Proposed criteria for acceptance of an application into an expedited pathway

Three criteria are proposed for the prescription medicines expedited pathways. All three criteria must be satisfied in order for a medicine to be eligible for Priority Review or Provisional Approval.

**Criterion one: Serious condition**

The medicine is indicated for the treatment, prevention or diagnosis of a life threatening or seriously debilitating disease or condition.

**Criterion two: Unmet clinical need**

The medicine addresses an unmet clinical need in Australian consumers.

**Criterion three: Major therapeutic advantage**

**For Priority Review:** there is substantial evidence demonstrating that the medicine provides a major therapeutic advantage in efficacy and/or safety over existing treatments that are fully registered in Australia.

**For Provisional Approval:** there is promising evidence from early data indicating that the medicine is likely to provide a major therapeutic advantage in efficacy and/or safety over existing treatments that are fully registered in Australia.

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

**Shire response:** Shire Australia Pty Limited believes amendments should be made to Criterion Three as follows:

"For Priority Review: there is substantial evidence demonstrating that the medicine provides a major therapeutic advantage in efficacy and/or safety over existing treatments that are fully registered in Australia for treating the same medical condition".

"For Provisional Approval: there is promising evidence from early data indicating the medicine is likely to provide a major therapeutic advantage in efficacy and/or safety over existing treatments that are fully registered in Australia for treating the same medical condition".

The underlined text proposed for insertion is important to remove ambiguity arising from the situation in which a fully registered medicine is being used off-label for treating a medical condition. It is highly unlikely that sponsors will conduct a clinical development program including an active comparator which has not been approved by regulatory authorities as this presents significant ethical as well as regulatory challenges.

Comment [VC1]: Please clarify how substantial will be defined?

Comment [VC2]: Please clarify how promising will be defined?

Comment [VC3]: Please clarify how will early data be defined? It is proposed those terms should be better defined with at least a few examples across some key therapeutic areas.
Question 2: What other considerations may need to be included?

Shire response: The TGA should consider offering Priority Review pathway to medicinal products that provide a significant contribution to patient care and quality of life (QoL). Take for example an application to register a paediatric dosage form that facilitates the accurate administration of a medicine used for treating a life-threatening condition in children. While such a medicinal product contributes to improving patient care just by common sense reasoning, it would be difficult for a sponsor to generate "substantial evidence demonstrating that the medicine provides a major therapeutic advantage in efficacy and/or safety over existing treatments (i.e. the adult dosage form in this example) that are fully registered in Australia. It is important for the TGA to be flexible in not enforcing "All three criteria must be satisfied in order for a medicine to be eligible for Priority Review or Provisional Approval" at all times.
**Designation process for the expedited pathways**

It is proposed that the expedited pathways will be available to prescription medicines containing new active substances or new uses for medicines (i.e. New Chemical Entities\(^1\) and Extension of Indications\(^2\)) that meet the specified eligibility criteria. TGA will implement a formal designation process for determining whether a medicine is eligible to enter one of the expedited pathways for prescription medicines. In line with TGA’s principles for expedited pathways, sponsors will be responsible for providing TGA with all the information necessary to get and support continued designation for the Priority Review or Provisional Approval pathways.

**Optional pre-submission meeting**

Pre-submission meetings will be recommended for sponsors intending to apply for designation to an expedited pathway. It is suggested that pre-submission meetings will occur 6-7 months prior to submission of the dossier for the registration process. Pre-submission meetings may not be needed for all applications, as this information could be gathered through phone or email communication.

**Application**

Similar to the EMA process, it is suggested that an application for designation for Priority Review or Provisional Approval is to be submitted to TGA approximately 10-12 weeks prior to submission of the dossier for the registration process.

One of the proposed principles for our expedited pathways is that sponsors will be responsible for providing all information necessary to receive and maintain the designation. For the Priority Review pathway, sponsors will need to provide evidence of Good Manufacturing Practice (GMP) compliance or show that they have applied to obtain the necessary GMP certificate or GMP clearance.

**Designation decision**

TGA’s Principal Medical Advisor will assess the information provided by the sponsor against the relevant criteria to determine whether a medicine should be granted a designation for the Priority Review or Provisional Approval pathway. It is proposed that we will have a target timeframe of 20 working days from acceptance and acknowledgement to the sponsor of a complete application to make the designation decision.

Successful designation of an application as either Priority Review or Provisional Approval does not mean that the medicine will necessarily be approved after evaluation and registered on the ARTG. Applications that are assessed as being ineligible may still apply for registration via the standard Prescription Medicines Registration Process.\(^3\)

TGA will work consult with industry to further develop details of the designation process.

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\(^1\) Prescription medicines containing a chemical, biological or radiopharmaceutical substance that have not previously been included in the ARTG.

\(^2\) Change to the approved therapeutic uses of prescription medicines registered in the ARTG. This includes a 'new use' where an existing medicine is approved for an additional therapeutic use and an 'extended use' where an existing medicine is approved to treat a broader range of consumers.

Question 3: Is the proposed process and timing of the designation steps appropriate?
Shire response: N/A

Question 4: What other considerations may need to be taken into account in implementing the proposed designation process?
Shire response: TGA should consider defining what “maintain the designation” involves.

Duration of designation

It is proposed that after a designation for Priority Review or Provisional Approval has been granted by us, the sponsor will be required to provide the full submission for registration within three months of being notified of the outcome in writing, otherwise the designation will lapse. This aligns with the principle that both the TGA and the sponsor will commit to expediting the application in the interest of public health, while accommodating any unexpected delays in submission.

Question 5: Should there be three-month 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.
Shire response: Not applicable.

Publication of TGA decisions

Question 6: Should we publish the outcomes of applications for Priority Review and/or Provisional Approval designation?
Shire response: The Priority Review and/or Provisional Approval designation will depend on the process to evaluate acceptability. Therefore, Shire would like to seek further details on how the review for designation will be conducted.

Question 7: Should publication of both ‘eligible’ and ‘ineligible’ designation decisions occur?
Shire response: Shire proposes TGA to publish only the eligible designations.

Question 8: Should we publish whether a medicine has been registered through one of the expedited pathways?
Shire response: The TGA should consider publishing this information after completion of registration.

Question 9: If so, how much detail should be published and when should TGA decisions be published?
**Shire response:** The TGA should consider publishing only top level summary in similar lines to those published by the EMA e.g. name (active substance, INN, common name, chemical name or company code), substance type, therapeutic area, therapeutic indication, type of data supporting request (whether nonclinical/clinical) and type of application.

This could be published at the time of AusPAR publication.

**Post-implementation review**

As the Australian regulatory context differs from our international counterparts, it is difficult to anticipate how the proposed Priority Review and Provisional Approval pathways will operate alongside our existing processes for the registration of prescription medicines.

It is proposed that a post-implementation review of the Priority Review and Provisional Approval pathways will consider whether the eligibility and exit criteria are fit-for-purpose in the interests of public health, any changes that may be needed to improve the designation and registration processes, and the extent to which our resources have been diverted from business as usual activities. Timing of the post-implementation review is yet to be determined.

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

**Shire response:** N/A