HTA125

Comparison of the Joint Clinical Assessment (JCA) dossier with the German Medicines Market Reorganization Act (AMNOG) dossier – what content remains to be presented in the AMNOG dossier after implementation of JCA?

Becker, M[a]; Maier, M[a], Ernst, I[a]; Böckmann, D[a]; Rauch, M[a]; Oberhauser, M[a]; Gallinger, P[a]; Bonduelle, D[a] ; Van Engen, A[b]

[a] IQVIA Commercial GmbH & Co. OHG, Munich, Germany [b] IQVIA, Amsterdam, NH, Netherlands

OBJECTIVES

Commencing 2025, new oncology medicines and advanced therapy medicinal products will be assessed at EU level. A JCA dossier template was published early this year, which was developed in close collaboration with German healthcare authorities.

Here, we compared and contrasted between the JCA and AMNOG dossiers and, based on this, aimed to answer the question of what content needs to be presented in the German AMNOG dossier beyond the content presented in the JCA. We furthermore wanted to investigate whether a distinct comprehensive German AMNOG dossier as currently mandated will still be required for HTA in Germany after the implementation of the JCA process at an EU level.

METHODS

We evaluated the content of the JCA dossier template included in the JCA Implementing Regulation Annex (as of 23/05/2024) [1] and the EUnetHTA21 submission dossier template [2] with the latest German AMNOG dossier templates [3]. First, the dossier templates were compared and screened for major differences. Subsequently, the derived differences were used to conclude what content is not covered by the JCA dossier and therefore needs to be included in an additional delta-dossier tailored for AMNOG.

RESULTS

All sections containing relevant discrepancies of the JCA dossier compared to AMNOG dossier are highlighted in Table 1.

The content and structure of the dossiers to be submitted in terms of JCA and AMNOG are highly similar. While JCA sections 1 and 6 content corresponds to AMNOG modules 1 and 5, the content of JCA section 2 is reflected in the content of modules 2 and 3 in the AMNOG dossier. Section 3, 4 and 5 of the JCA dossier match the content and principle of module 4 of the AMNOG dossier.

However, there are some differences between the JCA and AMNOG dossier content. Compared to the AMNOG dossier, in the JCA dossier template there are additional sections on the organisational and societal impact of the health condition, variations in clinical pathways between countries and the regulatory status of the medicinal product in all countries with corresponding HTA reports. Contrasting to AMNOG, no costs of therapy need to be presented in the JCA dossier.

Overall, the documentation requirements for analyses regarding methods, PRO endpoints, patient-relevance, subgroups and presentation are more extensive and specific in the AMNOG dossier than in JCA.

Table 1 – Overview of JCA dossier with key discrepancies between JCA and AMNOG dossiers highlighted

1 Overview	1.1 Information about medicinal product
	1.2 Previous assessments under HTAR – **additional section**
	1.2 Executive Summary (focused on assessment scope)
	Assessment scope, PICOs for which results not submitted w/rationale for omission; Summary of relative effectiveness/safety results for each PICO; whether direct or indirect evidence; degree of certainty
2 Background	2.1 Characterization of health condition to be treated, prevented or diagnosed
	2.1.1 Overview of the medical condition **– additional section with organizational and societal impact of health condition**
	2.1.2 Characterization of the target population
	2.1.3 Clinical management of the medical condition **- variations in clinical pathways between MS, listing of treatment guidelines**
	2.2 Characterization of the medicinal product
	2.2.1 Characteristics of the medicinal product
	2.2.2 Requirements/instructions for use
	2.2.3 Regulatory status of the medicinal product (EEA, AUS, CAN, CH, JP, UK, USA) **– additional section**
	2.3 JSC related to the JCA
3 Assessment scope	3 Description of assessment scope, identification of PICOs for which no results will be submitted w/reason for omission **– more extensive scope**
4 Methods used in the development of dossier content	4.1 Criteria for selecting studies for JCA (inclusion/exclusion criteria per PICO)
	4.2 Information retrieval and selection of relevant studies
	4.2.1 Information retrieval
	(1) Studies performed or sponsored by the HTD
	(2) Bibliographic databases
	(3) Study registries and study results registries (clinical trial databases) **– search in CTIS registry**
	(4) Submission files to the EMA **– additional section for pivotal studies**
	(5) HTA reports (EEA, AUS, CAN, UK, USA) **– additional section**
	(6) Patient registries **– additional section**
	4.2.2 Selection of relevant studies
	4.3 Data analysis and synthesis **– assessment of appropriateness of methods and model assumptions required**
	4.3.1 Description of the design and methodology of the included original clinical studies
	4.3.2 Description of the results from the original clinical studies **– additional information required**
	4.3.3 Direct comparisons by pairwise meta-analyses
	4.3.4 Indirect comparisons **– additional information required**
	4.3.5 Sensitivity analyses
	4.3.6 Subgroup analyses & other effect modifiers **- subgroup analyses for binary events per variable only if at least 10 events occurred**
	4.3.7 Specification of further methods as required **– additional section**
5 Results	5.1 Results from the information retrieval process
	5.1.1 Studies performed or sponsored by the HTD or 3rd parties
	5.1.2 Studies from bibliographic databases
	5.1.1 Studies performed or sponsored by the HTD or 3rd parties
	5.1.2 Studies from bibliographic databases
	5.1.3 Studies in study registries/study results registries (clinical trial databases) **– additional section**
	5.1.4 Studies from submission files to the EMA **– additional section**
	5.1.5 HTA reports **– additional information required**
	5.1.6. Studies from patient registries **– additional section**
	5.1.7 List of studies included overall and by PICO
	5.2 Characteristics of included studies
	5.3 Study results on relative effectiveness & relative safety
	5.3.1 Results for the patient population < i>: Results for all PICO(s) in patient population < i>
	5.3.1.1 Patient characteristics for PICO <i> **- standardized difference between the study arms necessary for non RCT**
	5.3.1.2 Health outcome results for PICO <i> and uncertainties in the results **– deviations on relevant outcomes and their presentation**
6 List of References	
Appendix A	Tabular listing & info on methods of all studies included in JCA
Appendix B	Info to assess degree of certainty (including but not limited to the RoB-assessment)
Appendix C	Results of the main study/studies from the clinical development program (if not included in PICO question(s)) **– additional information required**
Appendix D	Underlying documentation D.1 Full texts of reference / D.2 Documentation of information retrieval D3 Programming code for programs used for analyses **– for all analyses, not ITC only** D.4 Study reports for original clinical studies D.5 Study reports for evidence synthesis D.6 Clinical safety and efficacy data included in submission file to EMA D7 HTA reports of the medicinal product subject to the JCA **– additional section** D.8 Information on studies based on registries D.9 Information on JSCs **– additional section**

Similar content | **Minor deviation** | **Moderate deviation**

Discrepancies of the JCA content compared to AMNOG are presented in dark blue.

Abbreviations: AMNOG: Arzneimittelmarktneuordnungsgesetz [German Medicines Market Reorganization Act]; AUS: Australia; CAN: Canada; CH: Switzerland; CTIS: Clinical Trials Information System; EEA: European Economic Area; EMA: European Medicines Agency; EU: European Union HTA: Health Technology Assessment; HTAR: Health Technology Assessment Regulation; HTD: Health Technology Developer; Institute for Quality and Efficiency in Health Care]; JCA: Joint Clinical Assessment; JP: Japan; MS: Member States; JSC: Joint Scientific Consultation; PICO: Population, Intervention, Comparator, Outcome; PRO: Patient Reported Outcomes; RCT: Randomised Controlled Trial; RoB: Risk of Bias; UK: United Kingdom; USA: United States of America

DISCUSSION & CONSLUSION

The comparison of the HTA dossiers showed a high degree of similarity between the two HTA dossiers. The similarity between the dossiers reflects how much the German HTA authorities (Federal Joint Committee [G-BA] and Institute for Quality and Efficiency in Health Care [IQWiG]) have shaped JCA.

The majority of deviations are minor and due to the different focus of the dossiers. Since AMNOG is aimed at deriving an added benefit and prepare the associated price negotiation, the AMNOG dossier requires costs of therapy, guidelines and calculations of the target population in Germany, which are not part of the JCA and its scope.

Additionally, the scope of the JCA will be significantly larger compared to the AMNOG due to the fact that it needs to be relevant for all 27 member states, not just one and the resulting anticipated high number of PICO requests. It is possible that German authorities will demand additional PICOs not addressed within JCA, especially for specific subpopulations.

Since the information required by the G-BA does not fully overlap with the content in JCA, a delta-dossier will be required, nevertheless.

Specifically, the delta dossier would need to include an additional contextualization of the health condition, the applicable guidelines, the target population as well as the clinical management specific for the German health care setting to set the scene for the German benefit assessment. Additionally, as the JCA does not include the calculation of the cost of therapy, the great majority of cost calculation and budget impact analysis will remain part of the German AMNOG delta dossier.

It is therefore expected that modules 2 and 3 in the German AMNOG delta dossier will remain unchanged. Module 4 will need to reference the JCA report while presenting additional analyses specific to AMNOG (e.g., subgroups or effect measures) or for potential additional PICOs..

The delta dossier has not yet been specified by German health authorities. An updated AMNOG dossier template is expected by the end of 2024 [4].

References:
[1] EC (2024). Commission Implementing Regulation (EU) 2024/1381 of 23 May 2024.
[2] EUnetHTA (2023). D5.1 Submission Dossier Template – Medicinal Products. Version 1.0, 31/07/2023.
[3] G-BA (2024). Formulare und Vorgaben zum Download – Anlagen zum 5. Kapitel der Verfahrensordnung
[4] G-BA (2024). The benefit assessment of medicinal products in accordance with the German Social Code Five (SGB V), section 35a.

Poster presented at ISPOR Europe 2024 on 18th November 2024; Presentation Code: HTA125
For further information please contact: IQVIA | Real-World Insights | Marie.Becker@iqvia.com