Bridging the gap between national and EUnetHTA21 HTA methods

Are marketing authorisation holders ready for joint clinical assessments?

HTA356

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Background

From 2025, select pharmaceuticals will be mandated to undergo a joint clinical assessment (JCA) at the European level. Each JCA will consider multiple decision problems representing differing national treatment landscapes. In order to standardise the assessment process, the European Commission has tasked EUnetHTA21 (2021–2023) with developing a set of potential methodological guidelines that should be followed across assessors. Currently, countries that follow a HTA process have their own national methodological guidelines for assessing pharmaceuticals. However, there is limited information on how the methodological guidelines for JCA align with national HTA guidelines. This research compared the methods proposed by EUnetHTA21 to methods currently used by select national agencies. [1,2]

Methods

- Four EUnetHTA21 methodological guidelines (direct/indirect comparisons, endpoints, applicability of evidence; and validity of clinical studies) were reviewed alongside methodological guidelines published by national HTA agencies from Germany (G-BA), Italy (AIFA) and Denmark (DMC).[3] These countries/agencies represent one of each HTA market archetype (G-BA – comparative clinical efficacy; AIFA – budget impact; DMC – cost-effectiveness).
- Requirements on national guidelines were classified as similar, more stringent, less stringent and no specific requirement compared to JCA requirements.

Results

- Across the published guidelines, 12 domains were identified which could potentially differ between JCA and current national comparisons. The type of indirect treatment comparison (ITC) which is accepted and ITC specifications, acceptability of surrogate outcomes, requirements for safety reporting, quality of life (QOL) inclusion, PICO mismatch, risk of bias assessment, acceptability of trial types, use of real-world evidence (RWE), minimum clinically important difference (MCID) definition, subgroup requirements, sensitivity analysis of outcomes (Table 1).
- Across all domains, there was broad alignment in only two domains: acceptability of trial types and reporting of safety data (Table 1). [3]
- Overall, JCA guidelines were most aligned with the Danish guidelines; 8 of the selected domains within national guidelines were similar to the methods suggested by EunetHTA21 (3 were less stringent or with no specific requirements and one less stringent). Denmark is followed by the German (6 similar, 3 more stringent, 2 less stringent) and Italian (3 similar, one more stringent, 2 less stringent and 6 categories having no specific requirements) (Table 1). [4,5,6]

Table 1: Comparison of selected JCA requirements with national HTA guidelines

JCA Guideline	Requirement			
Validity of clinical studies	PICO mismatch			
	Risk of bias assessment			
	Acceptability of trial types			
	Use of RWE			
Outcomes	Surrogate outcomes			
	Required safety reporting			
	QOL inclusion			
	MCID definition			
Applicability of evidence	Subgroup requirements			
	Sensitivity analysis			
Indirect comparisons	Type of ITC which is accepted			
	NMA specifications			
Similar		3	6	8
More stringent		1	3	1
Less stringent		2	2	1
No specific requirement		6	1	2

Abbreviations: HTA: Health technology assessment; ITC: Indirect treatment comparison; JCA: Joint clinical assessment; MCID: Minimum clinically important difference; NMA: Network meta-analysis; PICO: Population, intervention, control, and outcomes; QOL: Quality of life; RWE: Real world evidence.

Conclusions

- While the EUnetHTA21 suggested methods are most similar to those used in Denmark, there is substantial variability between all agencies assessed.
- For pharmaceutical companies gearing up to start JCA submissions in 2025 there is a need to fully ensure that they understand the methods they will be assessed by in order to ensure a positive outcome when it comes to the JCA; as a negative JCA may have implications on national HTA outcomes and pricing negotiations.

REFERENCES

[1] EUnetHTA 21 2022. Individual Practical Guideline Document. D4.3.1: Direct and indirect comparisons.

[2] EUnetHTA 21 2022. Individual Practical Guideline Document. D4.5: Applicability of evidence-Practical guideline on multiplicity, subgroup, sensitivity and post hoc analyses.

[3] EUnetHTA 21. Individual Practical Guideline Document. D4.6: Validity of clinical studies.

[4] Danish Medicines Council 2021. The Danish Medicines Council methods guide for assessing new pharmaceuticals.

[5] Italian Medicines Agency 2020. Linee guida per la compilazione del dossier a support della domanda di rimborsabilita e Prezzo di un medicinale.

[6] Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen 2023. Allgemeine Methoden.; G-BA responsibilities and methods