Australian Government
Department of Health
Therapeutic Goods Administration

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Consultation submission

This form accompanies a submission on *Expedited pathways for prescription medicines: Eligibility criteria and designation process*

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☐ OTC medicines	☐ Medical devices	☒ Prescription medicines
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Category		
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MMDR consultation: Expedited pathways for prescription medicines
Reform Coordination and Support Section
Regulatory Services and Improvement Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

19 December 2016

Dear Sir/Madam

Thank you for the opportunity to respond on behalf of the innovative, research-driven pharmaceutical industry in Australia, to the Therapeutic Goods Administration's paper *Consultation: Expedited Pathways for Prescription Medicines: Eligibility Criteria and Designation Process* (Version 1.0, October 2016). The introduction of expedited pathways for prescription medicines will help reduce the gap between the availability of new data and access to medicines for Australian patients, in areas of high clinical need.

This submission has been prepared with the expert input of Medicines Australia's Regulatory Affairs Working Group (RAWG). Members of RAWG are selected for their regulatory experience and industry knowledge, and bring a whole-of-industry perspective to the consideration of regulatory issues that stand to impact our sector.

Medicines Australia agrees with the principles for the proposed criteria for Priority Review and Provisional Approval but suggests the following improvements be considered:

- limit the need for Australian specific requirements, data and review to the extent necessary to inform the applicability of a Priority Review/Provisional Approval designation to Australia, where a designation has been granted by a comparable overseas regulator such as FDA or EMA, in order to minimise the burden on both Sponsors' and TGA's resources, i.e. focus TGA consideration on Criteria 1 and 2;
- re-word Criterion 2 to ensure that a new medicine is not inadvertently deemed ineligible for an expedited pathway where there is an existing treatment, despite the new medicine offering a major therapeutic advantage over the existing treatment.

We would also note that alignment between expedited approvals pathways and reimbursement processes is critical to delivering faster access to new, innovative medicines for Australian health care consumers - a point that we emphasise in our separate submission to the TGA's targeted consultation paper on Priority Review (2016).

Our detailed feedback on the proposed expedited pathways is attached. As always, we are available to discuss our submission and look forward to further refinements being considered and consulted upon by the TGA.

We note that our member companies may make submissions in their own right to this paper, reflecting their own experiences and expertise, and that these should also be given due and proper consideration.

Finally, we acknowledge and thank you for the extension granted by the TGA to respond to this paper, to time with the due date for comments on the separate TGA targeted consultation paper on Priority Review (19 December 2016).

Yours faithfully

Larissa Karpish
Manager, Industry & Regulatory Policy

MEDICINES AUSTRALIA RESPONSE TO

TGA CONSULTATION ON

EXPEDITED PATHWAYS FOR PRESCRIPTION MEDICINES

Eligibility criteria

Question 1:
Do the proposed criteria for Priority Review and Provisional Approval address the objectives of the expedited pathways?

Response:
Medicines Australia (MA) broadly agrees with the principles of the proposed criteria for Priority Review and Provisional Approval. (Please note: MA will respond separately to the TGA's more detailed targeted consultation paper on Priority Review 2016, consistent with the overarching principles described herein).

However as currently written, Criterion 2 (unmedical medical need), could inadvertently make a new medicine ineligible for Priority Review or Provisional Approval designation where there is an existing treatment, despite the new medicine offering a major therapeutic advantage over the existing treatment.

Therefore MA proposes that the Criterion Two be reworded to state:
*Unmet clinical need **or** provides major therapeutic advantage in efficacy or safety over the existing treatment.*

Consequently, this specific text ("*provides major therapeutic advantage in efficacy or safety over the existing treatment*") could be removed from Criterion Three for both for Priority Review and Provisional Approval.

Question 2:
What other considerations may need to be included?

Response:

MA welcomes the TGA proposed mechanisms for expedited review being made available for both initial registrations as well as for extension of indications, and assumes that the pathways would equally be open to new routes of administration or dose forms, assuming that the criteria are met by the new innovation.

Designation process

Question 3:
Is the proposed process and timing of the designation steps appropriate?

Response:
MA agrees with the principle that the request for Priority Review or Provisional Approval designation is submitted by the Sponsor for TGA consideration prior to the dossier submission.

The content of the Sponsor's Designation Application should be a brief document (up to 20 pages, depending on extent of data) which addresses the following:

- justification that the medicine would address a life-threatening or seriously debilitating disease or condition, and
- unmet clinical need, commenting on current available treatments/standard of care in Australia, or
- discussion of top line data supporting the claim of major therapeutic advantage in efficacy or safety over the existing treatment.

The need for a meeting between the Sponsor and the TGA (either as face-to-face or teleconference) can be assessed on a case-by-case basis, depending on complexity.

A face-to-face meeting option with input from global representatives as appropriate, will provide Sponsors and the agency the best opportunity to have an in-depth and interactive discussion of the proposed application for which an Expedited Pathway for review will be sought. If any potential issues are identified during discussions, such a meeting will also facilitate timely agreement on how these will be addressed in the application. Ultimately, the TGA and sponsor should work towards reaching agreement on the likelihood of priority review designation at this pre-submission phase, and a flexible approach towards communication and correspondence should be taken in order to achieve this. Obtaining clear and unambiguous guidance at this pre-submission stage would allow more time for resource planning. This is a key consideration as Sponsors often have to compete for global resources with their affiliates in other countries making similar regulatory submissions.

Although Sponsors would generally have an estimate of clinical study completion, and would plan the regulatory filing accordingly, in cases where studies are completed earlier (e.g. due to demonstration of compelling benefit), there should be no barrier in the TGA proposed mechanism to allow for an earlier dossier submission.

The timing of submission of a designation application 10 – 12 weeks prior to dossier submission aligns with the EU requirement for seeking Accelerated Assessment based on a submission 2-3 months prior to filing.

In the event following evaluation, the TGA determine that a Priority Review designation no longer applies, appropriate dialog should be conducted with Sponsors before any decision to switch to a standard review process.

Question 4:
What other considerations may need to be taken into account in implementing the proposed designation process?

Response:
For Priority Review, MA proposes that the decision maker of the designation process should be the Clinical Delegate. The Delegate is closer to the nuances of the therapy area, and has an overview of past, current and future developments in the area. For a Priority Review designation, the question is purely one of appropriate speed and urgency, based on substantial evidence.

For a Provisional Approval, where an approval may be granted based on 'promising' evidence, due to the inherent risk associated with a provisional approval, this designation would be more appropriately escalated to the Principal Medical Advisor (PMA).

In both cases, the PMA & Delegate should consult each other as necessary.

Appropriate administrative mechanisms can be put in place to review the number of, and consistency between, such designation decisions.

Duration of designation

Question 5:
Should there be three-month (sic) limit on the duration for the designation for Priority Review and Provisional Approval? If not, please provide reasons and suggest what could be an alternative time period.

Response:
MA does not agree with a three-month time limit on the duration of the designation for Provisional Approval. This is because in such cases, the application is based on early data and l delays in data availability are therefore not unexpected. A flexible approach is therefore needed.

A defined period by which a dossier should arrive at the TGA post a Provisional Approval designation could result in a scenario where the Sponsor may not be able to meet this requirement.

MA believes that it would create an additional regulatory burden on sponsors should designations be allowed to lapse and for sponsors to have to re-submit these requests.

Publication of TGA decisions

Question 6:
Should we publish the outcomes of applications for Priority Review and/or Provisional Approval designation?
Question 7:
Should publication of both 'eligible' and 'ineligible' designation decisions occur?
Question 8:
Should we publish whether a medicine has been registered through one of the expedited pathways?
Question 9:
If so, how much detail should be published and when should TGA decisions be published?

Response:
MA supports the TGA's efforts to ensure transparency and therefore supports the publication of outcomes for applications for Priority Review and/or Provisional Approval designation. However, the timing of the TGA publication and its content needs to be balanced against considerations involving commercial-in-confidence information.

The EU publishes consideration of a Sponsor's request for Accelerated Assessment soon after a CHMP decision on the Accelerated Assessment request, as "pre-submission issues". However, very limited information on the Sponsor's proposed submission is published at this point. Full details of the application and evaluation are only published on the EMA website after completion of CHMP evaluation of the submission.

The FDA periodically publishes a list of products granted Breakthrough Designation, without any product/submission details.

MA would support the publication of decisions regarding Priority Review/Provisional Approval designation for specific drugs as part of the AusPAR.

Other considerations

Question 10:
What other key issues should be considered in developing the Priority Review and Provisional Approval pathways?

Response:
MA supports the TGA's initiatives in response to the Australian Government's response to the Medicines and Medical Devices Review.

The introduction of expedited pathways will reduce the gap between data availability and access by Australian patients in areas of high clinical need and MA looks forward to working with the TGA in developing these pathways further.

Developing clear and unambiguous definitions for "substantial evidence" for Priority Review and "promising evidence" for Provisional Approval is essential. The definitions for these terms should be consistent with TGA's established risk based approach to regulation, based on an assessment of the available evidence and in keeping with the standards applied to accelerated pathways by comparable overseas health authorities.

- The standard for "substantial evidence" should primarily rely on the strength of body of evidence, which would be presented by the sponsor in the pre-submission meeting and designation application. A medicine should not be ineligible for priority review based on a requirement for a replicate phase III study if the evidence presented from a single phase III study is sufficiently compelling and all other eligibility criteria are met. Repetition of strongly positive trials would also present certain ethical concerns.

- "Promising evidence" should rely on the likelihood that the sponsor will be able to provide comprehensive data to demonstrate that the benefits of the medicine for a life-threatening or seriously debilitating disease outweighs its risks and address an unmet medical need. This will give the TGA the much-needed flexibility to approve these medicines sooner on the condition where there is a clear unmet medical need using surrogate markers or early phase evidence. Moreover, this would be entirely consistent with accelerated pathways in comparable overseas regulators.

In implementing these expedited pathways, in such a way as to minimise the regulatory burden for sponsors whilst ensuring safety/efficacy and effectiveness for Australian health consumers, MA strongly recommends limiting the need for Australian specific requirements and/or data.

Where the Sponsor has been successful in obtaining a Priority Review/Provisional Approval designation in other (comparable) jurisdictions, such as the US and/or EU, the TGA's assessment of the Priority Review/Provisional Approval designation applications should focus on the applicability of the proposed product to Australia (that is Criteria 1 and 2 only). This would minimise the burden on TGA resources.