



**THE NICE HIGHLY SPECIALIZED
TECHNOLOGY ASSESSMENT:**

**A NEW METHODOLOGY FOR
ORPHAN DRUG REIMBURSEMENT
IN THE UK**

Introduction

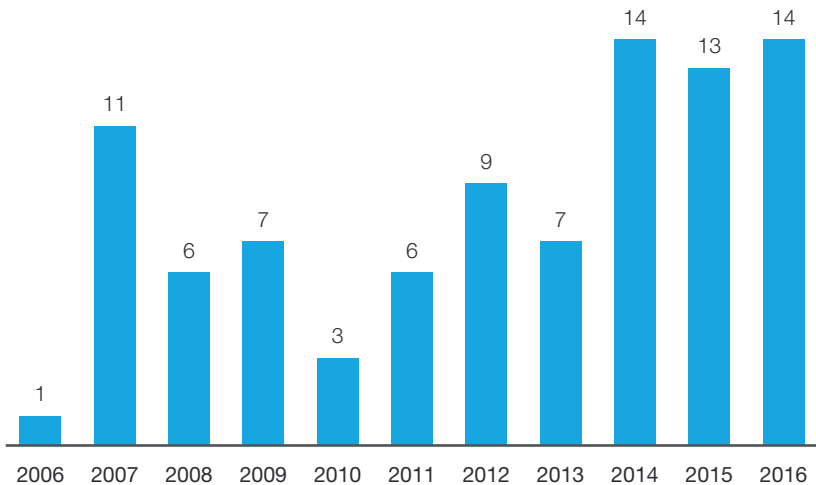
The key focus of the medical and pharmaceutical community today is finding treatment options for patients where there are currently none available; nowhere is this more relevant than in rare diseases. However, even when a treatment has been developed and approved, further challenges are posed when it comes to reimbursement and access. Regulatory approval does not necessarily guarantee success, with several recent high-price, high-profile innovations failing to gain market traction. Given the increasing number of products of this type being launched, the pricing of orphan treatments for rare diseases has come under more scrutiny. The underlying questions raised by this trend are how much both national and local budgets can bear to treat these rare diseases, and ultimately, the sustainability of the current rare diseases/orphan drug model.

Here, we look at the challenges associated with reimbursing orphan drugs and the recently updated process for balancing benefit and cost in the UK market, as an example of how reimbursement bodies are changing to meet the unmet needs of patients with rare diseases.

What are the growing challenges in funding orphan treatments?

The large number of orphan designations granted by the EU in recent years (Figure 1) demonstrates the continued interest in the orphan sector from the biopharmaceutical industry.

Figure 1. Number of orphan medicinal products in Europe with European orphan designation and European market authorization (MA) by date of MA¹



Reproduced with kind permission from “Lists of medicinal products for rare diseases in Europe”, Orphanet Report Series, Orphan Drugs collection, October 2017

The availability of more treatments for rare diseases is, of course, a good thing from a patient perspective. However, medicines intended for small populations require a high price per patient to recoup development costs and drive profitability, so many orphan drugs come with a high price tag. Despite financial incentives for development offered by the EU and individual countries, orphan products remain some of the most expensive on the market. Even considering the discounts offered by companies to reimbursement bodies (not usually published) it can be assumed that each new rare disease product represents a significant, and growing, cost burden.

Although each treatment is only for a limited number of patients, the approval of a small number of drugs can accumulatively lead to a significant budget impact. This means that regulatory/reimbursement bodies are looking for innovative ways to make these important medicines available, while limiting the potential cost burden and ensuring adequate resources are available across disease areas.

How are treatments for rare diseases assessed in England?

Due to the budget restrictions within the National Health Service (NHS), England (through The National Institute for Health and Care Excellence [NICE]) has had to become a world leader in managing the cost of pharmaceutical products. Many countries look to NICE approvals to assess products in their own markets. Given the increase in orphan products coming to market, and the need to provide treatment options for patients with these rare diseases, NICE has recently updated its approach to assessing such drugs. Importantly, and in a move from its previous stance, it accepts that therapies with only a few patients would rarely meet the restrictive cost-effectiveness criteria utilized for non-orphan drugs. Previously, orphan drugs were expected to meet the same cost per quality-adjusted life-year (QALY) threshold of £20,000–30,000.

Since April 2017, NICE has issued ‘highly specialized technologies (HST) guidance’ for new technologies when they are 15–20 months from marketing authorization. HST guidance is only developed for drugs for very rare conditions.

The process allows input from multiple stakeholders and is reviewed in a public forum, ensuring transparency in decision-making and giving patients a more prominent role. However, pharmaceutical companies sometimes feel the process is too restrictive and this has previously led to unsuccessful legal challenges from the Association of the British Pharmaceutical Industry (ABPI).⁴ No product has yet been assessed through the new process (as of October 2017).

NICE is keen to highlight that the HST process places most weight on the extent to which technologies demonstrate significant therapeutic improvement, described in HST methods as ‘overall magnitude of health benefits to patients and, when relevant, carers’.⁵ Therefore, NICE is attempting to move away from the perception they are purely focused on cost/price.

The majority of topics for assessment are identified by a national horizon scanning group (the National Institute for Health Research Innovation Observatory), which aims to notify the Department of Health of key, new and emerging healthcare technologies that might need to be referred to NICE.² This process identifies both products for HST and those non-orphan products to be assessed via the 'Technology appraisals guidance' process.³



Based on the list of provisional evaluation topics, the Department of Health and NICE work together to define the disease, the patients and the technology covered by the evaluation and establishes the questions to be answered through the assessment. Consultees and commentators are requested to comment on the draft scope.²



The manufacturer or sponsor of the technology is then invited to provide an evidence submission and all non-manufacturer consultees, which may include patient groups, physicians and other interested parties, are invited to submit a statement on the potential clinical effectiveness and value for money of a treatment.²



NICE then commissions an independent academic centre to conduct a technical review of the evidence submission and prepare an Evidence Review Group (ERG) report.²



The ERG report, plus any written submissions and personal statements from patient experts and clinical specialists, are then compiled into an evaluation report to be publicly reviewed by independent advisory committee (the Evaluation Committee).²



The Evaluation Committee then make recommendations.² If recommendations are more restrictive than the approved indication, they are detailed in the evaluation consultation document.²



Following public consultation, final evaluation determination (FED) on how the technology should be used in NHS England is produced.²



If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.²

How are the costs of these treatments managed in England?

NICE will fund HSTs up to £100,000 per QALY from routine commissioning budgets, five times greater than the lower end of NICE’s standard threshold range for non-orphan drugs. This allows for a significant additional cost over the standard care comparator for HSTs. For treatments above £100,000 per QALY, a QALY weighting may be applied. The QALY rating (Table 1) will progressively advantage treatments that offer greater QALY gains. Therefore, higher incremental cost-effectiveness ratios (cost per QALY) are only acceptable when associated with higher QALY gains.⁵ This highlights that the most important factor in decision-making is therapeutic benefit.⁵

Table 1. Weighting of QALYs in HST⁶

Improving quality of life for patients	Incremental QALYs gained (per patient, using lifetime horizon)	Weight versus 100k/QALY	Improving cost-effectiveness ratio
	≤10	1	
	11-29	Between 1 and 3 (using equal increments)	
	≥30	3	

For example:

Drug A has a cost per QALY of £110,000 and gives additional benefit of 18 QALYs over standard of care.

Therefore, using the new weighting:

$$£110,000 / 1.8 = £61,111 \text{ per QALY}$$

Which now falls within the acceptable threshold of ≤£100,000 per QALY

However, QALY gains over 10 are not commonly reported, with a few recent exceptions.

Managed access agreements (MAAs) are now often expected as part of an HST. These are schemes agreed between the pharmaceutical company and NHS England to enable patients to receive new treatments when limited data is available. The agreements usually involve some aspect of data gathering to support long-term reimbursement and price caps/patient caps/risk-sharing to ensure the budget impact is limited. There is little available guidance on the associated procedures but they are required to define:

- Patients most in need
- Patients most likely to benefit
- Start, stop and monitoring criteria
- Risk-sharing measures to protect the NHS if the technology does not work
- Commercial terms mutually agreed by NHS and the Company
- Quality of life benefits allowing for QALY calculation

In addition, from April 2017, NICE introduced a budget impact test for all technologies within the technology appraisal (for non-orphan drugs) and HST programmes. The aim is to assess the actual financial impact of a technology over the first 3 years of its use in the NHS in England. If the budget impact exceeds £20 million in any of the first 3 years, NHS England may engage in commercial discussions with the pharmaceutical company. Even if a product meets cost-effectiveness criteria, it may reach the £20 million budget impact in 1 year and trigger a discussion. These discussions are designed to mitigate the impact that funding the technology would have on the rest of the NHS.⁴ The ABPI has lost a legal battle against these changes, with NICE stating that, “rather than attempting to further frustrate NICE and the NHS’ work to ensure patients and taxpayers get maximum value out of the £15 billion pounds being spent on drugs, it now makes sense to work together [with pharmaceutical companies] towards that shared goal.”⁶

Key points

1. A cost per QALY of \leq £100,000 is acceptable for HSTs
2. For technologies with a cost per QALY of \geq £100,000, QALY weighting favours those with higher QALY gains
3. Sales exceeding £20 million in any of the first 3 years triggers discussions with pharmaceutical company
4. MAAs are required for most HSTs

Conclusions

Although the development of an increasing number of treatments for orphan diseases is a positive step for patients, it necessitates the development of new collaborative assessment methodologies, such as those recently developed by NICE. While financing reimbursement for these treatments is important, it cannot be to the detriment of other patients treated for more common diseases. This is the balancing act that reimbursement bodies are facing around the world and this UK example demonstrates how one market is trying to manage it. We would anticipate other markets also developing new assessment criteria over the coming years, making this one of the most uncertain and fast-moving environments for pharmaceutical products.

Whatever limitations reimbursement bodies place on these treatments, they will be subject to criticism by some. Hence methodologies need to be systematic, evidence-based and robust to allow for the defence of decisions and restrictions.

As the number of orphan drugs continues to increase, it is clear that further evolution of these tools and processes by market access bodies worldwide is expected to maintain sustainable reimbursement and ensure a fair distribution of drug budget for all patients.

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Glossary

Abbreviation	
ABPI	Association of the British Pharmaceutical Industry
ERG	Evidence Review Committee
EU	European Union
FED	Final evaluation determination
HST	Highly specialized technology
QALY	Quality-adjusted life-year
MAA	Managed Access Agreement
NHS	National Health Service
NICE	National Institute for Health and Care Excellence



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