# (ULTRA-)ORPHAN DRUG ASSESSMENTS IN POLAND: IMPACT OF PROPOSED CHANGES ON HTA OUTCOMES

*Dekkers R[1], Vaithyanathan G[2], van Engen A[1]*
*[1] IQVIA, The Netherlands, [2] IQVIA, Bangalore*

IMS Health & Quintiles are now IQVIA™

## OBJECTIVES

By the end of 2018, the Polish government is expected to implement its long-awaited amendment to its reimbursement system. [1] The amendment is expected to include a procedure dedicated solely to orphan drugs, which will allow for more relaxed reimbursement criteria in the assessment of ultra-orphan drugs. [2] Orphan and ultra-orphan drugs are generally defined as drugs targeting diseases that affect <5 in 10,000, and ≤1 in 50,000 people, respectively. [2]

Orphan and ultra-orphan drug manufacturers generally face challenges when applying for reimbursement via standard HTA procedures due to a mix of high uncertainty in the available evidence, low patient prevalence, poorly explored epidemiology, absence of comparable treatment alternatives on the market, and difficulty to meet cost-effectiveness standards.

Currently, ultra-orphan drugs follow the same HTA procedures as any other drug in Poland, meaning these drugs have to meet the same clinical and cost-effectiveness requirements as any other drug. This includes a strict willingness-to-pay threshold of three times the gross domestic product per capita per quality-adjusted life year (QALY) gained per capita (equalling to an ICER threshold of €35,220/QALY in 2017 based on a €11,740 GDP). [3,4]

Some countries have already implemented special considerations for (ultra-)orphan products and while details on the exact assessment criteria for ultra-orphan products in Poland are not yet published, a comparison between these countries and Poland can provide some insights on the possible impact on reimbursement outcomes of orphan and ultra-orphan drugs in Poland.

## METHODS

IQVIA's proprietary HTA Accelerator was used to identify drugs that received marketing authorisation by the European Medicines Agency (EMA) between 31 Dec 2012 and 01 Oct 2018. Original submissions, extensions of indication and resubmission HTA reports were identified for Poland (AOTMiT), and key HTA agencies that have established guidance and considerations for orphan disease products, including Canada (CADTH), Germany (G-BA), the UK (NICE, SMC) with a publication date between 31 Dec 2012 and 1 Oct 2018. HTAs were analysed for orphan designation by the EMA, indication prevalence, recommendation outcome and final decision drivers. [5]

## RESULTS

Between 31 Dec 2012 and 01 Oct 2018, the EMA granted marketing authorisation to 438 drug-indication combinations, 92 (21%) of which were attributed an orphan designation, and 13 (3%) met ultra-orphan indication prevalence criterion (Table 1).

The HTA agencies in scope (outside Poland) published 771 HTAs on the drugs approved by EMA, and AOTMiT published 175 HTAs. 161 (21%) HTAs published across all agencies (outside Poland), and 38 (22%) HTAs published by Poland were for orphan indications; 15 (2%) HTAs across all HTA agencies, and 1 HTA (4%) from Poland met the ultra-orphan indication prevalence criterion (Figure 1).

When looking at all HTAs, Poland provided comparable percentage positive recommendations (41%) when compared across all HTA agencies (outside Poland) (40%). Notably, more than half of the assessments (55%) published in Poland resulted in a negative recommendation, which is more than double compared with assessments conducted by HTA agencies with special considerations (23%).

The percentage of negative recommendations for orphan drugs across the HTA agencies is lower comparable with drugs for all indications (16% versus 23%). However, when looking at orphan drugs in Poland we see that these products have much lower chances of receiving positive recommendations (29%) compared to drugs for all indications (41%) in Poland or compared with orphan drugs in countries with special considerations for orphans (52%). Amongst the countries with special considerations, Germany had the highest rate of positive recommendations (88%; data not shown).

Poland only published one ultra-orphan drug assessment, providing a negative recommendation, thereby making a comparison with other agencies difficult. Across agencies with special considerations, ultra-orphan drugs generally received more positive recommendations (73%) compared with recommendation for all indications (40%) and orphan (52%) drugs. Ultra-orphan drugs received no negative recommendations, and less restricted recommendations compared with drugs for all indications (36%) and orphan drugs (31%) across all HTA agencies.

Positive recommendations for ultra-orphan drugs were mainly driven by clinical benefit and a general high unmet need in the patient population (Figure 2). Negative decisions were due to a mix of concerns related to uncertainties in the evidence presented and limitations in the economic analyses.

**Table 1: Products for ultra-orphan indication approved by the EMA**

| Therapeutic area | Brand (generic) | # HTAs |
|---|---|---|
| Blood and Immune System | Alprolix (eftrenonacog alfa) | 5 |
| | Coagadex (human coagulation factor x) | 0 |
| | Idelvion (human coagulation factor x) | 1 |
| | Strimvelis (autologous stem cells) | 1 |
| | Zalmoxis (genetically modified allogeneic t-cells) | 1 |
| Endocrine and metabolic diseases | Amglidia (glibenclamide) | 0 |
| | Crysvita (burosumab) | 2 |
| | Cystadrops (mercaptamine) | 2 |
| | Kanuma (sebelipase alfa) | 3 |
| | Lamzede (recombinant human α-mannosidase) | 0 |
| | Strensiq (asfotase alfa) | 6 |
| Infectious and Parasitic Diseases | Cresemba (isavuconazonium sulfate) | 2 |
| Oncology | Lenvima (lenvatinib) | 4 |

**Figure 1: HTA outcomes**

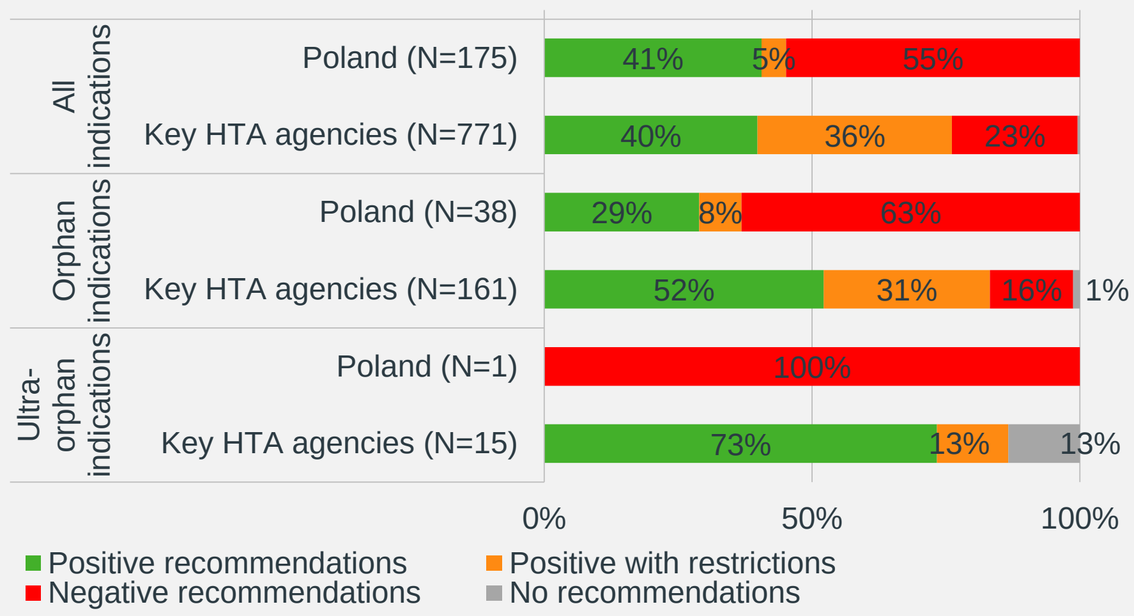
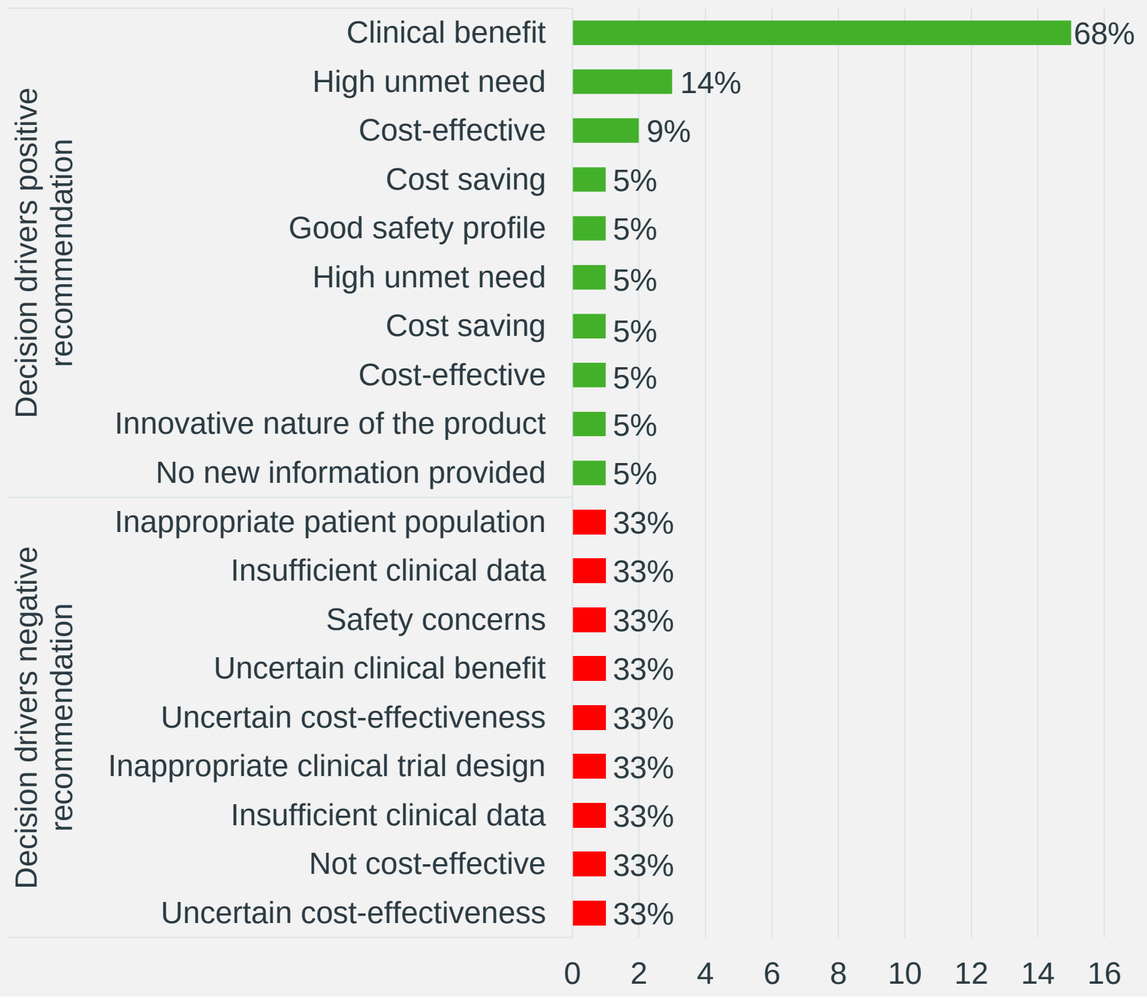



**Figure 2: HTA decision drivers for ultra-orphan indication drugs**




## Conclusion

**Generally, Poland is much stricter compared with other key countries. This research shows that special guidance for Poland is needed as currently (ultra-)orphan products face very high hurdles to become available to Polish patients. In other countries, the high unmet need and clinical benefit these ultra-orphan products bring are clear drivers for these products being recommended in almost twice as many cases compared with drugs for non-orphan indications. It remains to be seen what will happen in Poland when the new regulation come into effect, and so far developments have been slow, but it can be expected that these measures will have a positive impact on (ultra-)orphan drugs in Poland like we have seen in other countries.**

1. http://www.rynekzdrowia.pl/Farmacja/MZ-Narodowy-Plan-dla-Chorob-Rzadkich-najpozniej-do-konca-2018-r,181734,6.html; Published 28 Feb 2018, accessed 30 Oct 2018
2. K. Badora, Proposed changes to the reimbursement of pharmaceuticals and medical devices in Poland and their impact on market access and the pharmaceutical industry, Journal of Market Access & Health Policy, 2017, VOL. 5
3. http://www.aotm.gov.pl/www/hta/wytyczne-hta-2/; Published by AOTMiT in 2016, accessed 30 Oct 2018
4. The World Bank, https://data.worldbank.org/indicator/ny.gdp.pcap.cd?view=map, accessed October 22, 2018
5. IQVIA's proprietary HTA Accelerator

**ISPOR 2018 Barcelona**