For orphan drugs technology assessments, one size may not fit all

Will the implementation of JCA lead to increased access, or will it just lead to a duplication of work?

HTA206

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Background

Orphan drugs (ODs) face challenges demonstrating clinical value due to limitations in clinical trial design. In Europe, some health technology assessment (HTA) agencies have developed OD-specific frameworks/considerations. Joint Clinical Assessment (JCA) seeks to ensure consistent evaluation of the clinical evidence and reduce duplication of work, ultimately leading to faster and more equitable access to innovative health technologies. Currently, no OD-specific framework has been publicly disclosed for the implementation of JCA on ODs from 2028 onwards. This may cause some complications to address the unique challenges associated with rare diseases. This research aims to identify OD frameworks used at national level and explore challenges related to the JCA implementation in ODs using the current JCA framework.

Methods

National HTA websites and ISPOR website were screened, as well as supplementary desk research, between 2018 and 2024 to identify OD frameworks currently being used by national HTA agencies in Europe. The search included the following search terms: "HTA framework or consideration", "orphan drugs", "HTA assessment of orphan drugs" in combination with country names. The EUnetHTA and European Commission Websites were explored to identify any OD-specific considerations in the existing publicly available JCA framework.

Results

We identified two European countries with formal framework for ODs assessment (Germany and Scotland), and three countries applying special considerations (England, France, Sweden) (**Table 1**).

Table 1. Summary of ODs specific considerations in EU countries

Country & HTA body	OD-specific framework	Key rules or considerations for ODs	Key decision driver
Germany G-BA/ IQWIG [1-3]	**Yes**	• Additional benefit proven if total annual sales does not exceed €30 million • Lower statistical significance levels may be accepted (e.g., 10% for *p*-value) • Surrogate endpoints accepted	**Clinical value**
Scotland/ SMC [4,5]	**Yes**	• Single-arm trials often accepted • For ultra-ODs, following an initial assessment if a criterium for ultra-OD is met (1 in 50,000), the drug will be available 3 years on the NHS while additional evidence to be collected • Following that period, SMC will re-assess the drug and final advice will be published • For ODs and ultra-ODs, process may involve PACE, allowing patients/clinicians to influence decision making, considering factors like impact on patient QoL and effects on family or carers	**Cost-effectiveness**
England NICE [6,7]	**No**	• Single-arm trials often accepted • Under the HST process*, there is greater consideration on disease nature, impact on patients and caregivers, and available treatment options; a higher cost per QALY is also accepted • Acceptance of higher degree of uncertainty under both, STA and HST processes	**Cost-effectiveness**
France HAS [8,9]	**No**	• Severity of disease and unmet therapeutic need are general criteria favorable to ODs • Surrogate endpoints may be accepted if no other treatment options available	**Clinical value**
Sweden TLV [8,10]	**No**	• Single-arm trials often accepted • Surrogate endpoints may be accepted • Accepting higher cost per QALY, or higher level of uncertainty in economic evaluation	**Cost-effectiveness**

* It has restrictive eligibility criteria and a lot of ODs are assessed under STA: Single technology appraisal processes; Abbreviations: G-BA: Gemeinsamer Bundesausschuss (The Federal Joint Committee); HAS: Haute Autorité de Santé (French HTA agency); HTA: Health Technology Assessment; IQWIG: Institute for Quality and Efficiency in Health Care; NICE: National Institute for Health and Care Excellence; PACE: Patient and Clinician Engagement; OD: Orphan drug; QALY: Quality-adjusted life year; QoL: Quality of life; SMC: Scottish Medicines Consortium; TLV: Tandvårds- och läkemedelsförmånsverket (The Swedish Dental and Pharmaceutical Benefits Agency)

The current JCA framework for drug assessments does not include specific considerations for OD assessment [11,12]. Any additional criteria in accordance with the national HTA framework that may relate to ODs (e.g., disease rarity, severity, unmet medical need) should be considered at national level at the appraisal stage [13]. How JCA outcomes will be integrated into national OD assessments remains unclear. We summarized potential implications related to the lack of the clear OD framework at JCA level, in both, clinical-benefit and cost-effectiveness driven countries (**Figure 1**).

Figure 1. Implications of JCA current framework

Clinical benefit as key decision driver

Implications

- Risk of reassessment at national level due to different criteria for the clinical assessment for ODs (e.g., lack of acceptance of single-arm trials, acceptance of surrogate endpoints)
- Reimbursement delays possible as national agencies may request additional data beyond JCA requirements for ODs (e.g., RWD, natural history data)
- Negative JCA outcome due to lack of OD assessment framework may drive negative perception and impact negative decisions especially in countries without OD considerations

Recommendations

- Conduct early dialogue between manufacturers and both JCA and HTA agencies with specific OD considerations, as well as engagement with SMEs with relevant experience on OD assessments, can support the planning of relevant evidence generation and to understand potential discrepancies in requirements
- Develop strategic plan for potential national reassessments and additional data requests

Cost-effectiveness as key decision driver

Implications

- Uncertainty related to the effect of JCA outcomes on the decision making in countries applying OD-specific cost-effectiveness criteria
- Delay in time to market due to additional time needed to incorporate the JCA outcomes into C-E models (e.g., JCA-identified subgroups)
- Additional data may be required to bridge gaps between JCA clinical evaluations and national economic evaluations

Recommendations

- Conduct strategic planning for economic modelling early in the product lifecycle and early C-E model development, aligned with JCA timelines, to facilitate JCA outcome integration and identify key drivers and potential weaknesses for the pricing of ODs
- Identify potential data gaps between JCA and country-specific requirements for C-E models, and plan post-launch data collection strategy to support these
- Design innovative pricing models (e.g., outcome-based agreements)

Abbreviations: C-E: Cost-effectiveness; HTA: Health technology assessment; JCA: Joint clinical assessment; OD: Orphan drug; RWD: Real-world data; SME: Subject matter experts; HTA: Highly specialized technology

Conclusions

Manufacturers must consider the implications of JCA reports for HTA agencies that apply formal Orphan Drug frameworks and flexible approaches. In countries where only clinical benefit drives decisions, absence of Orphan Drug-specific frameworks may have minimal impact, although additional data clarification may be requested. For countries using cost-effectiveness criteria, the impact of JCA reports on orphan drug decisions remains unclear. In these markets, adapting C-E models to include JCA outcomes while meeting specific Orphan Drug market needs will be challenging, and will require appropriate data and model structures, while accounting for potential delays between JCA and local assessments. Early strategic planning on economic models or managed entry agreements can help navigate these complexities.

REFERENCES

[1] IQWIG General methods v6.1 (Jan 2022): https://www.iqwig.de/methoden/general-methods_version-6-1.pdf; [2] https://www.g-ba.de/downloads/40-268-9252/2023-02-02_AM-RL-XII_Aussetzung-Orphan-Drug-Ueberschreitung_TrG.pdf; [3] https://www.vfa.de/de/arzneimittel-forschung/woran-wir-forschen/orphan-drugs-medikamente-gegen-seltene-erkrankungen.html; [4] https://scottishmedicines.org.uk/media/6009/20201013-patient-group-participation-at-a-pace-meeting-v41_final.pdf; [5] https://www.gov.scot/publications/ultra-orphan-medicine-pathways-guidance/; [6] https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-highly-specialised-technologies-guidance; [7] Hale et al.: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10690432/; [8] Nicod et al.: https://www.valueinhealthjournal.com/action/showPdf?pii=S1098-3015%2817%2930167-5; [9] ISPOR (HAS representative presentation): https://www.ispor.org/docs/default-source/presentations/513.pdf?sfvrsn=b7019c08_1; [10] https://www.tlv.se/download/18.56bb14ac18b37f17d083e082/1697793328049/strenghened_access_to_medicines_for_rare_disesases_2023-10-19.pdf; [11] https://www.eunethta.eu/; [12] European Commission: https://health.ec.europa.eu/latest-updates/commission-facilitates-faster-access-medicines-clear-rules-joint-clinical-assessments-2024-05-23_en; [13] https://www.ema.europa.eu/en/documents/presentation/new-hta-regulation-key-elements-and-next-steps-flora-giorgio_en.pdf

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