Orphan Medicinal Products: Challenges faced by Companies in implementing the existing guidelines

Robert Morgan
Head EU Regulatory Strategy, Shire
EMA-EuopaBio Information Day, 15 October 2015

EuropaBio®
The European Association for Bioindustries

Outline of Presentation

I. Challenges in obtaining initial orphan designation

II. Demonstrating significant benefit at time of MAA to maintain orphan status

III. European Commission's planned review of its 2003 communication on the orphan legislation

The Impact of the EU Orphan Regulation

- The Orphan Medicinal Product Regulation (EC) 141/2000 has been a great success story providing patients with continuous treatment improvements in various disease areas:
  - *Stimulating the research and development of medicinal products to treat rare conditions successfully led to an increase in research investment in this field*
  - *More than 1,200 products in development granted orphan status*
  - *More than 120 orphan medicinal products are approved*

- The orphan designation and review procedures run smoothly

- The importance of Protocol Assistance in optimising the development programme is well established

I. Challenges in obtaining the initial Orphan Designation

- It must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating:
  - *"orphan condition" versus "therapeutic indication"*
    - *Regardless if there is a well defined mechanism of action (e.g. personalised medicine), designation must be justified for the full condition*
  - *Development of new products in the same indication*
    - *Limited incentives for Companies to continue development of alternative products in disease areas that still have unmet need*

- Prevalence of condition must not be more than 5 in 10,000:
  - *No significant challenges faced in demonstrating prevalence*
    - *Majority of orphans <3 in 10,000*
  - *Re-work of data for conditions already recognised as orphan condition*
    - *Introduction of list of recognised orphan conditions?*

I. Challenges in obtaining the initial Orphan Designation

- No satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorised, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition:
  - *Optimal timing of the orphan drug application (non-clinical, proof of concept, Phase II?)*
    - *Late submission of Orphan Designation will not allow early access to orphan incentives*
  - *The minimum level of data required to provide an assumption of significant benefit?*

I. Strategies to overcome challenges in obtaining the initial orphan designation

- Seek pre-submission meeting early in the process and ensure all items are covered, particularly
  - *(i) orphan condition*
  - *(ii) prevalence*
  - *(iii) significant benefit (if applicable)*

- Build sufficient time within the project plan to ensure that you can adapt to the feeedback that is received
  - *Full draft of the application is required to support pre-submission meeting.*

- Seek protocol assistance and ensure Company strategy to demonstrate significant benefit is accepted by COMP

II. Demonstration of significant benefit at time of MAA

- Level of data required to demonstrate significant benefit at time of Marketing Authorisation:
  - *Acceptance of alternative methods (such as indirect comparative data, historical data and adaptive designs) to generate the required level of evidence?*
  - *The release of further public information (EPAR?) on the assessment and decision-making of significant benefit performed by the COMP would allow other stakeholders to have visibility so as to facilitate market access*

- Ensure consistency from protocol assistance to CHMP opinion between EMA Committees with regard to the data required to demonstrate significant benefit:
  - *Industry supports strengthening input on significant benefit at the time of protocol assistance*
  - *Full alignment between SAWP, COMP, PDCO and CHMP (especially in context of conditional approval)*

II. Demonstration of significant benefit / orphan similarity at time of MAA

- In scenario of late approval of a product, it is challenging for the Sponsor to provide substantiation of evidence for significant benefit (particularly in situations of parallel submissions):
  - *Sponsor may not be in a position to justify the significant benefit against that new product (no direct comparative data available)*
  - *Timing of the COMP opinion post CHMP opinion puts the applicant in a challenging position in the event a negative COMP assessment of significant benefit and a positive CHMP opinion*
  - *Early COMP confirmation of significant benefit, before the CHMP opinion, would provide advantages to the Sponsor*

- Assessment of orphan similarity:
  - *Overlap of populations in some indications*
  - *Transparency on findings of similarity could help improve predictability of the system as questions on orphan similarity expected to increase in complexity*

III. Proposed Revision to the European Commission 2003 Communication

- The success of the orphan regulation since 2000 is well established
  - *Industry looks forward to partnering with EMA to build on this success story for the next 15 years*

- The review of the 2003 Communication on significant benefit and clinical superiority must be maximized so as to ensure that the orphan regulation continues to be a success so that patients with rare diseases continue to benefit from this important legislation:
  - *Should be driven by the need to accelerate development and approval of new therapies for rare disease patients*
  - *The revision to the 2003 Communication should be limited to only areas where clear issues have been identified*
  - *Continued flexibility with regard to the requirements of Sponsors is critical so as to maintain an environment conducive of innovation*