Introduction

The agency responsible for evaluating the clinical effectiveness and cost-effectiveness of new products / indications in England and Wales is the National Institute for Health and Care Excellence (NICE) and in Scotland is the Scottish Medicines Consortium (SMC). Whilst some aspects of the decision framework used by these two agencies are similar, many aspects of the process differ, particularly for products treating rare diseases. For example, NICE and SMC generally apply an incremental cost-effectiveness ratio (ICER) threshold of £30,000 per quality adjusted life year (QALY) gained, but if a product has European orphan drug designation or treats an equivalently small population, the SMC are not formally limited to this threshold and will accept higher ICERs (Figure 1). Conversely, NICE will officially only accept ICERs higher than £30,000 per QALY gained if the product meets end-of-life criteria or is for an ultra-rare condition and meets the criteria for the Highly Specialised Technology (HST) appraisal process. Recently proposed changes to the NICE process\(^1\) may mean that even ultra-orphan medicines evaluated through the HST programme will only be accepted if the ICER is below £100,000 per QALY gained (Figure 1). This would be the first time that a willingness to pay threshold is set for ultra-orphan medicines in the UK, which may reduce the unpredictability of appraisals for manufacturers.

Given the current and proposed difference in process for recommendations for rare diseases, the objective of this analysis was to review all recommendations made by NICE and SMC for treatments of rare diseases to evaluate whether one is more favourable.

Methods

All appraisals made by SMC\(^2\) (excluding non-submissions) and NICE\(^3\) (single, multiple or HST appraisals) evaluating drugs with EMA orphan drug designation or treating a disease included on the Orphanet list of rare diseases\(^4\) up to June 2016 were included in a database. Data on the appraisal type, indication, indication, therapeutic area as categorised by the British National Formulary (BNF) and recommendation were extracted.

Results

NICE have provided 92 recommendations for medicines with an orphan drug designation or that treat a rare disease, whilst SMC have provided 131 (Figure 2). The average recommendation rate (full or restricted) was significantly higher for NICE compared to SMC (76% versus 60%, p=0.014). However, it should be noted that 32 of the 131 SMC submissions were resubmissions: the original negative recommendation that resulted in the resubmission was included in the analysis along with the final recommendation so the final recommendation rates for SMC are likely to be higher.

The most common therapeutic area was malignant disease and immunosuppression (56%), followed by nutrition and blood (11%). Statistically significant differences (5% level) in recommendation rates between NICE and SMC were only observed for the following categories: musculoskeletal and joint diseases (89% vs. 33%, n=15, p=0.025), and nutrition and blood (100% vs. 44%, n=24, p=0.017), which is not expected given the small sample size in most categories (Figure 3).

Conclusions

A review of recommendations made by NICE and SMC for treatments of rare diseases show that the evaluation of these treatments can present challenges when ascertaining whether they represent value for money, NICE generally appear to be more favourable in recommendations for treatments of rare diseases. This difference may be eliminated following any changes to the SMC process for treatments for rare disease made once the current review of access to new medicines in Scotland is completed\(^5\).

A review of recommendation rates according to ICER would provide insight into the exact ICER thresholds used in decision making. Many manufacturers offer confidential patient access schemes, however, so the final ICER is not known. In addition, NICE considers both the ICER estimated by manufacturers and the ICER proposed by academic review groups so it is challenging to identify one base case ICER.

References: