



REAL CHANGE TO INCREASE ACCESS TO ORPHAN MEDICINES IN THE UK

This report was commissioned and funded by Biogen.

This material is intended for stakeholders with an interest in the current state of orphan medicines in the UK.

EXECUTIVE SUMMARY

Advancements in the diagnosis and treatment of certain rare diseases over the last decade have improved the lives of many patients and families. However, the process for assessing medicines for use on the NHS may not be keeping pace with the science, leading to people missing out on potentially life-changing treatment. This is disadvantaging the UK's reputation as an international life sciences leader, as well as an early launch market.

In this paper Biogen puts forward proposals for a new way of assessing a small group of rare disease medicines. These include:

- A new capped and budget-neutral scheme where certain medicines are reviewed on their clinical value and overall budget impact, linked to patient numbers.
- An early access approach grounded in risk sharing, so that patient access is prioritised and the benefits of early clinical experience can be realised.

If we can address these challenges the UK could stand to gain through:

- 1 Direct benefits to patients and their families**
- 2 Economic benefits through increased activity and job creation**
- 3 Creating a more attractive and sustainable environment in which to run clinical trials**



SEIZING THE OPPORTUNITY FROM SCIENTIFIC ADVANCES



Orphan medicinal products (OMPs) are medicines developed for the treatment of people with rare diseases – those affecting fewer than 5 in 10,000 people in the UK.¹ Many of those affected are children, with 30% not reaching their fifth birthday.²

Advances in diagnosis, clinical knowledge, and treatment, such as through gene and RNA therapies, have improved outcomes and provided hope. For example, an improved understanding of the genetic causes of disease could lead to the realisation that some diseases may be clinically distinct conditions that present similarly. A better understanding of the biological basis of diseases has led to the development of more targeted medicines in areas of high unmet need.³

However, capitalising on this scientific progress and making these medicines accessible to patients in the UK remains a challenge. Recent European Federation of Pharmaceutical Industries and Associations (EFPIA) data⁴ shows the UK lags countries like Germany, Italy and France in rare disease treatment availability. Between 2020-2023, only 50% of European Medicines Agency (EMA)-approved non-oncology orphan drugs were reimbursed in England (46% in Scotland) compared to 85% in Germany, 74% in Italy, and 67% in France. In addition, a 2023 BIA/ABPI survey found that about half of approved rare disease medicines are not reimbursed in England.⁵

There is a major opportunity for the UK if we can turn this tide. In 2022, industry-led clinical trials contributed £7.4 billion in gross value added to the economy, created 65,000 jobs, and generated £1.2 billion in NHS revenue.⁶ Faster access to treatments because of clinical trials also helped to avoid three million sick days, worth a further £0.9 billion to the UK economy. However, clinical trial initiation has significantly declined. Restoring trial activity to 2017 levels could add £3 billion to the economy, including £485 million in NHS revenue and 26,000 jobs.⁷ While the reasons for decline are multifaceted, ensuring the UK offers a swift and reliable route to market for medicines post-trial, through timely reimbursement, is critical to restoring confidence and attracting global trial investment. There is a crucial role for regulatory frameworks, which must actively support and incentivise orphan drug development. The U.S Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) offer a raft of incentives both pre and post approval for OMPs to encourage their development.^{8,9,10}

However, regulatory mechanisms alone are not sufficient to ensure patient access to treatments. The right evaluation and reimbursement processes must also be in place to enable promising treatments for rare diseases to reach patients. Existing initiatives like the Early Access to Medicines Scheme (EAMS), the Innovative Licensing and Access Pathway (ILAP), and the Innovative Medicines Fund (IMF) offer some promise, but fall short of their intended impact.

THE COST-EFFECTIVENESS DILEMMA



The UK has reformed its reimbursement system, with NICE (England) and the Scottish Medicines Consortium (SMC) adjusting their evaluation processes for orphan medicines. NICE introduced a severity modifier¹¹ and updated its Highly Specialised Technologies (HST) programme,¹² while SMC introduced an orphan modifier and an ultra-orphan pathway.¹³ NHS England established the IMF to support managed access arrangements for non-oncology treatments that NICE was not able to recommend for routine use.¹⁴

While these reforms demonstrate system recognition of the need to approach OMPs differently, these changes have not resulted in a step-change in the number of rare disease treatments being assessed or approved – for example only £2m of the IMF's £340m budget was spent to enable access to treatment in 2023/4.¹⁵

The stringent application of cost-effectiveness analysis and cost-neutrality is the nub of the problem. It explains the significant gap between the accelerated pathway offered by regulators and the number of medicines receiving full reimbursement in the UK.

These medicines will often come with a significant cost per patient, limited data and high levels of uncertainty, due to the rare and sometimes hard-to-reach nature of the population. This is particularly the case for first-in-class medicines, which represent scientific advancements, and which may deliver incremental clinical benefits.

The use of Quality Adjusted Life Years (QALYs) under a NICE Single Technology Appraisal (STA) may not sufficiently capture the nuances required to evaluate these medicines adequately and fairly.

Unless routed through NICE's HST programme (reserved for a very small number of medicines deemed to treat the very rarest of conditions), all medicines must meet the same strict cost-effectiveness thresholds. While some flexibility exists for rare diseases, most orphan medicines struggle to reach the willingness to pay threshold with enough certainty to be recommended for reimbursement.

The difficulties associated with developing OMPs are not unique to those treating the rarest of conditions, and yet we have created a chasm between what is an acceptable cost per QALY for the medicines routed through HST, and all other OMPs.

Other countries offer more pragmatic models. Germany recognises orphan status and assigns greater weight to incremental health benefits rather than strict cost-effectiveness.¹⁶ France offers temporary early access to innovative medicines through its *Accès Précoce* programme, enabling patients with serious, rare, or disabling diseases to receive treatment before the medicine receives European marketing authorisation, provided certain criteria are met (e.g. unmet need, innovation, and urgency of treatment).¹⁷ Then once an orphan drug receives regulatory approval, its therapeutic value is considered proven (i.e., no HTA is required) and it is made accessible to patients at a price set by the manufacturer, as long as its annual budget impact does not exceed €30 million (should it exceed the threshold, therapeutic value is assessed through the standard HTA process, which may be fast-tracked if the medicine is considered 'innovative').¹⁸

Are all QALYs equal?

Postma et al (2022)¹⁹ summarise the problem well with their comparison, which could be described as a person with a rare disease and a person with asthma. The person with the rare disease has a QALY baseline at 0.3 and the person who has asthma a QALY baseline of 0.7. The treatment for both conditions provide QALY gains of 0.3.

Under the current appraisal system, these QALY gains are considered equal, with the only thing separating them being the cost per QALY gain. However, the person with the rare disease started with a much poorer state of health and achieved 100% more QALYs, whereas the person with asthma started with much better overall health and achieved less than 50% more QALYs. The severity modifier seeks to address the issue of relative QALY gain, but as set out above, does not go far enough to address the fundamental challenges around the use of QALYs for rare diseases and the gap between STA and HST.



A NEW APPROACH TO NHS APPROVAL



The abolition of NHS England and the transfer of its responsibilities to the Department of Health and Social Care presents an opportunity for fresh thinking on the approval of rare disease treatments.

A new approach is needed to close the gap between regulation and reimbursement for certain orphan medicines. For a small group of medicines, there should be an exceptional yet standardised route to medicine approval on the NHS that exists outside of the traditional NICE process. This could ensure the UK achieves/returns to an R&D leadership position in life sciences and that people living with a rare disease are able to access what scientific discovery has to offer.



PROPOSED REFORM 1

Create a separate evaluation mechanism for Select Orphan Medicines

PROPOSED REFORM 2

Introduce reimbursement during early access through EAMS+

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Create a separate evaluation mechanism for Select Orphan Medicines

NHS England's Clinical Priorities Advisory Group (CPAG) evaluates medicines not topic selected by NICE, prioritising treatments based on its own set of assessment criteria, rather than cost-effectiveness assessment. However, CPAG is rarely used, lacks transparency, and applies only to specialised commissioning medicines.

In the new post-NHS England system, there is an opportunity to learn from what has worked well with CPAG, as well as where it could be strengthened to create a new mechanism that provides a more consistent, access route for rare disease medicines for which a NICE assessment is not viable.

This option would be only for an exceptional group of medicines that do not qualify for NICE HST but that meet agreed criteria, including those addressing a high clinical unmet need, which are indicated for a small numbers of patients, and where it is not possible to generate the level of evidence that NICE requires in its STA programme.

For this small group of medicines, it may not be in the interest of the taxpayer, patients or NICE for a full HTA to be performed. Limiting the impractical reliance on QALYs as a measure to determine the overall value of such medicines could release capacity and savings for NICE, while also being in the interest of patients.

A clearer, codified routing process led by the Department of Health and Social Care, working in partnership with NICE and the MHRA, could deliver a more efficient topic selection at NICE and a clearer and more transparent routing process than the current CPAG approach.

Biogen recognises that the introduction of a new access route would not be straightforward and that guardrails would need to be introduced to ensure that it did not become a mechanism through which NICE could be bypassed inappropriately. The following steps could be taken to provide clarity and certainty to industry, patients and the NHS on how the route would be used in practice:

- 1 Defining Eligibility:** Establish clear criteria for the routing of low-budget impact, high-unmet-need orphan medicines to the new assessment process. Involving the MHRA and NICE in the creation of the criteria could help to ensure alignment with existing regulatory processes, while mitigating the risk of inappropriate routing decisions.
- 2 Allocating Dedicated Funding:** Allocate a proportion of the Innovative Medicines Fund's £340m funding to be used to support access through the new route. A competitive process could allocate up to £10-£20m annually for eligible treatments, ensuring that the budget for the currently underspent IMF is used as intended to support access to orphan medicines, while not creating new spending pressures on stretched NHS budgets.
- 3 Industry Contribution:** Introduce a small fee for submissions to the new process, generating revenue to sustain the scheme and helping to ensure budget neutrality for the increased volume of assessments.



PROPOSED REFORM 2

Introduce reimbursement during early access through EAMS+

While a reformed access and reimbursement process should enable *better* access to medicines, a further initiative is required to ensure *fast* access is achieved.

This could be done in a way that shares risk fairly, while still achieving that goal of a more ambitious access environment for the UK. An adjustment to the Early Access to Medicines Scheme (EAMS) would apply for a limited number of products only. In the same way that typically only a small handful of products benefit from the early access system in France, strict criteria for this route would need to be defined and in place, including clear justification for going outside the standard EAMS process:

- 1 Before marketing authorisation**, companies supply medicines to the NHS at a discounted price (unlike current EAMS, which is free of charge).
- 2 After marketing authorisation**, the medicine remains in EAMS+ at the same discounted price, until NICE or the new access mechanism completes its evaluation.
- 3 If the final agreed price is lower than the interim price**, companies refund the NHS the excess. [Though if the agreed reimbursed price is higher, the NHS would not be asked to backdate the difference].



ENSURING NHS FINANCIAL SUSTAINABILITY

Any exceptional access scheme must safeguard taxpayers from unscrupulous pricing or rising costs. Existing budget controls such as the Voluntary Scheme for Branded Medicines Pricing, Access, and Growth (VPAG) and the Budget Impact Test (£40m threshold for new medicines) provide sufficient financial guardrails.

Eligibility criteria should ensure that only low numbers of medicines qualify – those addressing high clinical unmet need and targeting small patient populations, at low overall budget impact, would be considered. Additional considerations may include a company's commitment to UK clinical trials, real-world evidence collection, or academic investment.

CONCLUSION: THE TIME FOR CHANGE IS NOW



The UK must act decisively to improve access to orphan medicines, ensuring policy shifts translate into tangible benefits for patients. With the right reforms, the government can accelerate access while maintaining financial sustainability, unlocking the UK's full potential as a global leader in rare disease research and treatment.

These initiatives, if developed in collaboration with the wider rare disease community, could deliver on the twin government commitments to drive innovation and the ambition for the UK to lead the world in clinical trials.

Biogen remains committed to working with the government, regulators, and the rare disease community to make these proposals a reality.



If you have any questions or would like to discuss any of the issues raised in this report, please contact Jessica March, External Affairs Lead for Rare Disease at Biogen UK & Ireland, at jessica.march@biogen.com.

About Biogen

Biogen is a leading global biotechnology company that pioneers science and drives innovations for complex and devastating diseases. Biogen is advancing a pipeline of potential therapies across neurology, neuropsychiatry, specialised immunology and rare disease and remains acutely focused on its purpose of serving humanity through science while advancing a healthier, more sustainable and equitable world.

To learn more, please visit www.biogen.uk.com.

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