Differences in the reimbursement pathway for ultra-rare disease therapies in England and Ireland

Bal, Pratik Kumar[1]; Knight, Jennifer[2]; Barnes, Annie[2]; Prescott, Carl[2]; Dooley, Brenda[1]
1. AXIS Reimbursement Ltd, Dublin, Ireland; 2. AXIS Reimbursement Ltd, Manchester, UK

01. Introduction

Timely access to rare and ultra-rare medicines remains a persistent challenge, largely due to the complexity of health technology assessment (HTA) and reimbursement processes. Although both England and Ireland have established structured evaluation frameworks, significant barriers continue to impede the rapid reimbursement of treatments for rare and ultra-rare diseases.

This study presents a comparative analysis of HTAs conducted by the National Institute for Health and Care Excellence (NICE) in England and the National Centre for Pharmacoeconomics (NCPE) in Ireland for ultra-rare drugs (2013-present) and rare drugs between 2022 and 2025.

The key objectives of this research are:

- To identify and compare ultra-rare medicinal products evaluated by NICE and the NCPE between 2013 and 2025, encompassing the full operational timeframe of the Highly Specialised Technology (HST) pathway.
- To compare rare medicinal products appraised by NICE and the NCPE during 2022–2025, examining differences in evaluation outcomes, reimbursement timelines, and appraisal processes between the two HTA agencies.

02. Methods

A retrospective, descriptive analysis of secondary data was conducted to compare reimbursement processes and timelines for rare and ultra-rare disease therapies in England and Ireland (2013–2025).For ultra-rare therapies, all NICE - HST appraisals were identified and cross-referenced with corresponding NCPE assessments, as Ireland lacks a dedicated ultra-rare pathway.

For rare therapies, NICE guidance issued between 2022 and 2025 was cross-referenced with available NCPE submissions. The rare or ultra-rare status of each therapy was confirmed using the Medicines and Healthcare products Regulatory Agency (MHRA), European Medicines Agency (EMA), and Orphanet databases. Key data like appraisal timelines, outcomes, and reimbursement decisions, were manually extracted from the NICE, NCPE, MHRA, EMA, and Orphanet websites. All extracted information was systematically compiled and analyzed using Microsoft Excel (Office 365).

NCPE Website

Extracted Data
RR assessment outcome
HTA assessment outcome
Reimbursement date
Reimbursement outcome

NICE Website

Extracted Data
Type of submission
Date of NICE Final scope
Date of Final Guidance
Pathway followed
Reimbursement outcome

03. Irish Reimbursement Process

The key elements of the Irish reimbursement process, including the NCPE assessment and post-NCPE phase, are outlined in Figure 1.

Figure 1: Overview of Irish reimbursement process

NCPE Process

Rapid Review Assessment
- Document typically 20-25 pages
- Focus on clinical efficacy, place in therapy, and budget impact
- Five possible NCPE recommendations, which dictate pathway (e.g., HTA required, price discussions possible)

HTA
- Larger document
- Broader focus, including cost-effectiveness
- Multiple milestones including pre-submission meeting, dossier submission, preliminary questions and a Factual Accuracy Check
- Four possible HTA recommendations

Price Discussions (HSE-CPU)
- Meeting with HSE-CPU team members to discuss outcome to NCPE assessment
- Opportunity for applicant company to present commercial offering
- For certain products, opportunity for CPU to approve reimbursement at monthly products committee
- Products with uncertainty regarding efficacy and budget impact typically progress to HSE Drugs Group

HSE Drugs Group
- Multidisciplinary group of medical doctors, pharmacists, health economists, and patient representatives
- Assess applications at monthly meetings
- Will make recommendations for reimbursement, stipulate any restrictions required or advise if reimbursement not recommended

Reimbursement Approval
- Following Drugs Group approval, application approved by HSE leadership group/ Senior Leadership Team (SLT)
- Following positive recommendation, reimbursement granted within 45 days

04. NICE Reimbursement Process

The NICE have multiple reimbursement pathways for products:

- **Single Technology Appraisal (STA)** - Standard process for most applications.
- **Highly Specialised Technologies (HST) (Ultra-Orphan) Pathway** - Introduced to support access to medicines for patients with ultra-rare diseases.

The STA process is NICE's standard approach for evaluating most new medicines and indications. It is typically used for drugs intended to treat more common conditions and for which sufficient clinical and economic evidence is available at the time of marketing authorisation.

The HST process is considerably longer than the STA process, with an average appraisal duration of approximately 78 weeks (around 18 months).

Figure 2: NICE assessment process (for STAs)

Topic Referral
- Carried out by the Department of Health and Social Care (DHSC)
- NICE is formally notified that a new technology is to be appraised.
- Topic selection is based on relevance, disease burden, and anticipated NHS impact.

Scoping Phase
- NICE develops a draft scope outlining the PICO (Population, Intervention, Comparator, Outcome) framework.
- If deemed appropriate by NICE, a scoping workshop is held with stakeholders including the manufacturer, clinicians, & patient groups.
- The final scope is published to guide evidence submission.

Evidence Submission
- The company submits: Clinical trial data (RCTs, meta-analyses), Economic model (cost-effectiveness analysis, usually using QALYs), Budget impact analysis. An Evidence Assessment Group (EAG) independently reviews the submission.

EAG Report and Clarification
- The EAG critiques the company's evidence, model assumptions, and data inputs.
- NICE may request clarifications or additional analyses.

Committee meeting
- NICE committee meets to assess: Company submission, EAG critique, Stakeholder submissions (e.g., patient/carer groups). Committee assesses the Incremental Cost-Effectiveness Ratio (ICER) and quality of evidence and outcome: Final Draft guidance (FGD) is issued with provisional recommendation.

Final guidance
- Final approval by NICE
- Publication of advice on NICE website

05. Results

Ultra-Orphan Drugs Assessments

As shown in Table 1, the NICE-HST programme demonstrated a substantially higher rate of positive recommendations for ultra-rare disease therapies, with 93.3% (28/30) of submissions approved.

In contrast, the NCPE recommended 43.3% (13/30) of assessed ultra-rare therapies.

Moreover, 6 NCPE appraisals remain ongoing, and 11 therapies had not yet entered the Irish reimbursement process.

Orphan Drugs Assessments

For orphan drugs, Table 1 shows that NICE's STA pathway approved 73.9% (51/69) of submissions, whereas only 38.2% (26/68) of NCPE orphan appraisals resulted in a positive reimbursement recommendation.

Additionally, 42 NCPE assessments are still ongoing, indicating longer decision timelines consistent with findings from Table 1.

Overall, these results highlight significant disparities in appraisal outcomes and timelines, suggesting that patients in Ireland may face delayed access to orphan and ultra-rare disease treatments compared with those in England.

Table 1: Overview of NICE and NCPE Assessments

Group	Total (n)	Recommended, n (%)	Not Recommended, n (%)	Ongoing, n (%)	Terminated, n (%)	Did Not Apply, n (%)
NICE - HST	30	28 (93.3)	2 (6.7)	– (-)	– (-)	– (-)
NCPE - ultra rare	30	13 (43.3)	– (-)	6 (20)	– (-)	11 (36.7)
NICE - STA	69	51 (74)	7 (10.1)	– (-)	11 (15.9)	– (-)
NCPE - rare	68	26 (38.2)	– (-)	42 (61.8)	– (-)	– (-)

Comparison of NICE and NCPE/HSE Timelines

Table 2 presents a breakdown of the assessments conducted by both the NICE and NCPE drugs. The median appraisal time for ultra-rare drugs was 419 days under NICE-HST and 1,035 days under NCPE. Although the NICE-HST group included an outlier (maximum 2,226 days), the mean duration remained shorter (550 vs. 1,011 days).

For rare drugs, the median appraisal time was 446 days for NICE-STA and 717 days for NCPE, with corresponding means of 494 and 647 days. Overall, both mean and median values indicate shorter appraisal timelines under NICE compared to NCPE for both rare and ultra-rare drugs.

Table 2: Summary statistics (in calendar days) each group (For all reimbursed drugs)

Group	Median (days)	Mean (days)	Min (days)	Max (days)	Q1	Q3	IQR
NICE-HST	419	550	275	2226	334.5	553.3	218.8
NCPE - ultra rare	1035	1011	475	1625	891	1117	226
NICE - STA	446	494	154	1227	337	626	289
NCPE - rare	717	647	148	1299	340.3	864	523.8

06. Conclusions

This study highlights notable differences in appraisal timelines for rare and ultra-rare drugs between NICE and NCPE. Overall, NICE appraisals demonstrated shorter median and mean durations compared to NCPE, indicating more efficient decision-making processes. The NCPE timelines, particularly for ultra-rare drugs, were substantially longer, reflecting the complexity and resource demands of evaluating treatments for very rare conditions.

These findings underscore the need for greater efficiency and transparency within appraisal systems to ensure timely and equitable patient access. Strengthening collaboration between agencies and adopting adaptive approaches such as managed access agreements, may help address current delays while maintaining the robustness of economic evaluations.

In summary, addressing the identified challenges through system-level reforms is critical to ensuring timely and equitable access to rare and ultra-rare drugs, ultimately improving outcomes for patients with rare diseases in Ireland and beyond.

AXIS Reimbursement Ltd
22 Lower Baggot Street, Dublin 2, D02 X658
11th Floor, 3 Piccadilly Place, Manchester, M1 3BN

axisreimbursement.com
+353 (1) 529 2768; +447768740344
info@axisreimbursement.com