# A global comparative evaluation of health technology assessment outcomes for non-orphan, orphan, and ultra-orphan drugs

HTA279

Sarah-Jane Lyttle[1], Adelaide Shaw-Maguire[1], Jane Moorhouse[1]

*1. Initiate Consultancy, London, UK.*

## SUMMARY

### OBJECTIVES

- Orphan and ultra-orphan drugs may receive additional support or incentives during pricing and reimbursement, with some markets having adapted their health technology assessment (HTA) processes for these products.
- We sought to understand whether these adaptations have an impact on HTA decision-making for orphan drugs.

### METHODS

- We reviewed the HTA outcomes published in 2023 from across 13 markets with a range of HTA processes for orphan and ultra-orphan drugs.
- We analysed the likelihood of HTA success according to the presence of adapted or separate processes for orphan or ultra-orphan drugs.

### FINDINGS

- Orphan and ultra-orphan drugs had a reduced rate of HTA success when compared with non-orphan drugs across all markets in 2023.
- The likelihood of HTA success was greater for orphan and ultra-orphan drugs when assessed in markets with a separate ultra-orphan pathway or those which consider orphan status.

## BACKGROUND & AIMS

- Drugs can be designated as orphan if they meet certain criteria set by regulatory agencies:
  - The European Medicines Agency (EMA) defines an orphan product as one which is indicated for a life-threatening or chronically debilitating disease with a prevalence in the EU of no more than 5/10,000 people. The product must also provide significant benefit to patients affected by the disease in order for orphan designation to be granted.
  - The Therapeutic Goods Administration grants orphan drug designation under similar criteria for products assessed in Australia, but there is no such orphan designation available in at marketing authorisation level in Canada.
- Whilst there is no official definition of "ultra-orphan" disease, the term is typically applied to drugs treating diseases with prevalence less than 1/50,000. The term was officially introduced by the National Institute for Health and Care Excellence (NICE) in 2004[1] and is also recognised in Scotland[2].
- Some markets offer additional support or incentives for orphan drugs, and some have adapted the HTA process for orphan and ultra-orphan drugs.
- The aim of this study is to understand the impact of or these incentives and adaptions on HTA outcomes.

## METHODS

- HTA decisions published in 2023 in 13 markets across Europe, North America, and the Asia-Pacific were reviewed, using data collected as part of Initiate's 2023 Reimbursement Radar[3]; a database of global HTA outcomes published across 13 global HTA markets.
- The 13 markets included analysis were Australia, Canada, Denmark, England, France, Germany, Ireland, Italy, the Netherlands, Norway, Scotland, Spain, and Sweden.
- **Table 1** describes the incentives and adaptions made to HTA processes for orphan and ultra-orphan drugs in these markets.

**Table 1. Orphan product-specific HTA process across markets**

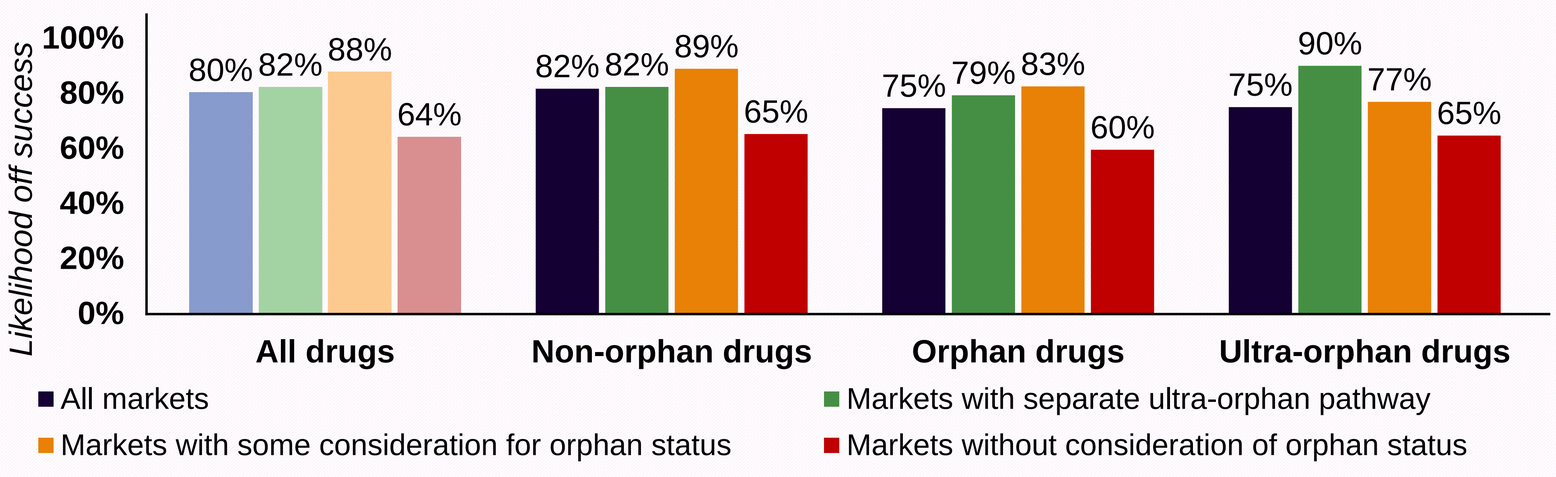
| National orphan product process | Markets |
|---|---|
| **Separate process:** *Dedicated assessment route for orphan products* | |
| **Modified process:** *Considerations made for orphan products including expedition of processes, pricing adaptations, reduced extent of assessment* | |
| **No process:** *No considerations made for orphan vs. non-orphan products* | |

- Data was extracted regarding appraisal type and decision. Drugs were categorised based on disease prevalence, as non-orphan (>5/10,000), orphan (<5/10,000), or ultra-orphan (<1/50,000).
- Decisions were analysed to evaluate the likelihood of HTA success given a modified or separate process for orphan or ultra-orphan drugs.

## RESULTS

- 896 submissions were included in the analysis: non-orphan (n=722), orphan (n=134), and ultra-orphan drugs (n=40).
- The breakdown of HTA outcomes by market type and orphan designation is presented in **Figure 1**.
- Across all markets, HTA success was lower for orphan and ultra-orphan drugs (both 75%) compared to non-orphan drugs (82%).
- Orphan drugs were more likely to be recommended in markets with a separate ultra-orphan pathway (79%) as well as those with some consideration of orphan status (83%) than in those without any consideration of orphan status (60%).
- Ultra-orphan drugs were also more likely to be recommended in markets with a separate ultra-orphan pathway (90%) as well as those with some consideration of orphan status (77%) than in those without any consideration of orphan status (65%).
- Interestingly, markets with a separate ultra-orphan pathway (82%) as well as those which consider orphan status (88%) had an overall higher positive recommendation rate than those without any consideration of orphan status (64%) for all drugs regardless of orphan status
- This trend also applied to non-orphan drugs: 82% were recommended in markets with a separate ultra-orphan pathway and 89% in markets with some consideration of orphan status, compared with only 65% in markets without any consideration of orphan status
- It is important to consider that the likelihood of HTA success ranges greatly across the markets without any consideration of orphan status, with Denmark and Ireland having the lowest overall likelihood of success of the 13 markets included in this analysis (43% and 6% respectively vs. an average of 85% for the other markets)
- As such, the inclusion of Danish and Irish HTA outcomes in this analysis may be accounting for this trend:
  - The likelihood of reimbursement in markets with no considerations increased after excluding Denmark and Ireland: 64% to 86% for all drugs, and 65% to 84% for non-orphan drugs.
  - This likelihood of success is in-line with that of markets with a separate ultra-orphan pathway (82% for all drugs and non-orphan drugs), as well as those which consider orphan status (88% and 89% for all drugs and non-orphan drugs respectively).

**Figure 1. Likelihood of reimbursement success by market and orphan designation**




## CONCLUSIONS

- Orphan and ultra-orphan drugs received a disproportionate number of negative HTA assessment decisions across global markets in 2023.
- Separate ultra-orphan pathways and consideration of orphan status were associated with improved HTA outcomes for orphan and ultra-orphan drugs.
- Despite this, only 54% of markets assessed take orphan status into account as part of their HTA processed, and even fewer utilise separate ultra-orphan pathway.
- There is a clear need to introduce more consistent and considered HTA processes, in order to better support successful outcomes for orphan drugs and meet the needs of patients with rare diseases.

### References

1. *NICE. NICE Citizens Council Report Ultra-Orphan Drugs. London, NICE, 2004.*
2. *SMC. Ultra-orphan medicine for extremely rare condition. https://scottishmedicines.org.uk/how-we-decide/ultra-orphan-medicines-for-extremely-rare-conditions/*
3. *Initiate Consultancy, 2023, Reimbursement Radar*

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*initiateconsultancy.com* *hello@initiateconsultancy.com*