Introduction

Rare diseases have become an important area of focus over the past decade due to the number of untreated rare conditions. Our objective was to review Health Technology Assessment (HTA) requirements currently in place for the reimbursement of rare diseases in 18 European countries (EU15, Nordic* and Poland), and to identify and compare differences between their approaches.

*EU 15: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and UK.

**Nordic: Denmark, Finland, Iceland, Norway and Sweden.

Methods

HTA requirements specific to rare disease treatments were obtained from HTA agencies in the selected countries. The information identified was supplemented by structured research in order to identify further reimbursement considerations relating to market access. These requirements were then compared.

Results

Our results showed that some countries have developed orphan specific criteria for HTAs, while others have adapted existing requirements to the orphan drug market, in order to facilitate pricing and reimbursement for orphan drugs.

Definitions of orphan (disease prevalence ≤5 in 10,000) and ultra orphan (disease prevalence ≤1 in 50,000) drug were similar in most countries. Germany applied a cap of 40,000 patients for orphan drugs and defines ultra orphan drugs as those for a condition with prevalence ≤1 in 30,000.1 In England, a cap of ≤100 patients is applied for ultra orphan drugs. Most countries granted market exclusivity for 10 years.3

The pricing and early access programmes for orphan drugs did not differ considerably from the non-orphan drug process3 -3 (no early access programmes were available in Iceland, Norway and Poland). HTA requirements applicable to orphan drugs varied by country (Table 1), including greater flexibility in pricing, fast track options (France) and greater leniency in the clinical data submitted (e.g. surrogate endpoints accepted in Germany, higher levels of uncertainty accepted in Sweden, England and Scotland), no cost effectiveness analysis required (Belgium and Netherlands), and separate HTA programmes for orphan drugs (Highly Specialised Technology (HST) appraisals in England).

In addition to the development of HTA-specific criteria, many countries had also implemented non-financial and financial incentives (Figure 1). Non-financial incentives were commonly observed, with many countries offering pre-licensing access (11 out of 18). Financial incentives, on the other hand, were less commonly seen, with only four countries (Belgium, France, the Netherlands and Spain) offering such an incentive in the form of tax exemptions, no registration fees and/or reduced rebates. Accelerated funding sources were also available for orphan drugs to account for the higher price in most countries (except Finland, Greece, Iceland, Luxembourg and Poland).

Conclusions

Over the past two decades there has been a shift in the pharmaceutical industry towards rare diseases, an area that was highlighted as having a high unmet need by the European Commission in 200910. Certain orphan drug policies exist throughout most of Europe, such as, orphan drug definitions, early access opportunities and pricing3. However, this review has highlighted significant differences in the HTA requirements between the European countries assessed, resulting in alternative recommendations and routes to market for the same drug in different countries. Harmonising HTA requirements through European-wide collaborations could decrease inequalities and timely access to treatments for rare diseases across Europe.

Market exclusivity has been a key policy in incentivising research and development of orphan drugs as it protects return on investment initially.

Evidently, understanding orphan drug specific reimbursement processes and what drives them is key for the industry to ensure that patients with rare diseases gain access to much needed treatments in today’s ever changing market.

This study was limited by the lack of data available in English on some of the HTA agency websites, which impeded access to information. Future studies could focus on individuals and different conditions to delving deeper into the rationale behind the different interventions implemented to promote orphan drug access and reimbursement.