Challenges in the German AMNOG Procedure: The need for national PICO transparency and optimized consultation windows in the context of EU-HTA

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EU-HTA Objectives

- Enhance timely access to new therapies for patients
- Avoid duplication of work (both for pharmaceutical companies and HTA authorities)
- Strengthen the quality of the clinical assessment and harmonise the clinical assessments of health technologies

PICO defines assessment scope for Joint Clinical Assessment (JCA)

- **P**opulation(s)
- **I**ntervention
- **C**omparator(s)
- **O**utcome(s)

The process begins when each European Union Member State (MS) submits its national PICO(s) to the PICO survey. Subsequently, the JCA subgroup is responsible for **consolidating these national requirements into PICOs at the EU level**. It is essential that the consolidated EU PICOs are inclusive and adequately reflect the needs of the various MS. Finally, **only the consolidated PICOs will be published**, not the initial submitted PICO(s) by each individual MS.

Challenge: Late-Stage Uncertainty Regarding Final National PICO Requirements

In the German AMNOG procedure, health technology developers (HTDs) can seek early consultation (G-BA advice) to clarify the national PICO and optimally prepare their dossiers for benefit assessment. However, the advice is not binding, and the requirements may change. A significant challenge arises when the European PICO is published and a mismatch between the advised national PICO and the final requirements becomes obvious.

Example of such mismatch from the PICO exercise 1 on Durvalumab in first line treatment of HCC (EC 2025):

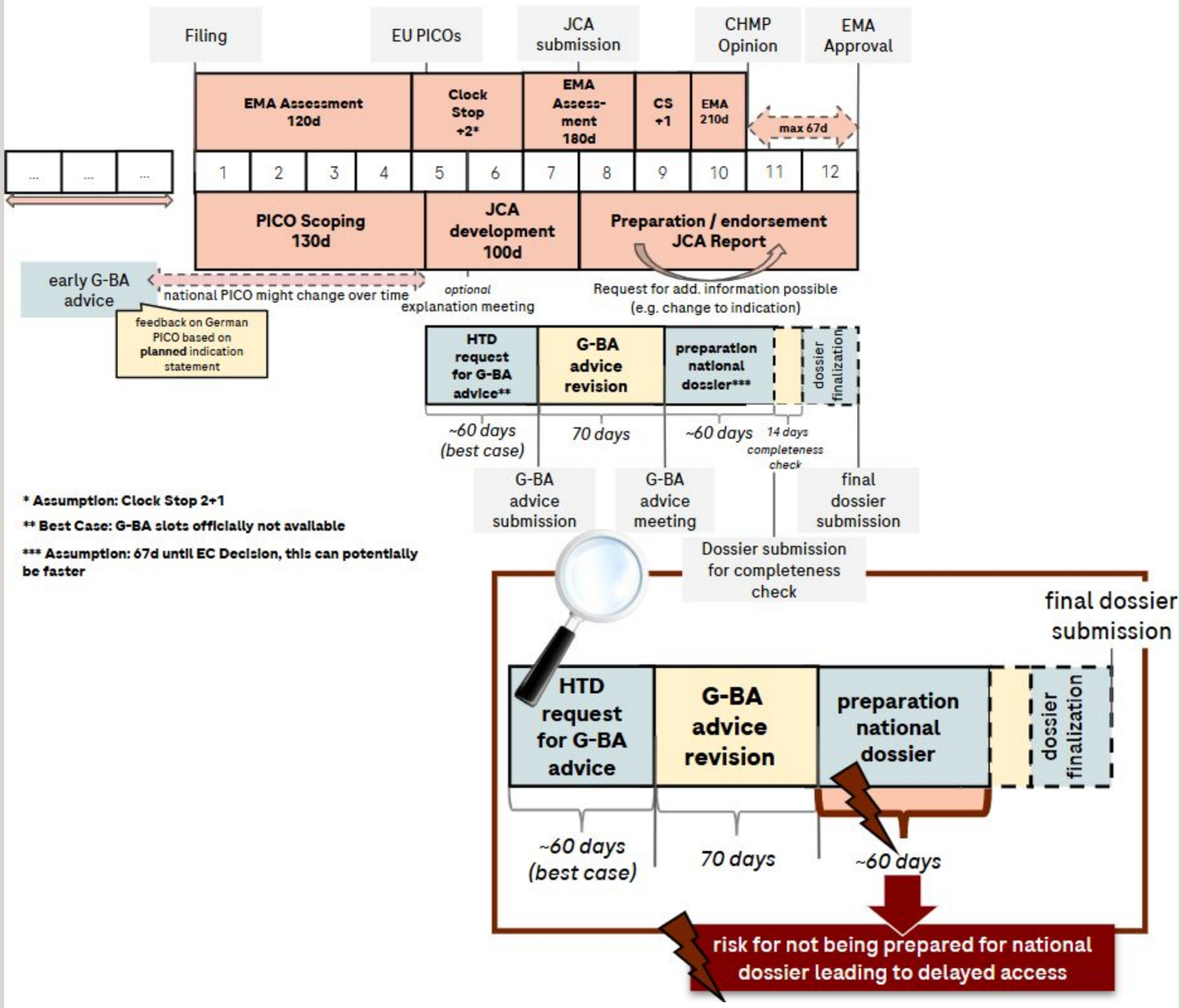
German PICO from AMNOG Dossier (2024):
Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy (Subpopulation B)

Final EU-HTA PICO (after consolidation) - PICO exercise (2025):
Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B *or Child Pugh C, with conditions for immunotherapy*, first-line therapy (PICO 13).

As the national PICO by member states are not transparently shared with the HTD, it remains unclear whether this mismatch arises from a change in the national PICO or from the consolidation of two similar PICOs. Consequently, the HTD is left uncertain about which patient population to address in the national dossier.

Because the time between the final PICO publication and the dossier submission deadline is extremely limited, seeking further advice within this critical window is not practicable. This late-stage uncertainty creates a systemic inefficiency that puts the timely submission of an appropriate national dossier and the product launch at risk. It also subverts the core objective of preventing work duplication, thus undermining the very efficiency the EU HTA Regulation was designed to achieve.

Inefficient national dossier preparation timelines due to lack of national PICO transparency

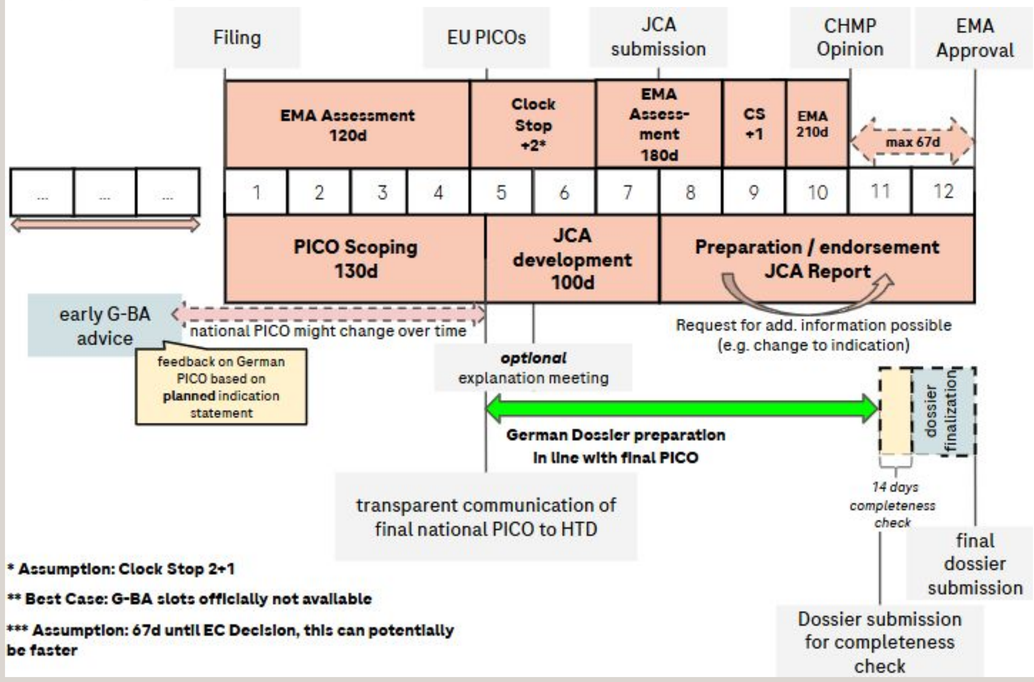


Conclusion

To enhance process quality and ensure the timely submission of high-quality national dossiers, achieving early clarity on final PICO requirements is fundamental.

The ideal approach is the transparent communication of the final national PICO to the HTD in parallel with the EU scoping process. Should this not be feasible, a pragmatic alternative must be established: a dedicated process for timely national advice or G-BA offering an explanation meeting (similar to EU HTA) immediately following the final EU PICO publication to reduce critical late-stage uncertainty.

Optimized national dossier preparation timelines through transparent communication of final PICO



Referenzen: EC 2025. *HTA PICO MP01: Methodological Guideline on PICO*. Verfügbar unter https://health.ec.europa.eu/document/download/322ae969-f3ca-4f23-ab8e-1b4bdf22528f_en?filename=hta_pico_mp01_en_0.pdf