Rare Disease Product Approvals: The Changing Regulatory And HTA Landscape Between 2018-2022

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Introduction

Globally, 7,000 rare diseases affecting 300 million people pose development challenges with small patient populations. Developing medicines for rare diseases requires innovation. Despite regulatory incentives, challenges for HTA and payers persist, such as surrogate endpoint, heightening evidence uncertainty. Alignment between agencies is required.

Understanding the current regulatory and HTA decision-making landscape for orphan products is essential for all stakeholders.

Method

Data on New Active Substances (NASs) approvals (2018-2022) by EMA, FDA, PMDA, Swissmedic, and TGA were collected from public domain, to analyse the timing, approval pathway and global rollout trend of orphan vs. non-orphan products. Follow-up included gathering HTA assessment data (2018-2022) from Australia PBAC, England NICE, France HAS, Germany IQWIG, Netherlands ZIN, Poland AOTMiT, Scotland SMC, and Sweden TLV, exploring synchronization in decision timing and 1st HTA decision. Comparative analysis encompassed decision frameworks and funding mechanisms for orphan products among HTA agencies.

Results

In the past decade, orphan drug approvals increased, the FDA having the highest designation rate at 55% (2018-2022).

Flexible pathways, mostly used by the FDA (92%) and PMDA (100%), expedite orphan drug reviews.

Figure 1: Proportion of NAS approvals by orphan designation for five regulatory authorities

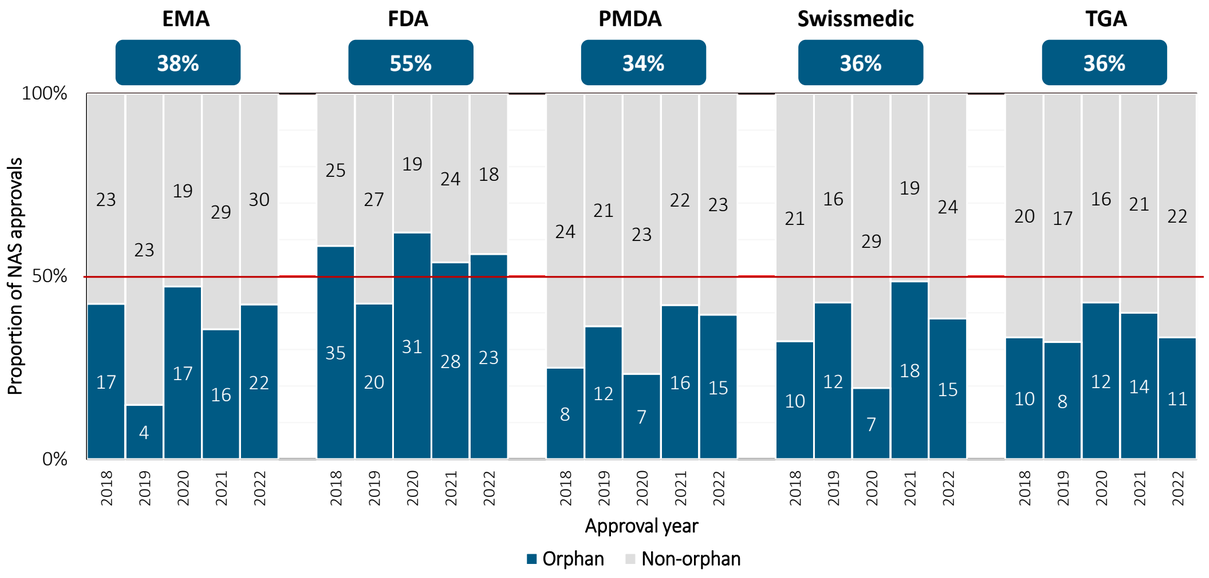


Figure 2: Proportion of Orphan products with at least one flexible regulatory pathway

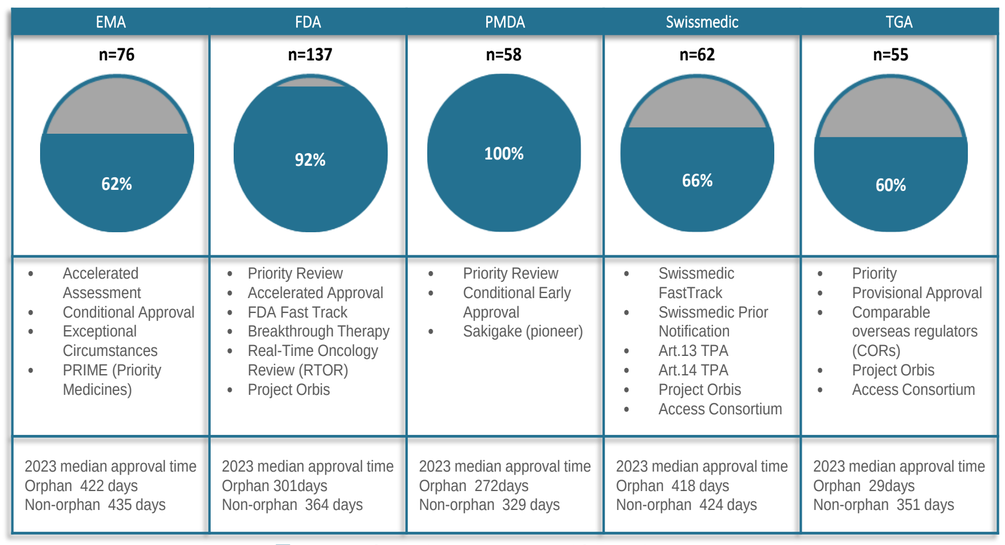
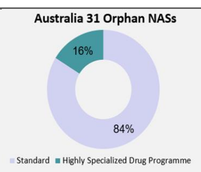
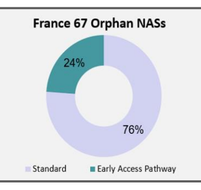
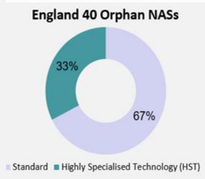
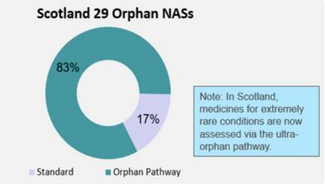


Figure 3: HTA framework for orphan products comparison 2018-2023

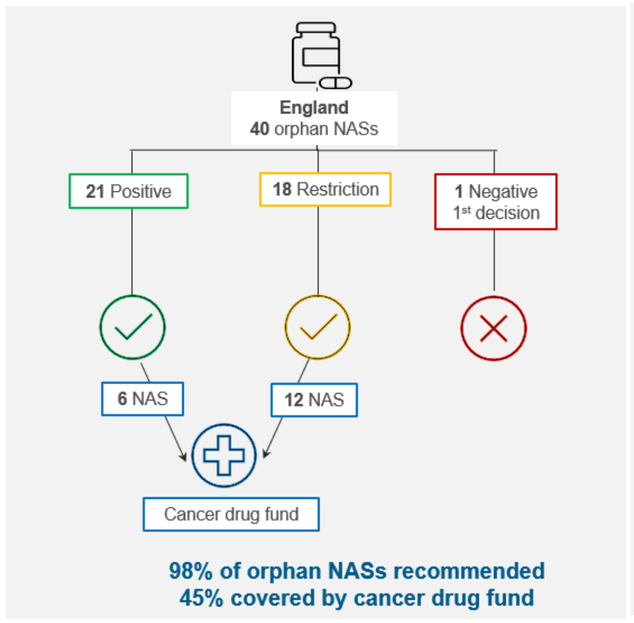
Jurisdictions	Agency	Orphan Specific Pathway	Other considerations	Orphan NASs assessed by HTA pathway
Australia	PBAC	N/A	Highly specialized drug Programme	
Canada	CADTH	N/A	Recognizes that there are exceptional cases where there is uncertain clinical and pharmacoeconomic evidence	
France	HAS	N/A	Early Access pathway	
Germany	IQWIG/ G-BA	N/A	Except from early benefit assessment： Orphan drugs will be subject to the full AMNOG process if their annual revenue exceeds €50m	
England	NICE	N/A	Highly specialized technology (HST)	
Scotland	SMC	Ultra-orphan pathway		

Divergence in rollout timing to HTA and recommendation resulted from varied submission strategies and review process.

Only SMC has a dedicated orphan pathway, while other HTA agencies may use alternative pathways/ criteria.

In addition, flexible funding mechanism such as England's Cancer Drug Fund facilitates patient access to orphan products.

Figure 4: Funding of orphan NAS in England through cancer drug fund



The Cancer Drugs Fund (CDF) is a source of funding for cancer drugs in England since 2016 to provide access to promising new treatments, via managed access agreement, while further evidence is collected to address clinical uncertainty.

Provides interim funding for all newly recommended cancer drugs, giving patients access to these treatments many months earlier than before.

Conclusion

The study showed a rise in global orphan drug approvals, underpinned by regulatory flexibility. Identified divergences in decision frameworks between regulatory and HTA agencies, as well as among HTA agencies, call for increased stakeholder alignment. This necessitates synchronizing evidence generation during development and improving decision frameworks for streamlined review and reimbursement processes.

Center For Innovation in Regulatory Science

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