24th November 2016
Reg ref: RegAffairs\consultation-commentary\30-consult-orphan-drug-14oct16

Medicines Authorisation Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Re: Consultation: Orphan Drug Program
2015 Consultation outcomes and 2016 Orphan Drug Program Proposal

Dear Sir / Madam,

AbbVie Pty Ltd welcomes the opportunity to review and comment on the above mentioned consultation.

Criterion one: Rare disease threshold or lack of financial viability and seriousness of the condition

EITHER
threshold of 5/10,000 (≈ 12,000 patients based on July 2016 population) (*less restrictive than status quo*, *more diseases may qualify as rare*) AND life threatening /chronically debilitating (*more restrictive than status quo*)

OR

life threatening/seriously debilitating or serious and chronic condition AND that without incentives it is unlikely that marketing would generate sufficient return to justify the necessary investment (*more restrictive than status quo*).

TGA Question 1: Do you support criterion one?

AbbVie Response

AbbVie supports criterion one and in particular welcomes the TGA proposal to increase the threshold to 5/10,000 patients for a rare disease. AbbVie also acknowledges that the

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disease should be life threatening/seriously debilitating or a serious and chronic condition with limited return on investment.

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Criterion two: Alternative methods of diagnosis prevention or treatment

There is no existing therapy (*more restrictive than status quo*)

OR

if there is existing therapy, the product represents a significant benefit over existing therapies (*more restrictive than status quo*)

TGA Question 2: Do you support criterion two?

AbbVie Response

AbbVie does not support criterion two with respect to the criteria that if there is existing therapy, the product represents a significant benefit over existing therapies.

Orphan Drug status should be granted based on the need for the treatment, prevention and diagnosis of rare diseases. Due to the complex nature of rare diseases, of which approximately 80% are genetically based, providing physicians with a range of treatment options is paramount to improving the health of patients. Additionally, many patients with rare diseases are paediatric patients and are less likely than adults to tolerate some of the existing therapies. A range of alternatives in the form of Orphan Drugs allows the flexibility to treat difficult conditions should the patient be intolerant or unsuitable to the Australian standard of care.

Furthermore, AbbVie believes that the TGA should encourage an arrangement where sponsors of New Molecular/Biological Entities applying for Orphan status are given the opportunity to present their case for improved outcome and/or unique modality of action of their development drug beyond the current marketed or recently approved therapies.

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Criteria three and four: Medical plausibility
A justification for medical plausibility is required to support the orphan indication and to support subgrouping of indications

Background
The orphan condition or disease needs to be based on aetiology, pathogenesis, pathophysiology, histopathology and clinical characteristics supported by international disease classification systems such as the WHO international classification of diseases code (ICD-10 code), where available.

In addition, any restriction of the proposed use of the orphan drug to a subset of a disease or condition would need to be supported by a justification of medical plausibility of why the use of the orphan drug would not be effective or safe when used in the rest of the population affected by the condition. Defining a subset by reference to the fact that the drug will (or has) only been tested in a subgroup of patients would not be considered a sufficient justification for the restriction to a patient subgroup.

TGA Question 3: Do you support criterion three and four?

AbbVie Response
AbbVie does not support criterion three and four. AbbVie does not support the statement regarding the restriction of the proposed use of the orphan drug, in particular the following statement

"Defining a subset by reference to the fact that the drug will (or has) only been tested in a subgroup of patients would not be considered a sufficient justification for the restriction to a patient subgroup."

This in reality is impossible to establish without performing some type of negative study to establish which patients are not eligible for the drug. If you take the example of a drug that targets a biomarker, the drug is not going to be efficacious in patients that do not have the biomarker on the cells that the drug is targeting. Therefore, it would be inappropriate to test the drug in the general population. An example of this would be a drug that targets the ALK gene (anaplastic lymphoma kinase) in Non-Small Cell Lung Cancer. It would be inappropriate to test a developmental compound in all NSCLC patients regardless of whether the patients had the ALK mutation.

Paediatric populations (Consultation item 4)

TGA Question 4: Do you support the proposed consideration of paediatric indications?

AbbVie Response

AbbVie supports the proposed consideration of paediatric indications.

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Modifications to the designation process (Consultation item 5)

TGA Question 5: Do you support the proposed changes to the designation process and the timing of automatic lapsing?

AbbVie Response

AbbVie does not support criterion 5, specifically the proposal that the orphan designation will lapse if an application to register the orphan drug is not lodged within a set period after designation (proposed to be between three to six months).

Due to the nature of rare diseases, recruitment for clinical trials is dependent on a limited number of available patients, can be unpredictable and lead to delays in the development timelines of a new therapy. This can occur with Oncology products especially if the new therapy is found to be particularly efficacious. This can result in a delay in reaching the primary objective of the study e.g. Overall Survival, and consequently delay the submission of the application to register the new therapy.

Automatically cancelling the orphan status after a limited time of 3-6 months will result in sponsors having to reapply for Orphan Status. The net result will likely be an increase in regulatory burden to sponsors in an area where the reward for orphan designation is already very limited.

AbbVie also believes it is premature to cancel all other orphan designations at the time of the first approval of a competitor product. It is advisable to measure each product on its own merit at the time of an Orphan Drug application to maintain and encourage access to innovative medicines for orphan conditions.

Furthermore, comparing the Australian environment to that of the EU framework developed by the European Commission i.e. EC Regulation 141/2000 (and in part implemented by the EMA recommendations) is also discouraged due to the imbalance in incentives between the two regions. It is instead recommended to compare the TGA process with that of a leading EU member state that has a balanced orphan access policy e.g. Germany or that of the US FDA.

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TGA Question 6: Are there any other key issues that should be considered in developing the changes to the orphan drug program?

AbbVie Response

The European system has additional complexities vs. the Australian (the significant benefit hurdle being one) which are to a point balanced with the European incentives, including, but not limited to, protocol assistance and 10 years of marketing exclusivity - as well as many national provisions that actually do help to expedite access to innovative therapies for patients suffering from chronic life-threatening or chronically debilitating conditions. Nonetheless, these additional complexities have directly led to delayed access to patients as evidenced by recent European examples. This has, in part, led to the European Commission issuing a public consultation to optimize the significant benefit provisions. The significant benefit hurdle creates an additional layer of complication with very limited benefit to patients and tightening this requirement contributes to de-incentivizing the orphan framework and as a consequence makes the orphan market less competitive. An orphan approach more broadly in-line with the USA FDA is a model worth considering that has successfully encouraged innovation in this space for the past 30 years. As of 24 November 2016, the FDA has granted 3915 Orphan Drug Designations of which 584 of these resulted in approved NDA/BLA's.

Should you have any queries regarding our submission please contact me by email at sean.duncan@abbvie.com or by phone on 0400 141 663

Yours sincerely

AbbVie Pty Ltd

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