Re: Consultation: Provisional Approval pathway for prescription medicines.

The Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) notes the development of Provisional Registration Approval pathway. It is delighted to have the opportunity to provide expert opinion with the Therapeutic Goods Administration (TGA) on registration matters. Overall, ASCEPT welcomes this work as it leads to opportunities to review and update some outdated but key aspects e.g. updating the product information (PI), improving the post-market monitoring scheme for medicines and medical devices,

Specifically, ASCEPT supports the reform of the PI. What is needed is a streamlined PI focusing on the clinical use aspects, with animal data at the end of the PI. It needs to be updated as new information becomes available.

ASCEPT is supportive of the introduction of the Black Triangle Scheme as a way of notifying practitioners that comparative safety and efficacy data is not available with this product. However significant resources are needed to ensure this the education of prescribers about this including liaison with the Medical Deans of Australia and New Zealand regarding teaching of medical students about the Scheme. The difference between Black Triangle and Black box is important for prescribers to be aware of.

However, ASCEPT remain concerned that some of these changes have been driven by a political agenda around support for fast tracking new products from Industry. It wishes to emphasize that we need to be sure any of these changes do not risk safety. Prescribers do need to know that new drugs on the Black Triangle Scheme do not have data usually associated with a registered product, and that notification of AEs is even more important than usual.
Also note however, that adverse events in Australia occur in three main groups – the elderly, those with comorbidity and children. A requirement to include observational data at least (clinical data best) should be mandated in these settings.

The proposed changes to Pharmacovigilance including inspection are supported, particularly compliance monitoring appear supportive in this regard. We support the plan to link with international regulatory authorities and share data and knowledge, particularly as new data becomes available to update the PI.

In summary, ASCEPT is supportive with the proposed improvements to the existing monitoring of medicines in Australia, but does have some concerns with the education for prescribers and the need for better and easier to use support systems regarding notification of AEs and collection of observational data.

ASCEPT is grateful for the opportunity to provide input into the Consultation. Please do not hesitate to contact the ASCEPT Secretariat at secretariat@ascept.org.au for any further information.

Yours sincerely on behalf of ASCEPT,

Data requirements for the registration application
Q1. Do you envisage any difficulties with the proposed clinical, non-clinical and quality data requirements or Provisional Approval registration applications?
- Main concern is lack safety and toxicity data

Q2. Do you envisage any difficulties in providing prospective advice on timelines for submission of clinical data?
- This could be useful if the TGA can work closely with sponsors to plan their phase 3 trials

Factors influencing our decision-making
Q3. Are there other factors that should be taken into account during the dossier submission and evaluation phase for Provisional Approval applications?
- It would be important to know the complete trial time line, to ensure there is timely completion of post-marketing trial

Q4. Are there other factors that should be taken into account to inform the registration

ASCEPT is the professional and independent society in Australia and New Zealand with expertise in the use and toxicity of medicines and chemicals
decision for Provisional Approval?
- Complete transparency of data/information is required from sponsors, imperative
- Thorough evaluation of international data for medicines already registered overseas

Conditions of provisional registration
Q5. Do you envisage any difficulties with the proposed requirement to collect and submit confirmatory data on efficacy and safety within the provisional approval period?
- The population group may not cover our population demographics and there may be inter-racial differences that will not have been identified in the phase two trials

Q6. What factors should be taken into account when determining whether the sponsor’s proposal for collecting confirmatory data is sufficient?
- The same requirements should apply as those for medicines being listed full registration

Q7. What other conditions or undertakings should be considered for provisionally registered medicines?
- Live updates of safety data from global and national market is required to prevent major adverse events

Enhanced risk communication
Q8. What information, communication and education activities should be considered to inform health professionals and consumers about provisionally registered medicines and the implications for patients?
- Provisionally registered medicines should be treated in a similar way to trial medication with a list of registers, health professionals should have access to all safety and efficacy data and be sent regular updates
- Patients need to give informed consent based on the above being disclosed and educated by their prescribers about the risks of provisionally registered medications

Q9. How might the TGA and sponsors communicate to patients and health care professionals the status of a medicine with a mix of fully and provisionally registered indications?
- Regular (second monthly)/ live updates as they receive information on adverse drug reactions and data on efficacy

Tracking and enforcement of registration conditions
Q10. What information should be published on the TGA website about the progress of RMP commitments, including confirmatory efficacy studies?
- There should be complete transparency of RMP

Lapsing or extending provisional registration
Q11. Do you envisage any difficulties with the proposed automatic lapsing after a two year period?
- This would be a good safeguard to assist sponsors with ensuring no delay in time for completion of post marketing trails (incentive)
- Problematic for patients who start treatment near the end of the two years and are mid-treatment cycle

Q12. In what circumstances do you envisage that an extension to the provisional registration period will be sought?
- For the above-mentioned patient group provided there is ongoing efficacy and safety data until the treatment cycle is complete

Q13. Under what circumstances should the TGA consider a modification of conditions or undertakings for provisionally registered medicines?
- Medicines listed in international market with years of extensive efficacy and safety data that has not gained registration in Australia

Transitioning to full registration
Q14. Do you envisage any difficulties with the proposed process for transitioning a provisionally registered medicine to full registration?
- enrolling patients in clinical trials to determine efficacy is more challenging than prior to approval, as patients may have been under the provisional scheme and enrolling in a trial may lead to random assignment as opposed to usual care

Legislative and regulatory amendment
Q15. Do you support the proposed amendments to limit appeal rights to certain TGA decisions and to the sponsor only
- yes,