HTA269

Paving the Path to Success for Joint Clinical Assessments – One Asset at a Time

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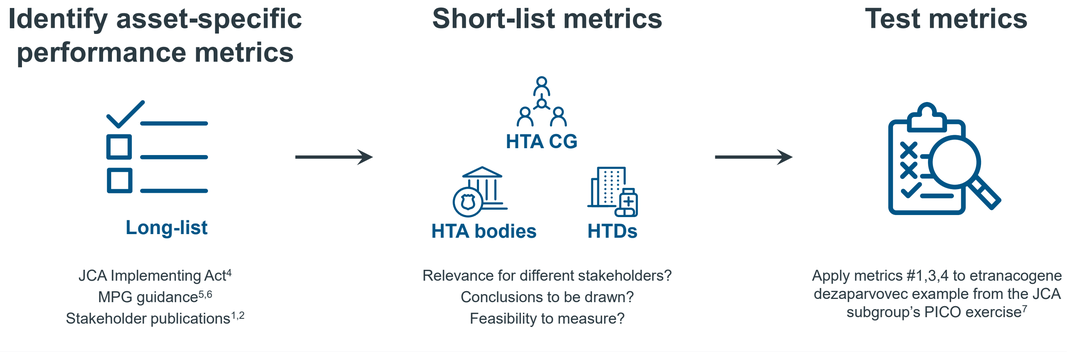
OBJECTIVES

- The first wave of Joint Clinical Assessments (JCAs) are currently ongoing, putting to the test the new processes introduced under the EU HTA Regulation.
- Appropriate metrics to assess their effectiveness are a prominent subject of debate[1,2]; however, it may take several years until enough JCA assets have launched across the EU to draw robust conclusions, which is why the new processes will only be formally reviewed in 2028[3]. Until then, which insights can be drawn from the initial JCAs?
- Our research aimed to identify metrics to measure performance at the asset level relevant for stakeholder decision-making (HTA Coordination Group, HTDs, national HTA bodies). The metrics were tested using one of the assets from the PICO exercises.[7]

METHODS



RESULTS

Asset-specific performance metrics

Metric		Conclusions to be drawn	Relevance (high, moderate, limited) HTA CG	HTA bodies	HTD	Source for metric	Addressing objective of the EU HTAR: Harmonized HTA methodologies?	Predictable HTA outcomes?	Avoid duplication of effort?	Accelerated patient access?
#1	**Overlap of PICOs requested at EU level vs assessed at MS level**	JCA scope meets local needs? Willingness to use JCA report?				JCA report, local HTA reports	✓	✓	✓	✓
#2	**Local relevance of evidence submitted for JCA**	Evidence accepted locally? Evolving acceptability vs pre-JCA?				JCA report, local HTA reports	✓	✓	✓	✓
#3	**Additional clinical data requested at MS level, beyond JCA scope**	JCA scope meets local needs?				Local HTA reports	✓	✓	✓	✓
#4	**Requested (sub-)populations, interventions, comparators, outcomes, subgroups**	Manageable analysis burden / effective consolidation?				JCA report	✓	×	×	×
#5	**Expert involvement during JCA**	Feasible amid short timelines & CoI rules? Even in rare indications?				JCA report	✓	×	×	×
#6	**Country / affiliation of assessors**	Consistently applied methodology, independent of assessors?				List of ongoing JCAs	✓	✓	×	×
#7	**Scope explanation meeting requested by HTD**	Need to clarify scope?				JCA report	×	✓	×	×
#8	**Time from EMA approval to local availability**	Accelerated patient access vs non-JCA assets?				EFPIA Patient WAIT Indicator, IQVIA Market Access Insights	×	×	✓	✓
#9	**JCA duration**	Timelines[5] feasible?				List of ongoing JCAs; JCA report (publication date)	×	×	×	✓
#10	**Regulatory timings**	Impact of delays on JCA timeline?				EPAR assessment report	×	×	×	✓

Test results: Overlap of PICOs requested at EU level vs assessed at MS level

Example: Etranacogene dezaparvovec[7]

For the treatment of severe and moderately severe Haemophilia B (congenital Factor IX deficiency) in adult patients without a history of Factor IX inhibitors **(note, only (sub-)populations, comparators, and safety outcomes shown here)**

PICO	Population	Comparator	*			**				***			
1	Adult patients with severe and moderately severe Haemophilia B without a history of Factor IX inhibitors: Full population	Recombinant FIX CFCs with SHL	●		○		●		●	●	●	●	
2		Plasma-derived Clotting FIX Concentrates	●	●	○	●		●	●	●	●	●	
3		Recombinant FIX CFCs with extended half-life	●		●		○		●	●	●	●	
4		Individualized treatment	●	○	○	○	○	○	○	○	○	○	
5		Eftrenonacog alfa	●	●	○	○	○	○	○	●	●	●	
6	Who are on prophylactic therapy with Factor IX CFCs – Subpopulation A	Prophylaxis with Factor IX CFCs	●	○	○	○	○	○	○	○	○	○	
7	Who are not on prophylactic therapy with Factor IX CFCs – Subpopulation B	Watchful waiting and episodic therapy with CFCs for acute haemorrhages	●	○	○	○	○	○	○	○	○	○	
8	Full population	Immunine 600 IU (plasma-derived preparation)	○	○	○	○	●	○	○	○	○	○	
9	Full population	Rixubis (recombinant preparation)	○	○	○	○	●	○	○	○	○	○	

Assessment scope: ● JCA PICO ● PICO requested / assessed – evidence provided ● PICO requested / assessed – evidence not provided ○ PICO not requested / assessed

HTA outcome: Full reimbursement recommended; Reimbursed with restrictions or conditions recommended; Reimbursement not recommended or no added benefit; No value judgement / no recommendation provided

Outcomes	Assessed by HTA body								
Any adverse event (AEs in total, per SOC and PT)	✓	✓	✓	✓	×	✓	×	✓	×
Serious AEs (SAEs in total, per SOC and PT)	✓	✓	✓	✓	✓	✓	✓	✓	✓
Severe AEs (severity graded to pre-defined criteria, reported in total and by SOC and PT)	✓	✓	✓	×	✓	×	✓	✓	✓
Death related to AEs	✓	×	✓	✓	×	×	✓	×	✓
Treatment discontinuation due to AEs	✓	✓	×	✓	×	×	✓	×	×
AEs of interest: Hepatocellular carcinoma	×	×	✓	×	×	×	×	✓	×
AEs of interest: Hepatotoxicity	×	×	✓	×	×	×	×	×	×
AEs of interest: Cancer	×	×	×	×	×	×	×	×	×
AEs of interest: Thromboembolic events	×	×	✓	×	×	×	×	×	✓
AEs of interest: Liver toxicity (e.g., ALT/AST increased)	×	×	✓	×	×	×	×	×	×
FIX inhibitor development	×	×	×	×	×	×	×	×	×
Durability of the therapeutic effect (up to latest follow-up data available)	×	×	×	×	×	×	×	×	×
A priori defined AESI	✓	✓	✓	×	×	×	✓	×	×
Assessed by HTA body, but not mentioned in exercise: Treatment-related AEs	✓	×	✓	✓	✓	✓	✓	✓	✓
Assessed by HTA body, but not mentioned in exercise: AE leading to treatment interruption	×	×	×	✓	×	×	×	×	×

Note: All outcomes from the PICO exercise were evaluated, but due to space limitations only safety outcomes are shown; countries may have assessed additional safety outcomes

Note on 'OR' comparators: PICOs with comparators for which evidence was submitted are marked with a green circle, while other OR comparators are shown as not requested (empty circle) since these were not required in addition to the submitted comparator
The following comparators are deemed appropriately: For **PICO 4** - recombinant FIX CFCs with SHL, recombinant FIX CFCs with EHL, plasma-derived Clotting FIX Concentrates; for **PICO 6** - plasma-derived FIX CFCs, recombinant FIX CFCs with SHL, recombinant FIX CFCs with EHL; for **PICO 7** - plasma-derived FIX CFCs, recombinant FIX CFCs with SHL, recombinant FIX CFCs with EHL; **Notes**: *HAS reviewed full EMA label population and listed several comparators combined with OR, with data provided vs FIX inhibitor (without specifying the type of FIX inhibitor used) and eftrenonacog alfa; **AEMPS, AOTMiT and ZIN reviewed single-arm trials only, with intra-individual comparison vs baseline in patients pre-treated with FIX inhibitor (the study inclusion criteria did not specify the type of FIX inhibitor used); ***Finland and Sweden reviewed full EMA label population and listed 'coagulation factor IX (FIX) replacement therapy', with data provided vs eftrenonacog alfa

CONCLUSION

What insights at asset-level reveal:

- Three out of the seven JCA PICOs have to date not been assessed in any MS HTAs
- Unclear terminology may pose a hurdle to local uptake of the JCA report
- Two additional PICOs were requested at MS level based on a review of 9 EEA countries
- JCA introduces new analysis requests that to date have not been needed for MS HTAs

Limitations:

- There is no JCA report for any of the products tested in the PICO exercises; therefore, it is not possible to test all metrics before the first JCA report becomes available
- The scoping exercises were conducted when certain MS HTAs were already in progress and when the scoping guidance was not finalized; hence, the JCA scope for etranacogene dezaparvovec may have been different

Why insights at asset-level matter: The objectives of the EU HTAR are long-term goals; to detect early signposts of change, granular asset-level data are required, covering the end-to-end process from JCA to national HTA outcomes; early indicators include

- Aligning terminologies / definitions used in the JCA scope and local HTA reports
- Increasing local acceptability of different types of evidence (e.g., ITCs, PROs)
- Evolving launch sequence across EU markets

Abbreviations

AESI: Adverse Event of Special Interest; ALT: Alanine Aminotransferase; AE: Adverse Event; AST: Aspartate Aminotransferase; CFC: Clotting Factor Concentrate; CoI: Conflict of Interest; EEA: European Economic Area; EHL: Extended Half-Life; EMA: European Medicines Agency; EU: European Union; EU HTAR: EU HTA Regulation; FIX: Factor IX; HCC: Hepatocellular carcinoma; HTA: Health Technology Assessment; HTA CG: HTA Coordination Group; HTD: Health Technology Developer; ITC: Indirect Treatment Comparison; IU: International Units; JCA: Joint Clinical Assessment; MS: Member State; NSCLC: Non-Small Cell Lung Cancer; PICO: Population, Intervention, Comparator, Outcome; PRO: Patient-Reported Outcome; PT: Preferred Term; SAE: Serios Adverse Event; SHL: Standard Half-Life; SOC: System Organ Class.

References

1. Wang, T., & McAuslane, N. (2025). Ensuring the Efficiency and Effectiveness of Joint Clinical Assessment in National HTA Decision-Making: Insights from the 2024 CIRS Multi-Stakeholder Workshop. *Journal of Market Access & Health Policy*, *13*(1), 9. https://doi.org/10.3390/jmahp13010009; **2**. European Access Academy Spring Convention 2025, Proceedings Issue (https://irp.cdn-website.com/e52b6f19/files/uploaded/Proceedings_EAA_04_2025-fe41db7e.pdf); **3.** 5th Meeting of the Health Technology Assessment Stakeholder Network 1 July 2025, Brussels Summary minutes (https://health.ec.europa.eu/document/download/0007ee07-3019-4d3c-9de2-83beeca430a4_en?filename=hta_20250701_mi_en.pdf); **4**. Implementing act on joint clinical assessment of medicinal products for human use (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202401381); **5**. Procedural guidance for JCA medicinal products (https://health.ec.europa.eu/document/download/0929cd01-619d-4456-a1c4-d8e33f9e36bf_en?filename=hta_jca_mp_procedural-guidance_en.pdf); **6.** Guidance on the scoping process (https://health.ec.europa.eu/document/download/7be11d76-9a78-426c-8e32-79d30a115a64_en?filename=hta_jca_scoping-process_en.pdf); **7.** PICO exercises carried out by the JCA subgroup in the Spring of 2024 (https://health.ec.europa.eu/publications/pico-exercises_en); all websites accessed 8 October 2025

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