HOW SAFE IS THAT ORPHAN DRUG DESIGNATION?

Implications for Pricing and Market Access in Europe

In Europe, applications for orphan status of a drug can be submitted at any stage of development. Because of this, most drugs will be at early clinical (or even pre-clinical) stages at the moment of applying for and obtaining the initial orphan drug designation (ODD). However, orphan designations will be re-assessed at the time of marketing authorization (MA) and in the past couple of years, we have been seeing an increase in the number of products that have received ODD, only to have that ODD status challenged or revoked just prior to receiving MA.

The procedure relating to Orphan Drug Designation in Europe is comprised of two phases:

01 Designation of the product as an orphan drug medicinal product

02 Reassessment of orphan designation at the time of marketing authorization

Most are aware of the basic conditions regarding the rarity of the clinical condition (i.e., EU prevalence < 5:10,000; inability to market the product without financial incentives) that determines whether a product could be eligible for ODD. However, this is only one of the requirements that must be met. The others being[1]:

- The intention to diagnose, prevent or treat a life-threatening or chronically debilitating condition
- No satisfactory method of diagnosis, prevention, or treatment of the condition, or if there are other products treating the same condition, then the new product needs to demonstrate a significant benefit over such existing products to those affected by the condition

It is the last condition that has recently created issues for several pharmaceutical manufacturers.

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1. Article 3(1)(a) of the Regulation (EC) No 141 / 2000 (the Orphan Regulation)

Pricing and market access strategies for some European countries can be dependent upon the ODD (e.g., Germany). Significant problems can arise if a company develops its market access strategy under the assumption of having ODD, then it discovers only months before launch, that their product may lose its ODD.

So how does a product demonstrate significant clinical benefit in comparison with existing treatments? EMA proposes three key questions that need to be addressed to resolve this question[2]:

1. Is it a new indication?
2. What are the existing therapies or satisfactory methods?
3. How does it compare to existing therapies?

Despite challenges in the orphan regulatory practice, existing therapies by and large refer to products authorized in the EU in the orphan condition as proposed for designation. When there are existing therapies, it is question 3 that is most pertinent. The manufacturer must convince CHMP that either there is:

- Clinically relevant advantage based on improved efficacy
- Clinically relevant advantage based on improved safety or
- A major contribution to patient care

While market access professionals are familiar with the most usual methods to address the first two points (i.e., direct or indirect treatment comparisons), they might not be always aware that demonstration of meaningful and clinically relevant changes that allow the product to be used in a broader patient population or previously excluded groups by the authorized products might also be a key argument for maintenance of the ODD. Thus, in some cases, demonstration of lack of satisfactory treatment for a subset of the targeted population might be considered per se as a clinically relevant advantage. Finally, the last point is a bit more qualitative in nature and potentially allows for strategic creativity, albeit with a reasonably high risk of failure given that significant benefit uniquely based on major contribution to patient care is seldom granted at the time of marketing authorization.[3]

The questions for market access professionals are:

- How certain are you that your product will be able to maintain its ODD at launch? If odds favor loss of ODD, your company might be better off not requesting it at all, and developing a launch strategy for a non-orphan drug from the beginning. For a 50-50 situation, a non-orphan strategy scenario would still be a prudent approach for planning purposes.

- What investments and strategies can be executed to increase the likelihood of maintaining the ODD upon marketing authorization? What is the trade-off between the investment in resources required vs. the benefit of the ODD?

Recommendations

In light of the above, how can a company assess the security of maintaining ODD in Europe? Here are some suggestions for market access professionals:

- Ensure availability of evidence to demonstrate significant benefit will exist at the time of marketing authorization: While payers might accept additional data at post-reimbursement decisions, this is not the case for ODD - there is no future chance to re-claim an orphan drug designation.

- Find ways to engage early with payers and HTA bodies; not just with EMA - Prior discussions/agreements are critical to ensure all data and evidence is meaningful to all stakeholders when commercializing, whether having an ODD is relevant in each market.

- Although the condition to demonstrate major contribution to patient care has more room for creativity, it is important to not forget that any claimed advantages around this will still need to be substantiated with data.

[2] Data exclusivity, market protection, orphan and paediatric rewards. EMA, 26 October 2018. Presented by Soia Ribeiro, Head of Regulatory Affairs Office, Human Medicines Evaluation Division

[3] Fregonese, L. et al. Demonstrating significant benefit of orphan medicines: analysis of 15 years of experience in Europe, Drug Discov Today (2017)

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Sean has more than 15 years of experience in pricing and reimbursement while at Amgen.

He has launched several products globally; and developed pricing and market access strategies for pharmaceutical products across the lifecycle. He has been a thought leader in developing strategies and tactics to combat International Reference Pricing; and providing advice to companies about what they can do to better prepare for reference pricing. He is the author of several publications in clinical and health economics journals and has been involved in the development of pricing defense strategies for several of the early Biosimilars launched in Europe. He was an early advocate in instituting value-based selling programs to bring pricing and Key Account Management teams closer together to foster shared goals in pricing execution. Sean is currently an Adjunct Assistant Professor at the University of Southern California in the Titus School of Pharmacy and Health Policy. Sean is passionate about introducing profit enhancing pricing analytics and decision tools into pharmaceutical and medical device companies to help drive improvements in company's bottom line.

About LatticePoint Consulting:

LatticePoint is a boutique consulting firm that focuses on pricing and market access for innovative medicines and medical devices. LatticePoint is led by former industry market access leaders who understand how to plan for the political, scientific, and financial realities that will be pivotal in negotiating product access. We work with biopharma companies and investors to help define, negotiate, and defend the value of their products in key markets around the world. The LatticePoint team has over 40 years of pharmaceutical and biotechnology industry experience. Led by former industry market access leaders and a high-caliber team with significant experience in the sciences, licensing, M&A due diligence and integration, venture capital and international affiliate operations, we have a depth of experience, both at the global and regional levels. Our multilingual staff of native German, French, Italian, Spanish, Portuguese and English speakers is experienced at handling negotiations in many key countries while keeping an eye on cross-border implications. We engage with payers, providers, hospitals, HTA bodies and EMA for early access, give feedback on clinical program design, and create and execute in-country reimbursement strategy negotiations in key markets around the world. We retain a Global Payer Panel for market research interviews.