PREDICTING ORPHAN DESIGNATION AND MARKETING AUTHORISATION BASED ON A REVIEW OF THE EUROPEAN MEDICINES AGENCY ORPHAN DISEASE REGISTER

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Introduction

Current projections of European[1] and worldwide[2] expenditure on orphan drugs are contrasting (Figure 1). We aim to identify trends in the orphan drug designations (ODDs) and marketing authorisations (MAs) awarded by the European Medicines Agency (EMA) following the introduction of the EU Regulation on orphan medicinal products in 2000[3], which incentivised development of orphan drugs, and to estimate the number of future ODDs and MAs, in relation to these expenditure projections.

Methods

EMA decisions on ODDs[4] and MAs[5] made between 2000 and 2015 were collected into a database, and stratified by outcome and British National Formulary (BNF) category. Regression analysis was performed to predict the volume of applications each year up to 2025 based on the historical number of ODDs and MAs, for which exponential, linear, logarithmic and polynomial curves were fitted and assessed using the coefficient of determination, R^2.

Results

We identified an increasing trend in both the number of ODD applications (14 in 2000, 190 in 2015) and the number of positive ODDs since 2000 (4 in 2000, 186 in 2015). The majority of applications to the EMA for ODD have been successful (97.9% in 2015) (Figure 2). Some designations are later withdrawn (often as the market exclusivity expires) so it appears that the number of withdrawals is lower for the latter years, but this could increase if currently positive decisions are withdrawn in the future. The BNF category with the greatest number of ODDs was 'malignant disease and immuno-suppression' at 36.2% over all years, with the smallest at 0.2% awarded to 'ear, nose and oropharynx' (included in 'others') (Figure 3). Although fluctuation occurred between years, an increasing trend was observed overall in the number of MAs granted since 2000 (Figure 4). It is predicted that in 2025, there will be 272 ODDs granted and 20 MAs for orphan drugs, an increase of 110 and 9 positive applications, respectively, from 2015.

Figure 1. European[1] and worldwide[2] projected expenditure on orphan medicines

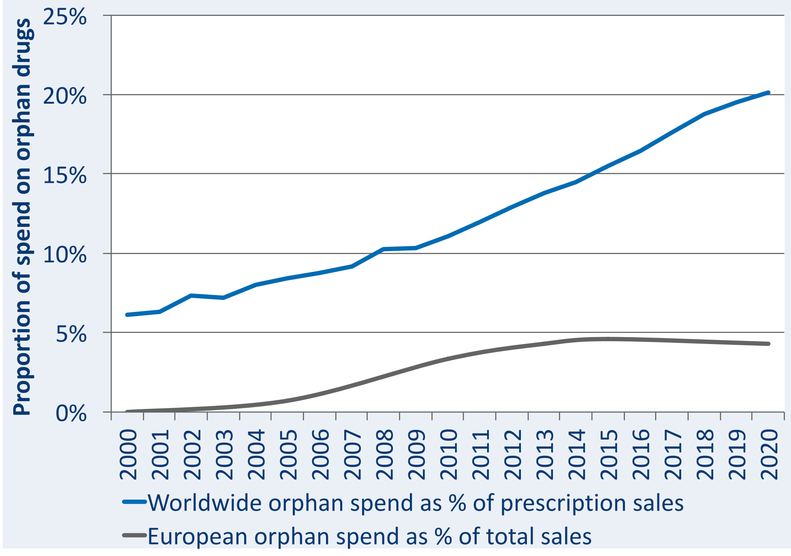


Figure 2. Number of positive, negative and withdrawn orphan drug designation decisions per year

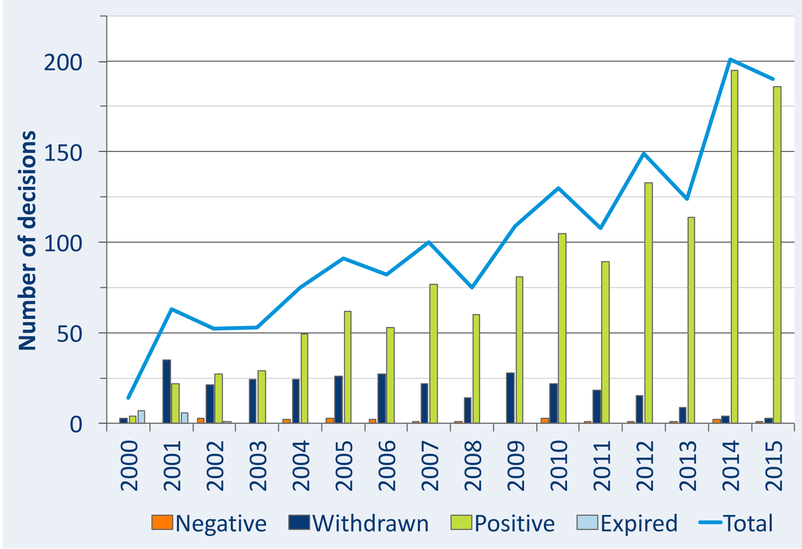


Figure 3. Orphan drug designations per BNF category

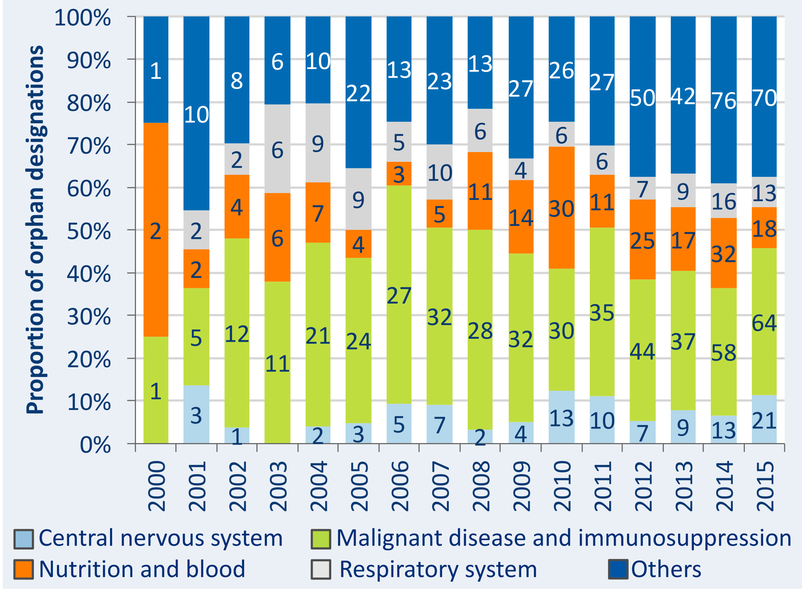
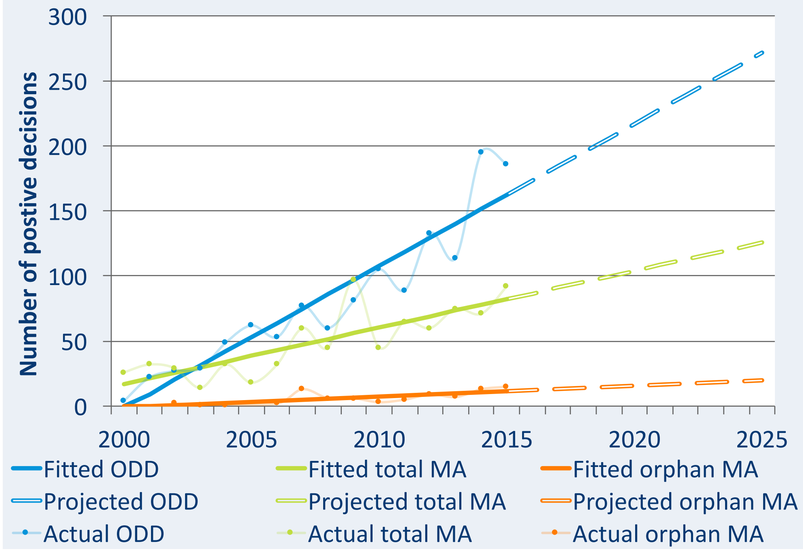


Figure 4. Projected EMA marketing authorisations (MA) and orphan drug designations (ODD) granted each year



Linear regression was chosen for the analysis. The polynomial and exponential curves had slightly higher R^2 values for ODDs and orphan MAs, respectively, but since the improvements were small and would have resulted in steeper increases, the linear estimates were chosen as the real world best fit overall.

Conclusions

This analysis has identified a rapidly increasing trend in the number of ODDs granted each year, which is expected to continue into the the next decade. The increase in MAs for orphan drugs is much slower with only a small proportion of medicines with ODD receiving MA. In reality, a plateau might ensue since there are a finite number of rare diseases (5,000 to 8,000[6]). We anticipate that new MAs for orphan drugs are likely to maintain the share of orphan drugs, rather than increase it, once development is aligned with that of the wider pharmaceutical industry, and especially if there is a shift in clinical research focus.

With an increasing number of ODDs and MAs granted by the EMA, it is necessary to consider the potential financial implications. Schey et al.[1] estimated a plateau would occur at approximately 5% after 2016 in the proportion of the European total spend on orphan drugs. It was reasoned that the expected annual increase in expenditure on orphan drugs is anticipated to be no faster than the growth in the greater pharmaceutical market. Our projections could align with this as not all medicines with MA will gain national reimbursement and the number of new medicines introduced for the same indication means spending is divided and not necessarily increased. Other research has estimated that worldwide, proportional expenditure on orphan drugs is set to increase to 20.2% by 2020, excluding generics[2]. These estimates do not replicate the plateau predicted for European spend, but do reflect the continued increases projected in our analysis.

The EU Regulation on orphan medicinal products has triggered increasing numbers of ODDs and MAs for orphan drugs to be granted each year. This trend is predicted to continue, but with contrasting expenditure forecasts, there is some uncertainty. Due to the lag between receiving ODD and MA, and achieving sales, further analysis could attribute MAs and sales to the year of ODD.

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