Real-world assessment of orphan drugs via the new Joint Clinical Assessment route in Europe

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Background and objectives

> Rare diseases can have a catastrophic impact on patients' lives, few are preventable, most are chronic and many result in early death.[1] Despite rare diseases emerging as a public health priority in Europe, disparities in reimbursement and patient access to orphan drugs (OD) across Europe still exists.[1,2]

> Due to the small populations, Health Technology Assessment (HTA) bodies are challenged to make reimbursement decisions with very limited clinical efficacy and cost data, and typically recommend high prices.[2] Additionally, there is heterogeneity amongst the factors considered by individual European HTA bodies regarding cost-effectiveness thresholds, budget-impact and efficacy measures.[3,4] As a result, decisions on reimbursement and the number of ODs reimbursed often differs between European member states.[2]

> The Joint Clinical Assessment (JCA), developed by the European Medical Agency (EMA), is already in its pilot phase. The JCA aims to replace the evaluation of clinical evidence by multiple HTA bodies and instead co-ordinate the clinical assessment of new technologies across all European member states.

Existing Joint HTA bodies

JCA	BENELUXA	Valletta Declaration	EUnetHTA	FINOSE	FAaP
All European member states	Austria, Belgium, Luxembourg, Netherlands, Ireland	Croatia, Cyprus, France (observer status), Greece, Ireland, Italy, Malta, Portugal, Romania, Spain, Slovenia	30 European countries and 80 government appointed organizations	Finland, Norway, Sweden	Poland, the Czech Republic, Hungary, Slovakia, Lithuania

Objective

> The objective of this research was to explore how the new JCA route has been implemented for ODs following publication of the new EMA regulations.

> To meet this objective, we conducted a literature review to identify publications which examined products which are currently being assessed for the treatment of orphan indications and highly specialized technologies (HST) for rare and ultra-rare diseases.

Adoption of Regulation on HTA

What does the new JCA HTA cover?

> Member States' HTA bodies will engage in **joint clinical assessments (JCA)** and **joint scientific consolations (JSC)** to advice technology developers.[5-7] — Individual patient experts and clinical experts

> **"Horizon scanning"** to help health systems to prepare for new promising health technologies.[5-7] — Individual patient experts and clinical experts

> **Additional cooperation** e.g. on health technologies other than medicines and medical devices, or on economic aspects of HTA.[5-7] — Patient and Health professional organisations

Next steps in implementing the new JCA[5-7]

2022

In January 2022, the new HTA regulation will enter into force.

2025

In January 2025, the new HTA regulation will be applied.
The 3-year period allows time:

- To set up the organisational framework of the HTA.
- To adopt the implementing and delegated acts and methodology guidance documents.
- For member states to adjust their national HTA legislation and processes.
- For HTA developers to familiarise and comply with the new requirements and framework.

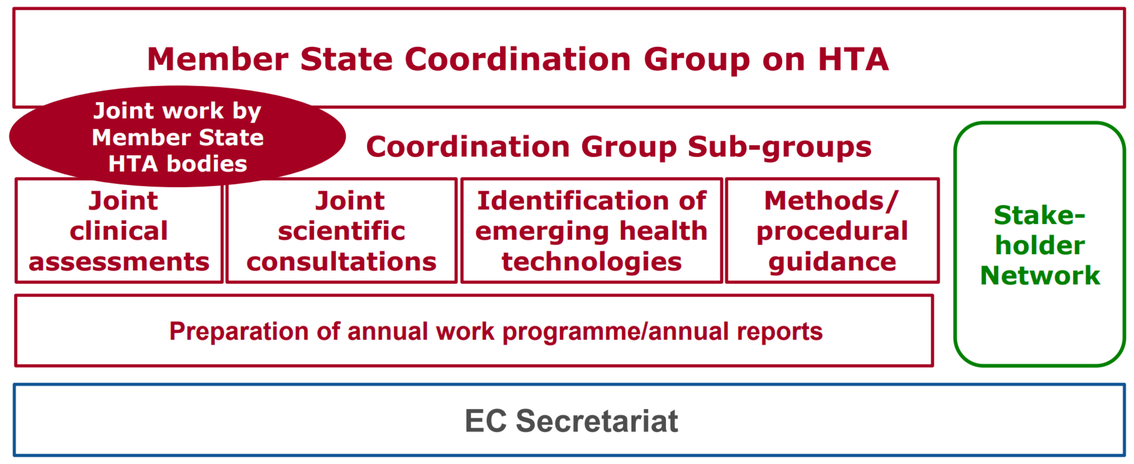
2030

Full joint HTA assessment scope in 2030.
The 5-year period allows time to:

- JSC + stepwise build-up of JCA scope for medicines. For orphan drugs this will be achieved in 2028, 3 years after application.

Adoption of Regulation on HTA - Continued

Involvement of external experts and stakeholder organisations[5]



> **External experts** (patients, clinical and other relevant experts): To provide input based on their specialised expertise (e.g. therapeutic area) during JCA and JSC.[5]

> **Stakeholder organisations** (e.g. healthcare professional organisations, insurers/payers, industry associations, patient groups, scientific societies): To provide input on horizontal and strategic issues and to regular meetings between Stakeholder Network and Coordination Group.[5]

Advantages of the new JCA

As the JCA focuses on clinical aspects of HTA i.e. problem definition, and clinical safety and effectiveness, the tasks of **national HTAs** reduce to:[5-7]

> **Complementary clinical analyses** if needed (more context specific, e.g. data on national disease epidemiology, patient registry in specific healthcare context).[5-7]

> **Non-clinical assessments** (e.g. economic, organisational, ethical aspects).[5-7]

> **Drawing conclusions** "appraisal" (taking into account the JCA and additional analyses, consideration of any additional criteria e.g. rarity of disease, severity of disease, lack of alternative interventions) and **conclusions on added value**.[5-7]

Literature review methods and findings

> A targeted literature review was conducted in Embase® (2017 – 2022) to identify publications investigating health technology assessments in rare diseases.

> The search strategy used a mixture of Emtree subject headings (biomedical technology assessment/, orphan drug/ and rare disease/) and free-text terms (HTA or JCA.tw etc.) to capture relevant publications.

> The Embase® search identified 201 potential abstracts. The screening of abstracts and full texts was completed by a single reviewer with consensus on any unclear articles provided by a senior reviewer.

> Overall, the literature review identified five relevant publications.

- Of these, only one described the landscape for approval of ODs via the new JCA route, three described joint assessment via other joint HTA initiatives such as EUnetHTA, FINOSE, BeNeLuxA, Valletta Declaration and FAAP, whilst the remaining one investigates a multitude of European programmes for ODs' assessment. One publication highlighted that only one advanced therapy medicinal product (ATMP) has been approved via the new JCA route, elivaldogene autotemcel for the treatment of cerebral adrenoleukodystryophy.[8-12]
- Whilst the three publications on other JCA routes indicated the clear need to align processes to ensure consistent evaluations and approvals within the EU, the article on the new JCA route calls for enhanced alignment of regulatory and HTA evidence requirements among others.

Discussion and Conclusion

> This review identified that no novel ODs were assessed via the new JCA EMA route for rare diseases in the pilot phase and access to ODs continues to vary across European Union member states.

> Although the EU is continuously pushing for harmonization relating to the implementation of the JCA, at present there is little momentum across EU countries to implement a multi-national approach to HTA.

> In future, the new EMA JCA route should provide a more homogenous clinical assessment across EU countries that could enable faster pricing and reimbursement negotiations specific to rare diseases.

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