ABSTRACT: IMPACT OF THE EU ORPHAN DRUG REGULATION ON THE DEVELOPMENT OF ORPHAN DRUG: A 15-YEAR ANALYSIS

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Background:

The European Union (EU) Orphan Drug Regulation was adopted on December 16, 1999 and became effective on April 27, 2000, to encourage the research, development and marketing of orphan drugs. It was estimated that the global orphan drug market totalled nearly $123 billion in 2014 and may reach nearly $191 billion by 2019.

Objectives:

To summarise and highlight what the EU Orphan Drug Regulation has accomplished since its inception.

Methods:

The European Medicines Agency’s (EMA) website was searched to collect all rare disease (orphan) designations evaluated. The European Public Assessment Reports (EPAR) for human medicines published by the EMA was also searched to obtain the number of approvals and refusals of orphan drug applications since 2000. The results of the two searches were cross-reviewed and then combined.

Results:

Since 2000, 1,563 compounds applied for orphan drug designation; 1,244 (79.6%) received positive opinion. However, in the past 15 years, only 97 (7.8%, 97/1,244) applied for central market authorisation in Europe, of these, 85 approvals were granted (87.6%, 85/97) and 10 were refused (9.7%, 10/97). Of the 10 refusals, 7 received comments on at least one aspect of inadequate trial design, which disallowed proper evaluation of the clinical benefits of the investigative drug.

Conclusions:

The provision of market exclusivity, protocol assistance, and fee reductions through the EU Orphan Drug Regulation have led to increased overall product availability for rare diseases in the past 15 years, year-over-year, as demonstrated by the high approval rate of market authorisation of orphan drugs. Of the few that had failed to receive a positive recommendation from the EMA, a common shortfall seemed to be the lack of fundamental trial design rigour. This may indicate the lack of knowledge on the sponsors’ part to fully utilise the resources offered by the EMA on protocol assistance, to minimise the probability of rejection on grounds of mere deficiencies in research methodology. Therefore, the promotion of these incentives through the Regulation remains critical in increasing the success of future and ongoing development of orphan drugs for rare diseases.