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Submission in Response to the Orphan Drug Program Consultation

22 November 2016

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Executive Summary

Amgen welcomes the Therapeutic Goods Administration's (TGA) proposal to amend the orphan drug program in a number of areas, including the proposed criteria and the designation process.

Whilst Amgen agrees with most of the proposals outlined in the paper, Amgen suggests some areas where improvements or further clarity would be beneficial. For example,

- TGA should make the criteria for establishing significant benefit over existing therapies clear to sponsors
- if there is a set period in which designation lapses it should be 'within 12 months'
- a set period of review of orphan designation applications should be introduced to enable efficient planning by sponsors

Introduction

About Amgen:

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's largest independent biotechnology companies and is developing a pipeline of medicines with breakaway potential.

Amgen Australia contributes disproportionately to the global clinical trial effort by being in the top ten countries for active clinical studies and in the top five for interventional studies. At any one time, Amgen Australia is involved in approximately 25% of interventional studies in the global clinical trial program.

Through its significant clinical presence, Amgen Australia conducts on average two First in Human (FIH) studies every year and almost half of its clinical trial activity is in early phase research (PI-PII). In 2015, we conducted 62 different studies at 347 sites across Australia and New Zealand, involving 1,645 patients trialing Amgen's innovative medicines.

Amgen Australia invests around $AU30-35 million in local research and development annually, which represents around 13% of its sales – this is very high compared with the industry average. One third of Amgen Australia's workforce is involved in research and development.

Amgen is committed to taking an active role in contributing to future public policy that is relevant to biologic medicines and industry development in Australia.

Response to the specific issues raised in the Consultation Document

For ease of reference, our comments are provided below in tabulated form with reference to the section of the consultation document in the left hand column.

Comments on the Orphan Drug Program Consultation Documents

Proposed criteria	Comments
A change to the rare disease threshold (from currently 2000 Australians to 5/10,000 which equates to ~12,000 Australians) Additional criteria: • rare disease and 'serious condition' or lack of financial viability and 'serious condition', and • alternative methods of diagnosis, prevention or treatment, and • medical plausibility of the orphan indication, and medical plausibility of subgroups	Amgen agree with the proposal to change the rare disease threshold to ~12,000 Australians Amgen agree with the application of additional criteria but has comments on these as outlined below
Proposed incentive	**Comments**
100% waiver of application and evaluation fees (status quo)	Amgen is in agreement with keeping the status quo ie 100% waiver of application and evaluation fees
Proposed process	**Comments**
1. Orphan designation lodged prior to registration (*current process*)	Amgen is in agreement with retaining the current process of lodging the designation request prior to registration
2. If the application for registration is not lodged within the set period (proposed to be between 3 – 6 months) after the designation, the designation lapses and the designation can be withdrawn or cancelled by the TGA if there is evidence that any criterion for orphan designation is no longer met (*new process*)	Amgen agrees with the concept of the orphan drug designation lapsing if the application for registration is not lodged within a set period, but does not agree with the proposed timeframe of between 3 – 6 months after the designation. Please see Amgen's response to Question 5 for further feedback on the timeframe Amgen agrees with the proposal that the designation can be withdrawn or cancelled by the TGA if there is evidence that any criterion for orphan designation is no longer met.
3. Decision on designation application and any subsequent review to be made by the TGA's Principal Medical Adviser (*status quo*) who can seek external expert advice (including from the Advisory Committee for Medicines) in relation to the criteria (*new process*)	Amgen agrees with keeping the status quo regarding the decision maker on the designation request and the introduction of the ability of the decision maker to seek external expert advice if required providing provision of such advice is timely, does not significantly delay the designation process nor the sponsor's ability to lodge a registration application for an orphan drug. Amgen also requests that TGA provide details on how sponsors will be informed that external advice will be sought, how sponsors interact with the expert and provision of information to assist the expert.

Proposed process	Comments
4. No fee for designation is planned (*current process*)	Amgen agrees with retaining the current approach to no fee for designation.
5. Lodgement of registration application with orphan status can occur through any of the registration pathways that are either currently available, or the priority or provisional pathways that will be implemented based on the Government's response to the Expert Panel Review of Medicines and Medical Device Regulation.	Amgen agrees with there being multiple avenues to lodge a registration application for an orphan drug, including via priority or provisional pathways to be introduced.
Questions 1-3	**Comments**
Criterion one: Rare disease threshold or lack of financial viability and seriousness of the condition	Amgen agrees with the proposal of either the 5/10,000 threshold and life threatening/chronically debilitating or life threatening/chronically debilitating or serious and chronic condition that is not financially viable providing that these terms are clearly defined, particularly serious and chronic condition, and criteria for financial viability (return on investment over how many years).
Criterion two: Alternative methods of diagnosis prevention or treatment	Amgen is in agreement with including both options for criterion 2. However, TGA should make the criteria for establishing significant benefit over existing therapies clear to sponsors, including the acceptability of non-clinical data and P1/2 studies. Data from P3 studies should not be required.
Criteria three and four: Medical plausibility	Amgen is in agreement with including both options for criterion 2. However, TGA should make the criteria for establishing significant benefit over existing therapies clear to sponsors, including the acceptability of non-clinical data and P1/2 studies. Data from P3 studies should not be required.

Question 4	Comments
Special circumstances for prevalence criterion for paediatric indications	Amgen agrees that additional allowances should be given to paediatric indications, including enabling the prevalence criterion to be met on just the paediatric population where the disease is different in paediatrics or specific to a paediatric sub-group, in addition to the whole of the disease. Furthermore, Amgen requests that special consideration be given for allowing orphan designation for drugs currently registered for adult indications and for which the paediatric population meets the prevalence criteria and of itself is not financially viable and designation has not yet been sought as the clinical evidence in paediatrics is still being gathered; that is a grandfathering provision.
Question 5	**Comments**
• the orphan designation will lapse within a set period if no registration application is made ▪ 3-6 months proposed • the designation can be withdrawn by the sponsor or cancelled by the TGA if any of the criteria are demonstrably no longer satisfied at any time	Amgen agrees with the proposal for orphan designation to lapse if no registration application is lodged within a set period, but Amgen does not agree with the proposed period of 3 to 6 months. We believe that this period is too short because it can take sponsors 3-6 months to prepare to lodge a registration application following the orphan designation. For a sponsor, the 3 to 6 month period prior to lodgment of a registration application involves - preparation and conduct of a presubmission meeting - preparation of Australian specific Module 1 documentation - preparation of appropriate Module 2 through 5 content. Amgen proposes the set period be 'within 12 months'. As evidenced by the data in the consultation paper, the majority of registration applications for orphan drugs are lodged within 12 month of the orphan designation. Furthermore, if orphan designation will lapse within a set period, Amgen requests a review timeframe be set for orphan designation applications to allow efficient planning of subsequent submissions, and prevent unnecessary delays to registration. Amgen seeks clarity on whether orphan designation for a product/indication prevents other products from being designated for the same indication. It currently appears that multiple products could be designated

	orphans, with only the first to submit for registration being eligible to have fees waived. Amgen also seeks an exemption to the set period to be given for the registration application for sub-population indications such as paediatrics or those with a specific biomarker, when orphan designation is based on the prevalence of the whole disease. Typically clinical evidence in subpopulations, such as paediatric populations, comes after the evidence in a major population such as adults. Sponsors should not have to reapply for orphan designation for the subsequent subpopulation indication.
Question 6	**Comments**
Consequences of adopting EMA orphan criteria	Amgen assume that TGA will accept an EU orphan drug application to which evidence of the prevalence in Australia is appended. This should be clarified.