

October 28, 2026

What International Drug Pricing Means for US Patients with Rare Diseases

Lessons from the UK's System

Key Takeaways for Policymakers

1

Rare disease therapies are not well suited to be assessed under conventional HTA frameworks.

Small patient populations, limited clinical evidence, and greater uncertainty around long-term outcomes make it more difficult for treatments developed for rare diseases to satisfy standard health technology assessment requirements.

2

Conventional cost-effectiveness thresholds can limit access.

Because rare disease therapies typically have higher upfront costs and fewer eligible patients, they are more likely to face prolonged negotiations, restricted reimbursement, or no routine NHS access despite regulatory approval.

3

Patient-defined benefit must inform treatment value and access.

Patients across all stages of disease should help identify meaningful outcomes, including preserving independence and remaining function, and participate directly in the development of pricing and coverage policies.

4

Delays carry irreversible consequences for patients.

Many rare diseases are progressive and life-limiting, meaning that every month without treatment can result in permanent loss of function, narrowing the window in which therapies can deliver their greatest benefit.

Introduction

In 2025, the Trump administration renewed efforts to implement ‘Most Favored Nation’ (MFN) drug pricing policies that would benchmark U.S. medicine prices against prices paid in other developed countries. The MFN concept, along with similar foreign-reference pricing (FRP) proposals offered by Sen. Bernie Sanders (I-VT) and others, has put a renewed focus on the implications of FRP for patients.

As is being increasingly recognized in U.S. publications, FRP creates a fundamental paradox: while the U.S. has resisted the explicit use of cost-effectiveness in healthcare decision-making, it risks indirectly importing the value judgements and access trade-offs that determine medicine prices in other countries.^{1,2}

In countries such as the United Kingdom, lower medicine prices are often achieved through health technology assessment (HTA) and reimbursement processes that influence not only what the healthcare system will pay for medicines, but also whether and when patients can access them.

These value judgements are particularly visible in rare diseases, where patient populations are smaller, unit prices often are higher, and evidence is harder to generate. As a result, patients with rare diseases often face restricted eligibility criteria, delayed access, or no routine NHS coverage at all.

As policymakers consider FRP proposals, the UK experience provides insight into the potential implications of benchmarking U.S. prices against markets that rely heavily on HTA-based pricing and reimbursement processes - including the possible impact on patient access, availability of innovative therapies, and long-term development of newer, better therapies for rare diseases.

How the UK HTA system works - and how it affects patient access

In the UK, medicines first undergo regulatory review by the Medicines and Healthcare products Regulatory Agency (MHRA), which assesses whether a treatment is safe and effective - similar to the role of the FDA in the United States.³

However, regulatory approval does not automatically mean patients can receive the medicine through the UK’s NHS.

Once a medicine is approved by regulators, it is then assessed by the National Institute for Health and Care Excellence (NICE), which evaluates whether the treatment meets the NHS’s cost-effectiveness requirements for reimbursement.⁴

This process is known as health technology assessment (HTA).

NICE evaluates medicines using a health economic methodology designed to assess whether a treatment provides sufficient value for money for the NHS. A central part of this process is the use of incremental cost-effectiveness ratios (ICERs), which are intended to estimate how much additional cost is associated with the additional health benefit a medicine provides compared with existing treatments.

To do this, NICE uses a metric known as the quality-adjusted life year (QALY). The QALY attempts to measure how much additional length and quality of life a treatment may provide to patients. To do this, the QALY assigns a value to the year of life, giving less value to a year of life with a disability.

NICE then compares the estimated cost-per-QALY against predefined willingness-to-pay thresholds that determine what the NHS considers acceptable value for money.

Since the QALY methodology devalues people with disabilities, the use of the QALY is banned in the United States to make coverage and reimbursement decisions due to its discriminatory implications. It is widely acknowledged to fail to engage patients across all stages of disease in identifying meaningful outcomes, such as preserving independence and remaining function.

In practice, these thresholds therefore represent the maximum price the NHS is willing to pay for a new innovative medicine. Treatments that exceed, or are interpreted to exceed, those thresholds will face prolonged negotiations, restricted reimbursement, or rejection altogether.

As a result, unlike in the United States, regulatory approval and patient access are not necessarily the same thing.

Medicines in the UK may spend months or years navigating additional reimbursement negotiations before patients can receive them through the NHS. Disagreements between manufacturers, NICE, and the NHS over how the value of medicines should be assessed and reimbursed remain a significant factor in these delays.

In practice, because QALYs combine survival and health utility, QALY-based evaluations such as those used by NICE may undervalue some interventions for older patients when standard measures are insensitive to meaningful quality-of-life changes and when shorter life expectancy limits the accumulation of QALY gains. Treatments for people with rare diseases face a similar disadvantage. Small patient populations generate limited QALY data, and the full scope of a medicine's benefit is rarely captured by NICE's standard instruments. The OHE found that approximately 70 percent of orphan and ultra-orphan medicines evaluated by NICE have a cost-per-QALY exceeding NICE's standard £30,000 threshold, meaning the standard pathway structurally blocks access for most of these medicines.⁵

What the data shows

Evidence from the UK and other markets that rely heavily on HTA-based pricing and reimbursement processes suggests that lower drug prices can be associated with significantly less patient access to these treatments, particularly for rare diseases and advanced therapies.

- While approximately **94% of rare disease medicines** are available to patients in the US, this drops to just 41% outside of the US.⁶
- Over the past decade, **88% of all new medicines** have been reimbursed in the US, compared with **46% in the UK**.⁶ Of those available in the UK, only 39% are available to the fully licensed population.
- Industry analysis suggests that while 20.1% of all NICE technology appraisals were stopped before a resolution was reached between 2020 and 2023, it is notable that **rare disease medicines accounted for 41% of those technology appraisals terminated between 2021/2022 and 2025/2026**.⁷
- On average, US patients wait approximately **3 months** from a medicine's global launch to Medicare reimbursement, compared with approximately **30 months** for NHS reimbursement in the UK.⁶

Together, these trends underscore how HTA-based pricing and reimbursement processes can affect not only the price of medicines but also whether patients can access them, how quickly they become available, and how broadly they are covered once approved.

Commentary on Funding Variation Request (FVR) process in the UK

*NICE is now consulting on formalising and expanding this process. Whilst they expect FVRs to remain the exception, they do also expect them to become more common as medicines get more innovative and expensive, which means more delays, more often, for patients waiting for treatments that have already been approved.*⁸

- Metabolic Support, UK-based patient organization

HTA pathway decisions can limit access

The Voxzogo case

The case of Voxzogo, a treatment for children with achondroplasia - the most common form of dwarfism – illustrates how NICE's decisions about *how* a medicine is assessed can significantly influence whether patients ultimately gain access to treatment.

Achondroplasia can lead to serious lifelong complications affecting bone growth, mobility, spinal health, and quality of life. For families, vosoritide represented one of the first therapies designed to target the underlying biology of the condition rather than simply manage complications after they occur.

NICE has a dedicated program for certain very rare conditions, the Highly Specialized Technologies (HST) pathway, which in 2025 was refined to make qualifying criteria stricter. Despite the rarity of the disease, NICE instead chose to evaluate Voxzogo through its standard technology appraisal (STA) pathway rather than this specialized route. This procedural decision carried important consequences.

Compared with the HST program, the standard appraisal pathway applies more restrictive cost-effectiveness thresholds, places greater emphasis on long-term data certainty, and is ultimately less flexible to the nuances or complications associated with rare disease therapy development.

Following NICE's scoping decision, the significant challenges of demonstrating cost-effectiveness under a framework less suited to assessing treatments for very rare conditions led the manufacturer to withdraw from the appraisal process. Consequently, despite receiving regulatory approval, the treatment remains unavailable through routine NHS commissioning for children in England.

The case illustrates how appraisal pathway decisions alone - not only final reimbursement recommendations - can shape patient access by determining the HTA framework through which rare disease therapies are evaluated. More broadly, it highlights how conventional cost-effectiveness approaches and evidentiary expectations may be poorly aligned with the realities of rare disease medicine development, which can lead to limited patient access to innovative therapies.

“The disproportion will be improved, and the knock-on effects to functionality and the activities of daily living and those challenges that kids and adults with achondroplasia live with will be much improved. It will stop some of those complications that require surgical intervention like hearing loss and glue ear requiring grommets and the obstruction to breathing requiring ear, nose and throat therapy. But most importantly for me is a reduction in the serious complications that can occur and lead to early death, so in infancy and medical complications that can occur later in life. This drug treatment should alleviate many of those complications and improve things on a day-to-day basis by making the daily challenges modified.”⁹

- Mary Andrews, co-founder of The MAGIC Foundation

The Duvyzat case

The case of Duvyzat, a treatment for Duchenne muscular dystrophy (DMD), illustrates how NICE's application of cost-effectiveness thresholds can result in reimbursement being restricted to specific patient subgroups, even after a medicine has received regulatory approval for a broader patient population.

DMD is a rare, progressive and fatal muscle-wasting condition that causes irreversible loss of muscle function over time. Children living with DMD gradually lose the ability to walk, breathe independently and carry out everyday activities. Since disease progression cannot be reversed, timely access to treatment is critical.

Duvyzat received FDA approval in the United States in March 2024 and UK regulatory approval from the MHRA later that year. However, NICE's appraisal process lasted almost two years before the treatment was recommended for routine NHS use in England in May 2026.

Throughout the appraisal, Duchenne patient organisations warned that delays to access could have significant consequences for families affected by this rapidly progressive disease.

NICE ultimately approved Duvyzat, but access was restricted to a subset of patients – those aged six and over who were capable of walking (ambulant) at the point they start treatment - a narrower group than the broader licensed population. Patient groups have expressed disappointment that non-ambulant patients remain excluded from routine NHS access, as the drug was approved as safe and effective for all Duchenne patients.

The case demonstrates that HTA-based reimbursement decisions can shape not only whether a medicine is funded, **but also which patients receive it. This selective restriction of which patients can benefit from new, potentially life-changing innovations is a direct consequence of restrictive guardrails designed to cut costs, not to serve patients.**

“It’s been utterly devastating knowing that there is a treatment out there that could slow down the progression of DMD and give Ben more time to do the things he loves, but not being able to access it.

“We are of course delighted that Ben will now be able to access this new medicine through the NHS, but it should never have taken this long and it’s vital that he can now do so without any further delay.”¹⁰

- Parent of child with Duchenne Muscular Dystrophy in the UK

The Orkambi case

The Orkambi dispute became one of the most prominent examples of how HTA and reimbursement negotiations can delay patient access to potentially transformative medicines, particularly for rare diseases where evidence generation is inherently more challenging.

Orkambi was approved in the United States in 2015 for patients with cystic fibrosis, a progressive genetic disease that causes irreversible lung damage and significantly shortens life expectancy.

However, **routine NHS access in England was delayed for four years** while NICE and the manufacturer negotiated a price deemed to be cost-effective for the NHS.

The delay reflected broader challenges in applying conventional HTA methods to rare disease therapies. Although Orkambi had demonstrated meaningful clinical benefit and received regulatory approval, uncertainty surrounding its long-term clinical benefits and whether it met NICE's cost-effectiveness threshold at the proposed price resulted in repeated appraisal discussions and prolonged commercial negotiations before reimbursement could be agreed.

During this period, clinicians and patient groups warned that children and young adults were losing lung function that could never be regained. For patients with cystic fibrosis, every infection and every decline in lung capacity can have permanent consequences. Patient organisations argued that while reimbursement negotiations continued, patients were becoming permanently sicker waiting for access to a medicine that was already available in other countries.

An agreement was eventually reached in 2019. **The case illustrates how conventional HTA approaches can be poorly aligned with the realities of rare disease therapies, where long-term evidence is often limited, patient populations are small, and delaying treatment may lead to irreversible disease progression.**

It demonstrates how the HTA process in the UK can delay access to regulator-approved medicines despite substantial unmet clinical need.

“When the state holds absolute power of provision over things that are essential for life, the state has commensurate obligations. British citizens are ‘prisoners’ of a monopolistic state healthcare system, which holds sole power to determine which treatments they will or won’t receive on the NHS.”

“To date, our government has failed him. As his parents, we must do better than that, even if it means uprooting ourselves to start again – moving somewhere where CF children are considered worth saving, despite the cost of doing it.”¹¹

- Patient & Family testimonies to Parliament compiled by Health and Social Care Committee secretariat in March 2019 leading up to approval after years of waiting.

Medicines may not launch at all

The Respreeza case

Patients with alpha-1 antitrypsin deficiency can experience progressive shortness of breath, repeated chest infections, and long-term lung damage. For many patients, treatment options are limited and focused primarily on managing symptoms rather than slowing underlying disease progression.

Respreeza received regulatory approval for use in the UK as a treatment to slow the progression of emphysema in adults with severe alpha-1 antitrypsin deficiency. However, following discussions with NICE during the technology appraisal process, the manufacturer decided not to launch the medicine in England and Wales. Respreeza is a plasma-derived therapy, which has is unique, complex, and costly to produce. NICE acknowledged this yet was unwilling to be flexible with the manufacturer to ensure patients were able to access the treatment. NICE subsequently terminated the appraisal after the company confirmed that it could not offer the product at a price that met NICE's current cost-effectiveness threshold.

As a result, patients in England and Wales did not gain routine NHS access to a therapy that is available in the United States. **The case illustrates how the application of conventional willingness-to-pay thresholds can leave manufacturers without a commercially viable pathway to reimbursement.**

For rare disease therapies, where development and manufacturing costs are often inherently higher with a smaller group of eligible patients, this can influence launch decisions and ultimately limit patient access to transformative innovative medicines.

Industry stakeholders have warned that such outcomes risk discouraging future launches, reducing patient access to innovation, and weakening the UK's position as a priority market for rare disease therapies.

“The only treatments currently available to patients with alpha-1 antitrypsin deficiency (AATD) in England are for symptomatic relief only. No disease- modifying treatments are available in the UK that slow or halt the progression of AATD-associated emphysema.

The therapy under consideration is the only licensed therapy with the potential to modify the course of AATD, and UK patients continue to die prematurely in the absence of any effective treatment options – since the previous scoping of human alpha1-proteinase inhibitor for evaluation under NICE’s STA programme in September 2015, 28 members of our patient charity have died, with an average age at death of 58 years (and 4 of these were below the age of 50).

In addition, patients with severe AATD have for many years had access to human alpha1-proteinase inhibitor in many European countries in the EU (incl. Germany, Italy, Spain, Austria, Portugal, Belgium, Switzerland etc.) and in the US, and comparison studies have shown improved clinical outcomes in patients treated with human alpha1-proteinase inhibitor compared to patients treated with standard therapy.

Patients in England therefore strongly feel that this technology should be considered by NICE as a matter of urgency in order to enable timely patient access to this therapy, if deemed appropriate, and to reduce the inequality of access to this therapy across Europe.”¹²

- Alpha-1 UK Support Group, 2023 comments to NICE during consideration

Implications of importing HTA-based pricing approaches into the United States

1. Reduced and delayed patient access

Linking US drug prices to countries that rely on centralized HTA systems could import not only lower prices, but also the discriminatory values and access restrictions that accompany those systems. For US patients, this could mean slower access to innovative therapies and fewer available treatment options as a consequence of deprioritized launches compared with other international markets.

2. Disproportionate impact on patients with rare diseases and severe conditions

Experience from the UK suggests that patients living with rare diseases, who often already face the greatest unmet medical need and the fewest available treatment options, are among the most vulnerable to delayed launches, restricted access, or decisions not to launch medicines at all.

Advanced therapies and gene therapies may be especially affected because they often involve smaller patient populations, greater evidence uncertainty, and higher upfront treatment costs.

3. ‘Reduced incentives for innovation

Policies that materially reduce returns on innovative medicines risk weakening incentives for future R&D investment. Since R&D investment decisions are closely tied to the predictability of pricing, reimbursement, and patient access, policies that disrupt this balance may reduce future investment in U.S. biomedical innovation, which would leave rare disease patients without treatments that would otherwise be within reach based on science alone.

4. Broader economic implications

The U.S. life sciences sector supports high-skilled jobs, clinical research, domestic investment, and global leadership in biotechnology innovation.

At a time of growing international competition, including from China, policies that weaken incentives for biomedical innovation may have broader implications for U.S. scientific and economic leadership.

The recently announced UK–U.S. trade agreement has sought to drive direct improvements to the UK’s restrictive HTA approach by increasing the ‘willingness-to-pay’ thresholds by up to 25%. However, this agreement fails to address the structural challenges and discriminatory implications for patients posed by the UK’s broader HTA-based pricing and reimbursement system, particularly for rare disease therapies.

The UK experience continues to highlight important considerations for US policymakers. MFN-style pricing policies risk importing some of the access hurdles and reimbursement pressures associated with HTA-based pricing approaches for potentially life-saving innovative and rare disease medicines. In an increasingly competitive global life sciences environment, this could contribute to delays, reduced R&D investment, and more restricted access to medicines for the patients who stand to benefit most.

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