EU HTA JCA and JSC - Updates to Guidance

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Internal Use Only

Overview

9 procedure guidances and templates released on 28th November 2024

Guidances

1. Procedural guidance for JCA medicinal products
2. Guidance on the scoping process
3. Guidance on filling in the joint clinical assessment (JCA) dossier template – Medicinal products
4. Guidance on the appointment of assessors and co-assessors for Joint Clinical Assessment (JCA) and Joint Scientific Consultation (JSC)
5. Procedural Guidance for Joint Scientific Consultations (JSC) on Medicinal Products (MP)
6. Guidance for the selection of Medicinal Products (MP) for Joint Scientific Consultations (JSC)

Templates

1. Briefing document template for Parallel HTA Coordination Group (HTACG)/European Medicines Agency (EMA) Joint Scientific Consultation (JSC) for Medicinal Products (MP)
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Procedural guidance for JCA medicinal products

- Assessment scope shared with HTD on day 87 (relative to submission to EMA for standard procedure) – was day 130 previously
- Day 52 for accelerated procedure
- Endorsement of the JCA by HTA CG at 406 days

Guidance on the scoping process

- A PICO that includes several possible comparators (i.e. where more than one treatment is suitable for all patients in the population), 2 scenarios exist
    - Effect estimates against each comparator required i.e. (c-1 PICOs), where c is the number of comparators
    - Effect estimates against at least one (any) comparator, i.e one PICO (e.g. c1 OR c2 OR c3 etc..)
        - Effect estimates should be provided for each comparator separately, as well as combined for all comparators, where methodologically appropriate
- Comparator treatments may or may not be licensed
- The overall acceptability of data submitted on an individualised treatment comparator (i.e. the population cannot be split into a limited number of meaningful subpopulations) will be assessed at the national level

Guidance on joint clinical assessment (JCA) dossier template

- Guidance on filling in the joint clinical assessment (JCA) dossier template – Medicinal products
- Annex 1: Table template collection
- Annex 2: Technical specifications for dossier submission

- Additional documents:
  - Table template collection – Filled-in examples
  - Editable (Word) table template
  - Editable (Word) dossier templates

Guidance on joint clinical assessment (JCA) dossier template

- Comprehensive description of what is required per section, particularly surrounding the statistical results to be included
- However, in places quite ambiguous
  - Some section titles (e.g. “Description of methods/results from the original included studies”, “Study results on relative effectiveness and safety”)
  - Regarding which parts should be included in which section (e.g. methods in section 4, section 5 and appendix?)
- RoB signalling questions to be conducted and reported (Cochrane, ROBINS-I)
- Results for all outcomes on all data cut-offs to be included
- Every outcome should report if pre-specified, alpha level used, control for multiplicity
- Analyses of AEs comparable with AMNOG (i.e. effect measures, p-values etc by SOC/PT) to be included in the appendix (for each PICO?) if > 5% frequency. Frequencies only in main text sections.
- Appendix B includes considerable and comprehensive list of tests/diagnostics to confirm statistical assumptions

Guidance on joint clinical assessment (JCA) dossier template

- Annex 1: Table template collection
  - Appear to be comparable (or identical?) to EUNetHTA21
  - Very detailed e.g. references to footnotes
- Annex 2: Technical specifications for dossier submission
  - Nomenclature of documents and filenames to be submitted

Annex 1: Table template collection example

Table 21: Relative effectiveness results (dichotomous outcomes) – direct comparison: K-mab vs. L-mab

Time point Outcome Study reference/ID	K-mab N	K-mab Patients with event n (%)	L-mab N	L-mab Patients with event n (%)	K-mab vs. L-mab RR [95 %-CI] p-value	K-mab vs. L-mab Hypothesis testing	K-mab vs. L-mab RD [95 %-CI] p-value	K-mab vs. L-mab Hypothesis testing
Week 52								
Mortality								
CLINEVID 15[a]	189	5 (2.6)	187	2 (1.1)	2.47 [0.49; 12.59] 0.256	1: NS - 2: NP - 3: NC	0.02 [−0.01; 0.04] 0.256	1: NS - 2: NP - 3: NC
CLINEVID 16[b]	179	3 (1.7)	181	2 (11.0)	1.52 [0.26; 8.97] 0.644	1: NS - 2: NP - 3: NC	0.01 [−0.02; 0.03] 0.644	1: NS - 2: NP - 3: NC
Total[c] (p_H = 0.691; I^2 = 0 %)					2.00 [0.61; 6.58] 0.255	1: NS - 2: NP - 3: NC	0.01 [−0.01; 0.03] 0.245	1: NS - 2: NP - 3: NC

Reading the "Hypothesis testing" columns:
1: Statistical significance: S = Statistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nominal p-value
2: Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified
3: Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled

a: data cut-off: 11.11.2020
b: data cut-off: 29.06.2020
c: calculated from meta-analysis with Mantel-Haenszel fixed effect model
d: Number of patients with an improvement in BCVA by ≥ 10 ETDRS-letters in week 52 compared to baseline on a scale from 0 to 100 points; increasing values correspond to an improvement of symptoms.
e: Number of patients with an improvement in NEI VFQ-25 sum score by ≥ 15 points in week 52 compared to baseline on a scale from 0 to 100 points, increasing values correspond to an improvement of health-related quality of life.

BCVA: Best Corrected Visual Acuity; CI: confidence interval; EDTRS: Early Treatment Diabetic Retinopathy Study; N: number of patients in the analysis; n: number of patients with event; NEI VFQ-25: National Eye Institute Visual Function Questionnaire-25; p_H: p-value from heterogeneity-test based on study*treatment in the meta-analysis; RD: risk difference; RR: relative risk

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Procedural guidance for joint scientific consultations

- Outlines how to apply for a JSC and the respective procedural timelines
- Possible to request a HTACG (only) JSC or a parallel HTACG/EMA JSC

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Procedural guidance for joint scientific consultations

Two eligibility conditions for a JSC:

- Date of future application for a marketing authorisation is expected to be after the respective date referred to in Article 7 (2) of the HTAR (2025, 2028, or 2030) and therefore subject of a JCA
- Clinical studies and clinical investigations are still in the planning stage. This implies that the pivotal study has not yet started and is still at a stage where the scientific recommendations of the HTACG could be taken into consideration (i.e. the protocol has not been submitted yet to any regulatory authorities).

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