



The PBS Post Market Review team
PBAC Guidelines Review
Pharmaceutical Evaluation Branch
Department of Health, Canberra, ACT

PBSPostmarket@health.gov.au

5th April 2016

Dear Sir / Madam,

Re: Public Consultation on the draft revised Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines (Draft Version 5.0)¹

For more than 230 years, Takeda has been committed to serving the community through healthcare solutions from prevention to care to cure. Takeda has a broad portfolio of more than 700 products spanning a variety of therapeutic areas, including cardiovascular/metabolic, immunology/respiratory, central nervous system, general medicine and oncology. Takeda also aspires to deliver medicines that address unmet medical needs, such as our current highly specialised medicines in the therapeutic areas of haematological malignancies and Inflammatory Bowel Disease, and has a large research and development (R&D) program investigating a number of new medicines.

As an interested stakeholder, Takeda thanks the Department of Health (DoH) for enabling the public consultation on the draft of Version 5.0 of the Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines (hereinafter referred to as Draft Version 5.0). As one of the member companies of Medicines Australia (MA)², Takeda fully supports the content and recommendations contained in MA's submissions to the draft Guidelines process, including the comprehensive technical review lodged 24th February 2016 and the 5th April 2016 submission which contains a broader overall consideration of the review and identification of issues the pharmaceutical industry considers to be key in the current draft.

Before commenting on Medicines Australia's recommendations for consideration (with which Takeda is in accord), Takeda wishes to commend all the parties involved in the Guidelines Review for the breadth of their review, the extensive work involved in the short time-frame of only approx. 6 months and for the review's recognition of many of the issues originally tabled by Medicines Australia in mid-2015, recognition of which has resulted in the incorporation of some of these into Draft Version 5.0. However, Takeda is in accord with Medicines Australia that there are a number of outstanding areas still in need of

¹ See at: <http://www.pbs.gov.au/info/reviews/pbac-guidelines-review> and <http://www.pbs.gov.au/info/reviews/pbac-guidelines-review-public-consultation>)

² Medicines Australia represents the research-based pharmaceutical industry in Australia, which brings new medicines, vaccines and health services to the Australian market.

consideration by the Guidelines Review Steering Committee (GRSC) and Adelaide Health Technology Assessment (AHTA), as follows:

1. Consider draft Version 5.0 against the initial goals for the review, including achieving world's best practice Guidelines;
2. Consider key guidance in the draft Version 5.0 requiring further consideration; &
3. Consider arrangements for the transition period from Version 4.5 to Version 5.0, how the Guidelines will be updated on an on-going basis and the provision of appropriate education for users of the Guidelines.

1. Consider draft Version 5.0 against the initial goals for the review, including achieving world's best practice Guidelines:

As the sponsor of several medicines for rare and less common haematological malignancies, Takeda notes the recommendations which were made in September 2015 by the Senate Community Affairs References Committee's inquiry into "Availability of new, innovative and specialist cancer drugs in Australia"³ (referred to as the Senate Inquiry hereinafter), whose Report stated: *"enhancing and formalising mechanisms for consumers and clinicians to play a more central and substantial role in the evaluation of new medicines and new indications for already listed medicines."* Takeda highlights that the Inquiry's recommendations do not appear to have been accounted for in Draft Version 5.0. Nor does Draft Version 5.0 appear to have incorporated international best practice HTA methods / approaches, as suggested by Takeda and other sponsors in their initial submissions to the Review in July 2015.

Notably, the approaches used in other international HTA jurisdictions do attempt to address the issues raised during the Senate Inquiry and their adoption would enable the current PBAC process to move towards meeting the Senate Inquiry's recommendations. Therefore, per Takeda's initial submission, we respectfully reiterate our request that the DoH, GRSC and AHTA consider the following:

- The creation of a supporting unit for the PBAC (within the DoH) similar to the Decision Support Unit (DSU) implemented by the National Institute for Health and Care Excellence (NICE) in the UK (<http://www.nicedsu.org.uk/>)⁴.
- The creation of a clinical panel which can provide expertise to the PBAC as required, similar to those in place for the Canadian HTA system (CADTH)⁵ and the Scottish Medicines Consortium (SMC - the HTA body responsible for the funding of medicines in Scotland)⁶. In fact, the remit of such a clinical panel would be similar to that of the current Australian Technical Advisory Group on Immunisation (ATAGI)⁷, whose role is to provide advice to the PBAC on vaccines. This clinical panel could be used to gain advice from clinical experts throughout Australia, both early on in the submission process (perhaps including involvement in the pre-PBAC submission meetings which are requested by sponsor companies) and on an on-going basis during the evaluation period when

³http://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

⁴ The DSU is commissioned by NICE to provide a research and training resource to support the Institute's Technology Appraisal Programme. The DSU (a collaboration between the Universities of Sheffield, York and Leicester with members also from the University of Bristol, London School of Hygiene and Tropical Medicine and Brunel University) provides a variety of services which support the formal NICE evaluation process. The sections under the DSU 'umbrella' include Methods Development, Appraisal Specific Projects and Technical Support Documents. The public availability of this information (which is an academically rigorous synthesis of the agreed position for each topic) provides clarity and certainty to all the persons / entities involved in developing and evaluating a reimbursement application. The DSU also provides training on behalf of NICE, with this training being available to the NICE technical team and appraisal committee members and also to those submitting evidence, including industry, consultancies and academic groups. The training covers general issues around technology assessment and appraisals, the application of specific methods in areas such as evidence synthesis and the use of software for decision modelling.

⁵ <https://www.cadth.ca/>

⁶ https://www.scottishmedicines.org.uk/About_SMC/What_we_do/index. The Patient and Clinician Engagement (PACE) process enables patient groups and clinicians to have a stronger voice in SMC decision making, especially for medicines used to treat cancer and very rare conditions. From May 2014 pharmaceutical companies have been able to request that SMC convenes a PACE group to review their medicine following the issue of the draft report from the formal SMC process.

⁷ <https://www.ausgovboards.gov.au/boards/australian-technical-advisory-group-immunisation-atagi>

clinical points requiring clarification arise. This would be particularly helpful for therapeutic areas which are not represented by the members of the PBAC themselves.

- The need for the 'patient voice' towards the PBAC's decision-making was noted to be of particular importance during the Senate Inquiry. Whilst the PBAC process has recently enabled this, it is still 'ad hoc' in nature, and it was made clear at a recent public forum ('Room with a Patient View', Sydney, March 2016) that patient organisations feel there is room for improvement. The Scottish PACE model could be an excellent approach whereby the patient voice is incorporated.

2. Consider key guidance in the draft Version 5.0 of the Guidelines requiring further consideration;

Takeda agrees with the three main Guidance issues highlighted by Medicines Australia:

- 2a) Revised guidance on the selection of the Main Comparator;
- 2b) Guidance not adequately covered in draft Version 5.0; and
- 2c) Procedural elements not adequately covered in draft Version 5.0.

A brief comment on each follows.

2a) Revised guidance on the selection of the Main Comparator (page 16)

Takeda is in total agreement with Medicines Australia's vigorous opposition to the inclusion of the wording 'least expensive alternative medicine' in regard to the selection of the main comparator in Draft Version 5.0, which supplants the wording 'Therapy that prescribers would most replace' in Version 4.5. As outlined by Medicines Australia, Takeda concurs that the requirement for a sponsor to select the main comparator based on price (and not on actual clinical practice), has the potential to:

- Compound existing concerns re comparator erosion & linkages between the F1 and F2 formularies;
- Raise reference pricing implications for all PBS-listed medicines linked by therapeutic relativity if a new proposed drug is compared with the least expensive comparator within a reference group;
- Further devalue 'innovation', examples of innovation being the targeted new medicines. This is not in accord with the Government's stance on innovation.
- Delay, or even prevent, Australian patients being able to access new medicines.

Moreover, Takeda believes the proposed wording is not in alignment with international best practice, nor is it in alignment with the remit of the PBAC as specified in the National Health Act. Takeda therefore strongly supports Medicines Australia's recommendation that the current text (re selection of main comparator) in Version 4.5 be retained in Version 5.0 of the PBAC Guidelines.

2b) Guidance not adequately covered in draft Version 5.0

Although Draft Version 5.0 does address some areas that were identified by the pharmaceutical industry in mid-2015 at the commencement of the Guidelines Review process, Takeda supports Medicines Australia's concerns that some have not been covered in the new Guidelines, with the two of particular interest to Takeda being i) evolving clinical trial design and ii) the inclusion of methods which account for the broader value of medicines.

i) Evolution of clinical trial design: Takeda has first-hand experience of regulators (including the Australian TGA) approving one of our breakthrough medicines for a therapeutic area with high unmet clinical need on the basis of uncontrolled, non-Phase III evidence. Whilst acknowledging the current pragmatism and flexibility evident in the PBAC decision-making process, Takeda believes (like Medicines Australia), that Draft Version 5.0 does not provide sufficient information about what the PBAC requires to inform their decision-making when the available evidence is not from a controlled Phase III clinical trial. Takeda therefore supports Medicines Australia's request for the need for

comprehensive guidance on this topic. Takeda believes that having this information would facilitate the provision of exactly what the PBAC needs for their decision-making, particularly in the situations where uncontrolled data (on which the product was registered) form the basis of the application.

ii) Inclusion of methods related to broader value of medicines: Takeda reiterates its previously expressed opinion that the new Section 3 (the economic evaluation) should allow for the inclusion of the perspectives of the patient / carer / society in the economic evaluation via the use of indirect costs and patient preference methodologies, which is the accepted practice in many other HTA jurisdictions. This is particularly relevant in the context of a decision-making process which uses the cost per quality adjusted life year (cost / QALY) as a base metric because, in the majority of disease areas, the utility weights which drive the cost / QALY reflect the various stages in the disease state itself and do not incorporate the patient's preference. For example, whilst the EORTC QLQ-C30 instrument is used to assesses the quality of life of cancer patients, it does not capture the 'utility' afforded to a patient by a new mode of administration such as being able to take a tablet at home rather than have to go to the hospital to receive an infusion. Whilst the cost offset of not having to go to hospital can be incorporated into the economic evaluation, the other, highly patient-relevant factors (such as the time saved by not having to travel to the hospital – time that may instead be productively spent at work/ the greater convenience / the lack of impact on the carer) cannot.

Takeda therefore supports Medicines Australia's request for inclusion of contemporary and thorough guidance on assessments relating to the full societal impact of a new medicine. Takeda notes that it, along with other members of our industry and other key stakeholders have long called for greater attention to these factors. As noted by Medicines Australia, although guidance on patient-relevant and societal factors has been included in draft Version 5.0 (e.g. patient preference, productivity gains, other indirect costs) we are also disappointed that Draft Version 5.0 does not outline how the PBAC will consider such "supplementary" information in its decision-making process.

2c) Procedural elements not adequately covered in draft Version 5.0.

Takeda is in general accord with Medicines Australia's comments on the 'procedural' elements not addressed in sufficient detail in Draft Version 5.0. Of these, Takeda is particularly concerned about the need to facilitate / optimise input from clinicians and patients throughout the evaluation process (which was referred to above) and also about the processes associated with a submission to the PBAC, including during the pre-lodgement phase (the Pre-PBAC processes) and those activities that happen after the PBAC's meeting, regardless of the latter's decision (the Post-PBAC processes). In Takeda's initial submission to the PBAC Guidelines Review, Takeda (and many other sponsors) noted the omission of these from the Review's remit and, whilst appreciating the DoH's viewpoint that these 'processes' do not lie within a revision to the Guidelines themselves, Takeda maintains that the 'processes' associated with a PBAC submission and the Guidelines (for preparing a PBAC submission) must be in alignment to ensure optimisation of the reimbursement process in Australia. Via this submission, Takeda wishes to reiterate the need for formal / ratified guidance on these processes and requests that the DoH provide a comprehensive 'processes' document (which should be a 'living' entity updated on a regular basis by the DoH) in the near future.

3. Consider transition arrangements, on-going updating of the Guidelines and appropriate education for users of the Guidelines

Transition: It is likely that sponsors will require advice for the transition period between the use of Version 4.5, the current version, and Draft Version 5. Takeda aligns with Medicines Australia's request that this period span at least two full PBAC cycles. In addition, Takeda respectfully requests that some flexibility be allowed for sponsors preparing resubmissions. Because a resubmission addresses issues

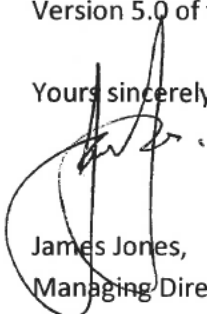
raised in regard to a previous application, the use of the new format as presented in Draft Version 5.0 could create additional complexity for the evaluation. In this circumstance, it may be more practical / efficient to continue with the previous format, with the incorporation of the additional requests for information required by Draft Version 5.0.

Updating: In regard to 'transition' and the future, Takeda notes the need for regular monitoring and reporting on how the PBAC Guidelines are being used in practice. Takeda also supports the regular and on-going updating of the Guidelines, particularly in regard to methodological / technological updates regarding clinical and economic comparisons. Doing this would ensure the Guidelines remain consistent with the updated literature, thereby meeting Minister Ley's objectives when the Guidelines Review was initially announced in April 2015 (see Items 1 and 2⁸). To this end, Takeda again highlights the approach taken by the UK's National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU), via which methodologies are updated easily outside of the Guidelines document itself. As outlined in many of the initial submissions to the review (from Medicines Australia, Takeda and other sponsors), adopting this type of approach would reduce red tape and ensure the Guidelines remain contemporary and 'world's best practice' through more regular updating, rather than allowing the Guidelines to become outdated over time, as has happened since the last major change in the early 2000s.

Education: Takeda also supports Medicines Australia's recommendation that comprehensive education be offered to industry, evaluation units and other key stakeholders. In addition, Takeda suggests that other important stakeholders such as key clinical bodies and patient organisations also be included in these educational initiatives, particularly as the latter's 'voice' is now formally included in the new Section 1 in Version 5.0. Takeda agrees with Medicines Australia that it is vital for all interested parties to have a common understanding of the Guidelines and their interpretation, including their intersection with the PBAC remit as outlined in Section 101 of the National Health Act (1953). As was the case for previous significant changes to the PBAC Guidelines, joint stakeholder workshops not only provided the necessary educational component, they formed an ideal forum for the exchange of ideas and information between the various stakeholders. Takeda aligns with Medicines Australia's recommendation that joint stakeholder workshops also occur with the roll-out of Version 5.0.

Finally, Takeda thanks the GRSC, the AHTA and the DoH for the opportunity to comment on Draft Version 5.0 of the PBAC Guidelines.

Yours sincerely,



James Jones,
Managing Director, Takeda Pharmaceuticals Australia,
Email:

⁸ The following Items will be included in the Guidelines Review:

1. Review of the Guidelines content identifying the methods and current research. Identify significant new developments for methods in relevant sections of parts II and III of the current Guidelines (i.e. since 2008). In undertaking this service the Contractor will consider the relevance to PBAC practice of existing guidance documents on relevant methodologies contained within guidelines published by comparable international health technology assessment agencies, regulators and internationally recognised authorities in the assessment of evidence.
2. Preparation of a technical paper for discussion on each issue for the revision, including identifying any issues of scientific debate and consideration of Australian and International best practice. Recommendations on editorial and obsolete matters for deletion. Preparation of proposals for how to address each technical issue for the revision of the Guidelines undertaken by the Contractor for consultation with the Guidelines Review Steering Committee. The current version 4.4 of the Guidelines is a long document and the PBAC is seeking to develop a more concise, clear, focused and up-to-date methods Guidance to replace Parts II and III of version 4.4.