Rare DISEASE DAY 2025

DOLON

How might JCA impact orphan sustainability in Europe?

Innovation in rare diseases has transformed the lives of many patients, yet significant unmet need remains. Among the 300 million people living with a rare disease in Europe today, a substantial number are without an approved treatment option, experience shortcomings with existing treatments, or struggle to access these.

To mark Rare Disease Day 2024, Dolon published a series exploring what it will take to see continued rare disease innovation in Europe.

This year, we turn our attention to EU Joint Clinical Assessment (JCA), which is now upon us and has the potential to transform the evaluation of medicines in Europe, including orphans. Building on our recent publication "Joint Clinical Assessment: The finger on the scale for orphan sustainability in Europe?", we explore the potential impact of JCA across three key dimensions important to sustaining investment and launch of new rare disease treatments in Europe.

#1 Breadth of access

#2 Efficiency of process

#3 Predictability of outcomes

#1 Breadth of access

Achieving the broadest possible access for a new rare disease treatment is a priority for patients and developers alike. A key objective of the JCA is to improve availability of innovative health technologies for EU patients by harmonising HTA across Member States. If JCA works as intended, it stands to reduce access disparities across countries driven by variations in HTA. However, if JCA processes and requirements are not calibrated to account for orphan specificities, this may lead to negative assessments and more restricted access to rare disease treatments.

Current JCA guidelines present a few areas of concern for orphans. One is the strict evidence hierarchy and the lack of formal adaptations for rarity.

If German-like evidence requirements are applied within JCA and trickle down to countries that do no have German-like exemptions for pricing and reimbursement, the result may well be constrained access. Another is the inclusion of off-label comparators within the assessment, which is likely to drive more challenging P&R negotiations at country level. This may potentially delay access or lead to unsustainable prices.

It is critical that JCA methods can recognise the full value of medicines and offer tailored flexibility where evidential uncertainty is impossible to avoid. If reasonable orphan flexibilities are not ensured at the JCA level, it will fall to Member States to incorporate these into their processes so that these vital medicines can be accessed.

#2 Efficiency of process

Reducing time to access to orphan medicines is a pivotal concern within the rare disease community. Part of the vision for JCA is to reduce duplication and make HTA more efficient by providing a centralised HTA report on the comparative safety and efficacy of a new product.

As a best case, the availability of a JCA report will speed up national HTAs by providing a robust foundation on which to base further economic assessment. Indeed, JCA runs parallel to the regulatory approval process with the aim of providing a clinical assessment around the point where many national HTA processes begin.

However, realising these efficiencies requires two things: that the JCA process can be completed within the projected timeframe, and that national HTA agencies are accepting of JCA findings. There is a risk that the inherent complexities within this process designed to aggregate diverse clinical situations across countries will render JCA less efficient than hoped. This is likely to be exacerbated for orphans, owing to the heterogeneity of the standard of care, potentially diving a high number of PICOs and data requests.

Given that rare diseases are frequently severe and life-threatening, avoiding delays is of the utmost importance. It is therefore imperative that JCA works for orphans and that complexity of implementation does not pose additional access barriers or delays.

#3 Predictability of outcomes

Drug development is a costly, lengthy, and above all risky endeavour. Business predictability is a crucial element influencing investment in the development and launch of new medicines. JCA seeks to improve "business predictability" in Europe by harmonising HTA across Member States, as stated in the Regulation.

For rare diseases, the risks are elevated due to the added challenges to clinical development [1]. Hence, it is even more critical to have in place a predictable HTA system that rewards innovations which deliver added value for patients.

Ideally, JCA will harmonise evidence standards across Member States over time, and the PICO framework will offer transparency on key drivers of the assessment. However, in the near term it is unavoidable that JCA will increase uncertainty, by introducing significant shifts in national HTA processes and significant uncertainty on how findings will be applied and inform reimbursement decisions at country level.

For long-term orphan sustainability, the vital thing is that JCA process and evidence standards are suited to orphan specificities, and that adaptations for rarity are formalised and predictable.

1 *Wong et al. 2019. https://pubmed.ncbi.nlm.nih.gov/29394327/*

Compounding effects of JCA and other reforms in Europe.

JCA is just one element in a broader evolving European policy landscape that is becoming increasingly challenging for orphan development.

Ongoing revisions to core EU Pharmaceutical Legislation and specific orphan provisions will likely see a significant overall reduction in the scale and certainty of key IP protections for rare disease medicines. Dolon has published impact assessments showing the potential impact of these revisions on future availability of innovative medicines in Europe (available here and here).

At country level, there are instances of reduced flexibility for orphans within HTA and P&R processes (e.g., decreased award of ASMR I-III in France since the financial crisis), as well as rising use of cost-containment measures (e.g. extensive use of clawbacks). Broadly, these trends are underpinned by a general scepticism of industry orphan pricing.

As multiple substantial reforms break on rare diseases at the same time, their effects cannot be considered in isolation from each other, nor from the broader trend of declining European attractiveness. JCA needs to be viewed in this context, as it ultimately presents a unique opportunity to revisit established national HTA and P&R policies and make them better for orphans than before.

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