PRECISION AQ™

EU Joint Clinical Assessment: Uncertainties and actions to ensure that drug developers do not fall behind

The EU Joint Clinical Assessment (JCA) has been designed to help streamline and harmonize access between different European countries in order to facilitate faster, better, and more equitable access to novel medicines. By publishing a JCA report shortly after regulatory approval, the EU seeks to provide a critique of population, intervention, comparison, and outcome (PICO) specific analyses that have been requested by national member state payer bodies and prioritized by the JCA Coordination Group.

In the wake of the publication of the first draft Implementation Act for the EU JCA, we wanted to revisit the JCA's key aims and challenges, as well as what capacities and collaborations companies should already be establishing, now that we are less than a year from the EU JCA taking effect.

We have identified four challenges that have the potential to significantly undermine the objectives of the JCA. These challenges can, in turn, be addressed by four responses. These are illustrated in Figure 1 and described in the text.

Challenge 1 – Complexity

- The number of PICOs that companies may be required to assess may be very large—with some potentially being improper, given a lack of ongoing discussion with manufacturers in the process
- Comparisons may be requested that deviate from the target population for the key trial(s), resulting in underpowered analyses and creating potentially misleading results
- Given that the time at which data are requested will be earlier than standard health technology assessment (HTA), comparisons may require complex indirect comparison methodologies, consideration of surrogacy, or additional outcomes to evaluate medium-term clinical efficacy and be unnecessarily onerous on manufacturers if choice of comparators is not judicious. Thus, there is a concern that a large amount of time and resources will be required to generate these data, which will be of potentially very limited usefulness

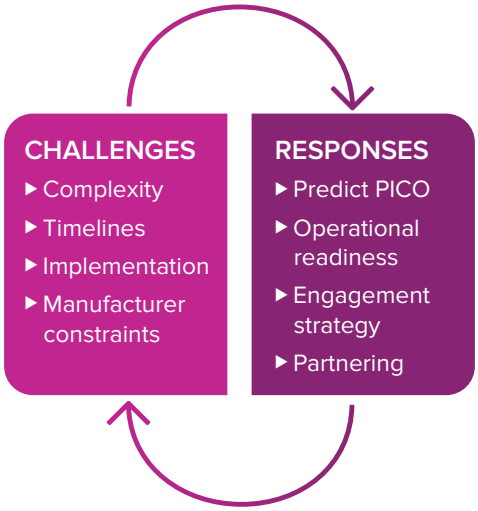
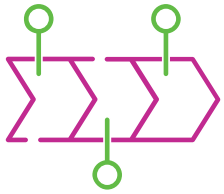


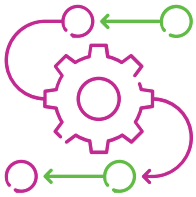
Figure 1. Challenges and responses to ensure success as the EU JCA approaches.

Challenge 2 – Timelines



- Though the draft Implementation Act provided clarity on some timelines, it also highlighted remaining uncertainties
- Companies will only have 90 days to develop the dossier (60 days in the case of products assessed under the European Medicines Agency (EMA) accelerated procedure). It is mentioned that this can be extended; however, it is unclear under what circumstances the HTA secretariat would agree to this
- The complexity and number of analyses required may be very challenging to complete within such timelines. In addition, the turnaround time for clarifying responses may be unrealistic, given the breadth of comments provided
- Further, the reform of the EU pharmaceutical legislation (which has been touted as the most significant reform to the EU's pharmaceutical legislation in over two decades) that is currently going through European Parliament may further put pressure on these JCA timelines due to the following proposals: (i) the maximum time for EMA assessment of marketing authorization applications (MAA) to reduce from 210 to 180 days, and (ii) the European Commission time to authorize Committee for Medicinal Products for Human Use (CHMP) recommendations to reduce from 67 to 46 days

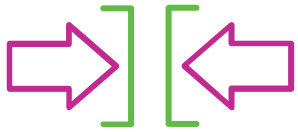
Challenge 3 – Implementation



- Member states must "give due consideration" to JCA reports, annex these to national HTA reports, and report on how each JCA was used
- However, this is subject to interpretation; many national HTA bodies (especially for the major markets) already have established evidence standards, and there is a concern to what level these countries will use JCA reports. Conversely, there is also the potential for JCA reports to be leveraged by HTA bodies/payers/regulators/other stakeholders outside of the EU
- Given a lack of recourse by the JCA for manufacturers that do not undertake the JCA process in good faith, what will be the uptake or effort put towards the JCA submission?
- Even where companies do engage in good faith, if companies cannot address all PICOs in the required timeframe (this may especially be an issue with small/emerging pharmaceutical companies):
  - Companies will not know which PICOs were requested by what markets, so there is no opportunity to prioritize accordingly
  - "In justified cases" extensions may be allowed—but no details are provided as to what constitutes an appropriate justification
  - The submission template allows for manufacturers to ''clearly identify any PICO(s), for which results were not submitted and explain the reasons for their omission,'' but again, no details are as yet available for what an appropriate justification may be

Challenge 4 – Manufacturer constraints

- The first Implementation Act specifies more company involvement in the PICO process:
  - Companies submit the proposed Summary of Product Characteristics (SmPC) and the clinical overview section of the EMA submission file to the HTA secretariat at the same time they submit an MAA to the EMA. This information will be used to develop the assessment scope/PICOs of the JCA
  - If deemed necessary, the HTA secretariat can invite the manufacturer to provide further information relevant to the development of the assessment scope/PICOs
  - If deemed necessary, the HTA secretariat can invite the manufacturer to an assessment scope/PICOs explanation meeting with the JCA Subgroup



- Nevertheless, there is no scoping meeting as part of the standard process or any other opportunity for companies to routinely input into the process—these are only at the discretion of the HTA secretariat
- Companies may require earlier capacity building to develop and support JCA-related workstreams and include consideration of broader market PICOs when designing key clinical trials

Response 1 | Predict PICOs

Given the tight timelines, companies need to make efforts to anticipate likely PICOs, which can be achieved through a combination of:

- HTA review of analogues
- Local country access team engagement
- Joint Scientific Consultations (which provide parallel regulatory and EU-wide HTA advice—although few slots have been available to date)
- National early scientific advice
- Monitoring the first products that go through JCA

Response 2 | Operational readiness

In order to meet the demands of the JCA to the required timelines, companies need to ensure that their operational structures and resources are in place to engage the right internal teams at the correct time, and that sufficient preparatory work is conducted to give health technology developers (HTDs) the best chance at submitting a comprehensive dossier.

Response 3 | Engagement strategy

Some of the key JCA documents are still being developed and are subject to consultations (including the first Implementation Act—still being finalized—with 5 more implementation acts to follow). There are also many working groups/industry associations trying to provide input into the process; that is, companies need not be passive actors but instead can help shape the evolving environment.

Response 4 | Partnering

The JCA is a complex, dynamic endeavor that will likely challenge all involved. Thus, selective partnering with a firm that has an integrated, interdisciplinary practice including experience across market access, HTA, HEOR, and health policy will be critical.

Conclusion

The argument for greater pan-EU efficiency in HTA makes sense; however, as with so many complex organizational endeavors, the devil is in the details. Some elements of the JCA are simple, logical, and quite feasible, but others are less so. We believe that a grounded approach to understanding the issues, preparing for the various scenarios (likely and unlikely), and partnering with colleagues who have dedicated their careers to understanding the technical standards, rules, guidance, and nuances of EU HTA will be a wise move for all involved.

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