HTA 164

Get JCA-Ready: Mastering PROs for Market Access Success

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Background & Objectives

- With the implementation of the JCA in January 2025, in parallel to the EMA regulatory process, HTDs are faced with increased evidence needs in the form of PICOs. This shift underscores the need for early, strategic planning to align with new evidence demands.
- PROs are a critical focus within JCA, with a strong emphasis on PROs in the outcomes requested. In addition, further detail and justification on the choice of PROs is required in the JCA dossier. With HTA bodies increasingly prioritising PROs for delivering patient-centred insights beyond traditional clinical endpoints, HTDs must proactively generate PICO-aligned data suitable for comparative evaluations.
- We therefore explored how evolving JCA PROs evidence requirements are reshaping the evidence landscape for HTDs with the aim of generating actionable insights to help HTDs navigate JCA requirements, align PRO strategies with regulatory expectations, streamline submissions, and ensure readiness for future JCA evaluations.

Methods

- We conducted a review of the MPG on outcomes and the JCA dossier template instructions[1,2]. Evidence expectations within the JCA framework were assessed and key considerations for reporting PRO evidence were collated. Practical insights from our experience with developing JCA dossiers informed actionable recommendations for HTDs to support JCA evidence planning and submission readiness.

Results

JCA reporting needs for PROs

- MPG guidance on outcomes requires HTDs to define each outcome and how it is measured (covering instrument details and supporting evidence for PROs - validity, reliability, and interpretability) [1-5] *(Table 1)*. For commonly used instruments, this data is often readily available; for new, less established PROs or where the instrument is used in a new context, evidence must be developed to meet JCA standards, which requires planning and adequate time allocation. Mitigations for challenges arising from JCA for PRO planning are summarised in *Table 2*.
- Insights from confirmed JCA scopes shared in 2025 indicate consistent requests for four PRO elements: disease symptoms, overall health status, and HRQoL assessed through both a generic and a disease-specific questionnaire. It is essential to clearly distinguish disease symptoms (e.g., pain caused by the condition) from treatment-related effects (e.g., chemotherapy-induced pain) where possible, with medical input ensuring accurate differentiation.
- Additionally, many instruments overlap in content domains and can address multiple aspects, including health status, disease symptoms, and other disease-specific domains. Therefore, careful selection and justification of instruments are critical to meet outcome requirements, as well as ensuring alignment on result interpretation.

Table 1. JCA reporting needs and key considerations[1,2]

JCA needs	Definition	Key considerations
Definition of Outcomes	Define each outcome: concept, source, measure, timing, response	• Ensure relevance to the target population and intended use
PRO instrument description	Describe the purpose and structure of the instrument	• Confirm appropriateness and coverage of key aspects • Provide references and, if possible, full instrument and instructions • Specify the main source of information (healthcare professionals, medical technology, patients) for answering items
Validity	Extent to which an instrument measures what it is intended to measure (e.g. anxiety PROM should reflect anxiety)	• Multi-dimensional, including content, criterion, and structural dimensions, assessed through ongoing research • Depends on score interpretation and intended use (contextual); not a fixed property across applications • Development should involve patients, caregivers, literature review, qualitative studies (identify relevant concepts), and statistical methods • Poor validity can lead to indirectness (measuring the wrong concept) and bias (systematic error) • Instruments must be culturally adapted when translated; reports should include structure and validation evidence
Reliability	Demonstrate consistency and reproducibility of outcome measurements	• Provide evidence of internal consistency (e.g., Cronbach's alpha) • Report test–retest reliability and inter-rater reliability where applicable • Justify reliability for intended population and context
Interpretability	Ability to assign clinical meaning to PRO scores	• Define and justify meaningful change thresholds (using published literature, validation studies, or expert consensus) • Use consistent and transparent scoring systems (clarify if higher scores mean improvement or decline, and apply consistently) • Contextualise PRO findings within the clinical narrative • Address missing data and its impact on interpretation • Ensure alignment with PICO and study endpoints and provide population-level and individual-level insights
Context of Use	Specify target population, study context, objectives	• Evidence must be specific to the JCA application

Early planning for PRO evidence

JCA reporting requires early planning and incorporating PRO strategy early in clinical development (as early as Phase 2, *Figure 1*). For all JCA submissions, the following components are advised:

- ✓ (if time permitting) **HTA scientific advice** (before pivotal trial initiation) to seek input on PRO relevance, instrument choice, and statistical analysis plans
- ✓ **PRO SAP and targeted narrative** (ideally before pivotal trial) aligned with JCA to ensure methodological transparency
- ✓ **Pragmatic PRO dossier** (compiled during trial) to provide the agreed upon narrative.

If a clear PRO strategy (i.e., identifying concepts of interest, fit-for-purpose PRO instruments, and psychometric evidence) was not generated prior to registrational trial, HTDs should follow a tailored approach to ensure alignment with JCA expectations:

- ✓ **Gap analysis and TLR** to identify payer-relevant PRO needs
- ✓ Address **evidence gaps** and guide the **selection of appropriate PRO instruments.**

Figure 1. EU HTA readiness plan: evidence generation and JCA strategy and JCA strategy development

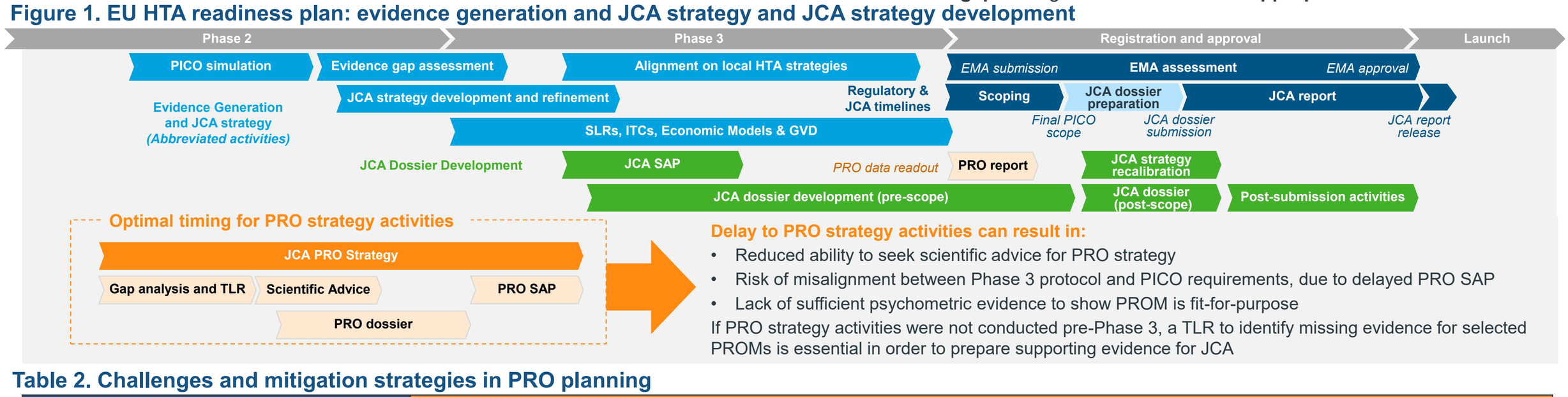

Table 2. Challenges and mitigation strategies in PRO planning

Challenge	Mitigations
1. JCA process runs in parallel with regulatory timelines in Europe	• Evidence generation activities including anticipation of PICOs and summary of the existing evidence justifying the use of the PICOs-related PROs will need to begin early, ideally from Phase 2; JCA dossier should be started **at least a year prior** to anticipated submission
2. JCA covers PICO evidence needs from 27 member states	• Develop a PRO strategy for **all** anticipated PICOs, including aspirational PRO value proposition and messages. Develop a separate PRO SAP that details all expected analyses (modelling, subgroups, missing data) to handle complexity
3. Evidence for validity, reliability and interpretability is required for all PROs	• Assess gaps in PRO strategy-supporting evidence early • If not already planned for regulatory submission, develop a separate PRO SAP that details all expected analyses (modelling, subgroups, missing data) to meet the expected requirements of the different HTA members

Conclusions and implications

- Meeting JCA requirements and achieving successful submission requires HTDs to embed PRO strategy early from Phase 2, ensuring timely outcome definition, instrument selection, and psychometric validation—especially crucial when using new or context-adapted instruments that demand additional evidence for JCA compliance
- JCA submissions preparations must include PRO SAP, a targeted narrative (ideally before the pivotal trial), and pragmatic PRO dossier compiled during the trial. Where feasible, HTA scientific advice should be sought early to validate PRO relevance, instrument choice, and analysis plans.
- JCA challenges—such as limited guidance on PROs, tight timelines, and cross-jurisdictional inconsistencies—can be mitigated through tailored planning, targeted evidence generation, strategic use of FDA benchmarks where MPG lacks structure, and alignment with consistent PRO expectations seen in 2025 PICO scopes.

Abbreviations: COA: Clinical Outcomes Assessment; EMA: European Medicines Agency; EU: European Union; FDA: Food and Drug Administration; GVD: Global value dossier; HRQoL: Health-related quality of life; HTA: Health Technology Assessment; HTD: Health Technology Developer; ITC: Indirect treatment comparison; JCA: Joint Clinical Assessment; MPG: Methodological and Procedural Guidance; PICO: Population, Intervention, Comparator, Outcomes; PRO: Patient-Reported Outcome; SAP: Statistical Analysis Plan; SLR: Systematic literature review: TLR: Targeted literature review.

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