, and how it may be implemented.

Provision of additional information on prior evaluations or reviews

For many disease areas a wealth of information has been gathered through previous evaluations and/or reviews. It has been our experience that certain documents have on occasion been provided to Sponsor companies by the DoH with commercial-in-confidence material appropriately redacted (e.g. DUSC analyses). Consideration could be given to the type and extent of information that could be released to Sponsor companies and guidance provided in the updated Guidelines.

2. PBAC Guidelines- relevant issues for in-submission activities:

- *Products with interdependencies on MBS items*: guidance on how to treat these in the submission process. The current process for co-dependent listings i.e. testing for targeted therapy is well defined. However, there are circumstances where an MBS item is required for drug delivery and although an existing MBS items is available that could be used by clinicians, this does not adequately represent the deliver needs or remuneration to support the new PBS item. Further clarity on the process, requirements and timing where a changed to an existing MBS item or new MBS item is required would be helpful
- *Hidden comparator prices*: guidance on how to handle pricing aspects in submissions where the comparator price is hidden would be useful. For instance, companies can either try and predict the market price of a product at which to conduct CE calculations, or choose the list price. Neither is optimal from a submission perspective because of the asymmetry of information, and neither approach benefits the evaluators. Being privy to such information prior to a submission, through a confidentiality agreement, may be a way to make a Sponsor's submissions more effective. Alternatives may exist- e.g. a standardised recommendation for approaching the pricing and health economic aspects of a submission when the comparator price is unknown.
- *Utilisation of macros in models*: while the general guidance is not to use macros in models, on some occasions companies may use them and have positive commentary from the evaluators (i.e. while the Guidelines do not encourage the use of new approaches, the evaluators may find the use of these technologies beneficial, provided their function is transparent and well explained). Having an updated guidance on use of macros in models- rules on use, data sources, transparency etc- would greatly benefit the user community for the PBAC guidelines, and potentially allow for improved modelling outcomes for submissions.
- *Adoption and implementation of new technology*: The ability to implement beneficial modelling techniques to submissions may improve the overall quality and applicability of submissions. Techniques such as network meta-analysis, discrete event simulation, probabilistic sensitivity analysis, etc allow users to interpret evidence provided in submissions in more meaningful ways, and the diffusion of such technologies into the evaluation process may allow for a more rigorous debate on new products. The PBAC Guidelines review offers the opportunity to evaluate the use of such new technologies, and may offer an opportunity to define how future new technologies may be evaluated and implemented without waiting for successive PBAC Guidelines reviews.
- *Guidance on methods of use of data sources other than RCT*- e.g. observational data, real world evidence, Registry data, single arm analyses, historical controls etc: while RCT's will remain the gold-standard of evidence analysis, a range of data sources are either available, or required, or available, to consider the merit of pharmaceutical interventions. The PBAC Guidelines review offers the opportunity to comment on non-RCT data sources and to specify circumstances of use for such data and how these are to be presented.
- *Guidance when there is a change in clinical practice*: Exactly how to factor such a topic into the PBAC Guidelines may be difficult, but the issue represents an important methodological matter for new products. When, for example, a change in clinical diagnostic evaluation occurs for a disease (e.g the change from the Poser criteria to the McDonald criteria in multiple sclerosis), the basis for evaluation in RCTs also changes. This creates potential issues with future submissions, where the comparator may have been anchored in older diagnostic criteria, while a new product is anchored in the new criteria. The recommendation for listing for the older product remains in use for an older diagnostic language, while the new product may need to 'fall

back' to the older diagnostic language, thus not representing contemporary diagnosis. While the problem lies in the relevant evidentiary basis, the application of the problem may lead to difficulties in clinical practice when trying to balance the needs of the prescriber/ patient with the rules governing PBS supply of medicines. Should a Sponsor submit on the basis of the new criteria (and potential create a schism in the language used for prescribing across the same condition), and if so, how would the PBAC react to the adoption of new language? Should all 'older' products be allowed to morph to the new criteria upon a diagnostic change? Advice in the PBAC Guidelines on such scenarios would be helpful to provide context to this particular issue.

- *Comparator pricing guidance*- particular products or a 'basket of goods' approach: As the design of RCTs often happens many years in advance, and without the consideration of Australia *per se* as the driving force behind the requirements for evidence, it often eventuates that the comparator in an RCT is not necessarily the comparator or is only one of many equivalent comparators that becomes evident in clinical practice in this country. In such cases, a Sponsor has a number of considerations when choosing a comparator- use the best evidence available (i.e. the RCT), choose the comparator that is most evident in Australia, or use a 'basket of goods' approach based on the relativities of the products. Formal guidance on choice of comparator in such situation would be welcomed as a part of the new PBAC Guidelines.
- *Treatment algorithm drift*: There are often examples where the structure of existing, historical PBS listings creates an Australian-specific, artificial treatment algorithm. On occasion, such algorithms result in the requirement to draw a comparison with a product where evidence cannot be generated (e.g. it would unethical to conduct an RCT with the historical agent as a comparator) nor is there an appropriate common anchor therapy to draw indirect comparison from. Guidance around how to use such comparators as a frame of reference without mandating the requirement for their inclusion as a comparator with full economic analysis would allow for submissions to more accurately describe the true, current place of therapy.
- *Guidance on biosimilar comparisons*: This is a very contemporary topic that was not considered as a part of the current PBAC Guidelines, and the provision of specific information in the new PBAC Guidelines is very timely. While the principles have been outlined by the PBAC already, a specific section of the Guidelines that relates to the evaluation of biosimilar products may be highly beneficial as the medical community navigates the emergence of new biosimilar technologies (including those products that may offer benefits over the comparator).
- *Edification of what constitutes a minor submission vs a major submission*: while this may seem a small issue, it would be recommended that the current Guidelines be reviewed at the appropriate section to ensure that the guidance provided for what constitutes certain types of submissions (particularly for resubmissions) is clear and represents the most current thinking for DOH.

3. Post-submission activities

Listing dates: Although the final outcome of listing depends on the Minister's approval, it has been noted recently that the process has become quite ambiguous in terms of when the actual listing date will occur (or not). Specifically, there are clear instances of Sponsors receiving notice of updates to the Schedule in the middle of the month prior, when the reasonable expectation is that the advice will come one month before the change. As listing of a product on the PBS post-submission (and

post-recommendation) is linked to a number of critical events, including physician and consumer expectation, product import and supply, wholesaler and pharmacy stock in, product related marketing activity and publication etc, it is of critical importance to have a window of notice prior to listing. A clear guidance on this issue as a part of, or separate to, the PBAC Guidelines would be welcomed by many, to allow for the efficient supply and launch of a product on the PBS.