Integration of Germany's AMNOG Framework with the Joint Clinical Assessment Process

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Background and Objective

- Joint Clinical Assessment (JCA), implemented in 2025 under the European Health Technology Assessment (HTA) regulation, requires that European national HTA processes align with the newly established JCA process.
- Manufacturers must submit an EU HTA dossier on comparative clinical evidence before receiving market authorization.
- This dossier and the subsequent JCA report along with complementary national submissions will be considered in national evaluations and decision making.
- To explore adaptations made and potential challenges in Germany the established AMNOG framework and its integration with JCA submissions has been investigated.

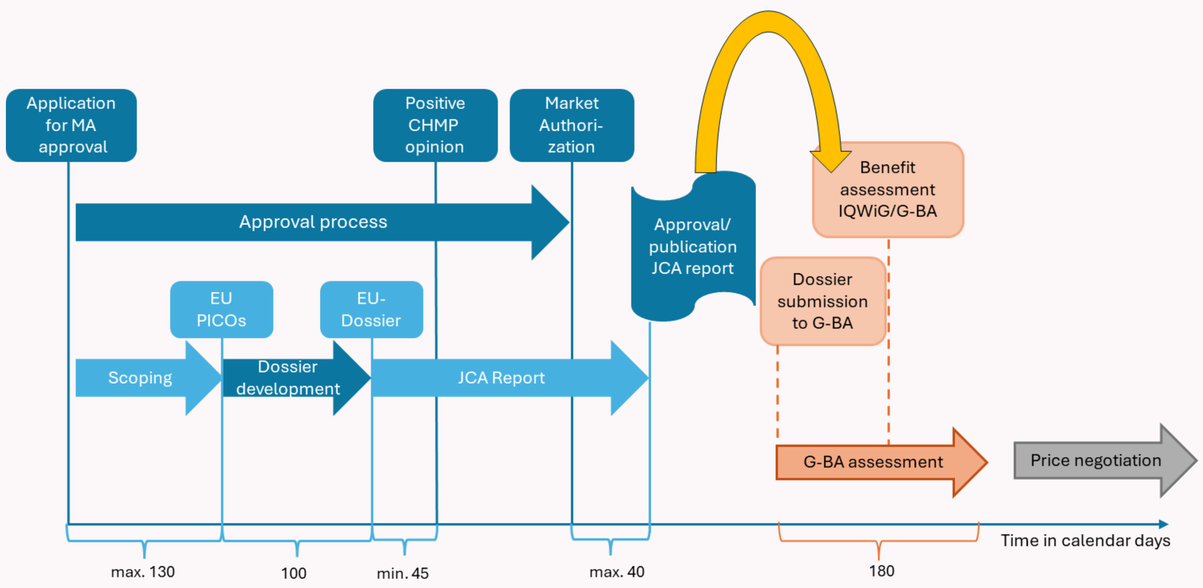
Methods

- The guidance document on filling in the JCA dossier template[1] including technical specifications for dossier submission, the JCA dossier submission template, and table templates have been reviewed and compared to the AMNOG template[2].
- Based on publicly available information[3-6] on adjustments made and remaining submission requirements according to AMNOG law the commonalities and differences between JCA and AMNOG submissions have been assessed and potential challenges identified.
- In addition to document templates, timing of both HTA processes, interdependencies and implications have been investigated.

Results

- A national dossier (AMNOG dossier) according to §35a SGB V must be submitted to G-BA (Federal Joint Committee) in any case, irrespective of a prior JCA.
- The G-BA has created a formal referencing bridge from AMNOG to JCA via changes of the Drug Benefit Assessment Regulation (AM-NutzenV[7]).
- Few adjustments in evidence requirements of the AMNOG submission have been made to better align with JCA requirements (e.g., searches in study registries, reporting of adverse events and subgroup analyses); referrals to data presented in JCA submission are permitted.
- Additionally, information such as indication, derivation of the ACT, patient numbers, therapy cost, derivation of additional benefit (modules 1-4) must be presented without referral.
- Comparator therapies, clinical outcomes, AE reporting, and dossier structure have been aligned where feasible, while preserving German-specific requirements, timelines, and decision sovereignty. Table 1 on the right maps the respective key categories.
- Timing of JCA report and AMNOG benefit evaluation: Figure 1 depicts the JCA process and interplay with regular AMNOG process

Figure 1: JCA and AMNOG processes



Results (ctd)

- Timing of JCA report and AMNOG benefit evaluation:
  - AMNOG dossier must be submitted latest at product launch which can follow immediately after receipt of market access authorization.
  - 6 months period for G-BA benefit evaluation is followed irrespective of JCA report availability.
- PICO provided by G-BA/IQWiG during JCA scoping reflects the AMNOG requirements.
- Information from JCA submission dossier and AMNOG submissions feed into evaluation.
- JCA report will be considered in evaluation if available before benefit assessment; JCA report published after hearing cannot be considered in decision on additional benefit.
- Publication of the JCA report and benefit evaluation according to AMNOG may diverge occasionally risking that the JCA outcome does not feed into the appraisal.

Table 1: Key areas of alignment and divergence between AMNOG and JCA dossiers

Category	AMNOG Integration with JCA Requirements
Appropriate Comparative Therapy (ACT)	• General requirements according to AMNOG methodology prevail • No ACT defined for orphans (but provided in PICO scoping) while JCA provides ACT for all products irrespective of orphan status • Selection of one therapy option for additional benefit demonstration possible while JCA requires comparison against all identified ACTs
Outcomes	• Categories defined in AMNOG are retained: mortality, morbidity (events/symptoms measured by validated instruments), health-related QoL (disease-specific and/or generic), and safety; fairly aligned with JCA • Patient-relevant outcomes are preferred corresponding to patient-centred outcomes preferred by JCA
Adverse events reporting	• Presentation of a priori analyses of AESI/SMQ eliminated in AMNOG for harmonization with JCA • Reporting of severe AEs (CTCAE ≥ 3) to align with JCA • Presentation of overall AEs ≥ 10% of patients in any study arm remains while JCA requests reporting of events with ≥ 5% incidence • Additionally, AEs in at least 10 patients and at least 1% in a study arm required in AMNOG dossier
Subgroup analyses	• Mandatory reporting of subgroup analyses for key parameters (age, gender, disease severity, center) in AMNOG dossier as well as all protocol-specified subgroups, according a priori definitions • Justified additional effect modifiers may be included-in AMNOG dossier as needed • JCA dossier also requires reporting of all protocol-specified subgroup analyses, aligned with AMNOG's requirements • In addition, JCA requires consistent presentation of subgroup results across all relevant PICOs
Evidence identification and cut-off dates	• For both AMNOG and JCA, the literature search cut-off is 3 months before submission • An updated search may be needed for the AMNOG dossier if search for JCA was > 3 months ago at submission • JCA methods may be referenced in the AMNOG dossier where appropriate

Conclusions

- The integration of JCA submission dossiers and JCA reports within the German AMNOG framework has been formalized by the G-BA and Ministry of Health through respective adaptations of the Drug Benefit Assessment Regulation (AM-NutzenV).
- The adapted AMNOG template allows manifold reference to the JCA submission dossier, especially in module 4, presenting clinical evidence. However, a dossier with additional information including additional benefit claim must be submitted.
- Some revisions to AMNOG requirements have been made to align with JCA submission but specific requests need to be addressed, and German law prevails.
- The initial adjustments maybe amended in future once first experiences with the new process have been made.
- Consideration of the outcomes of the JCA report in the benefit evaluation depends on its availability and may occasionally not be published early enough.
- Appraisal process and decision making follow the national requirements.

Legend

- ACT: Appropriate Comparative Therapy
- AESI: Adverse Event of Special Interest
- AMNOG - Act on the Reform of the Market for Medicinal Products ("Arzneimittelmarkt-Neuordnungsgesetz")
- AM-NutzenV: Ordinance on the Benefit Assessment of Medicinal Products ("Arzneimittel-Nutzenberwertungsverordnung")
- CHMP: Committee for Medicinal Products for Human Use
- CTCAE: Common Terminology Criteria for Adverse Events
- G-BA: Federal Joint Committee ("Gemeinsamer Bundesausschuss")
- HTA: Health technology Assessment
- HTACG: Health Technology Assessment Coordination Group
- IQWiG: Institute for Quality and Efficiency in Health Care ("Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen")
- JCA: Joint Clinical Assessment
- MA: Market authorization
- MS: EU member state
- PICO: Population, Intervention, Comparator(s), Outcomes
- SMQ: Standardised MedDRA Query
- SOC/PT: System Organ Class Preferred Term

References

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