ChatGPT

Europe's New HTA Era: Integrating Evidence Generation in the Post-JCA Landscape

Introduction

January 2025 marked a pivotal shift in how new therapies are evaluated for reimbursement across Europe. The EU's new Health Technology Assessment Regulation introduced the **Joint Clinical Assessment (JCA)** – a centralized HTA process aiming to standardize the clinical evaluation of medicines across all 27 EU member states [1]. Under this framework, companies launching new drugs (starting with oncology and advanced therapy medicinal products in 2025, expanding to orphan drugs by 2028 and all medicines by 2030) will face a single EU-level clinical assessment that informs all national decisions [2] [3]. The JCA focuses strictly on **clinical** outcomes – analyzing relative effectiveness and safety – while **member states retain authority over value judgments**, such as cost-effectiveness and pricing, in their own contexts [4] [5]. This convergence promises *faster patient access* by eliminating redundant country-by-country clinical reviews and ensuring greater transparency in how data are interpreted [6] [7]. However, it also fundamentally changes how **health technology developers (HTDs)** must plan evidence generation. No longer can manufacturers "learn as they go" with sequential country launches; instead, they must meet the evidentiary needs of regulators, the JCA, and multiple national HTA bodies *simultaneously*. This necessitates a proactive, **Integrated Evidence Generation Planning (IEGP)** approach to development – ensuring that from early clinical trials through real-world studies, evidence is generated with an eye toward every major decision-maker's requirements.

Integrated Evidence Generation Planning (IEGP) has emerged as a strategic response to this challenge. IEGP is a cross-functional, end-to-end approach to planning evidence generation that aligns the needs of regulators, payers, and other stakeholders into one cohesive strategy [8]. It is about breaking silos: bringing together clinical development, HEOR, medical affairs, market access, and even commercial teams to define *all* the evidence needed for a product's success, and mapping out how to produce it efficiently [9]. The cost of poor planning is high – missing data, misaligned study endpoints, or delayed analyses can lead to **missed opportunities, protracted launches, and lost trust** [8]. In this paper, we explore how the new JCA-driven landscape demands an IEGP mindset. We discuss the adaptations required in trial design, development programs, and real-world evidence (RWE) strategies to satisfy the **European Medicines Agency (EMA)**, the JCA process, and national HTA bodies all at once. Key topics include whether transparent EU-level assessment will reduce divergent HTA outcomes, how agencies will handle evidence transferability to local contexts, and how early stakeholder engagement can build more comprehensive and **simultaneous market access strategies** across Europe.

A New Reimbursement Evaluation Landscape in Europe

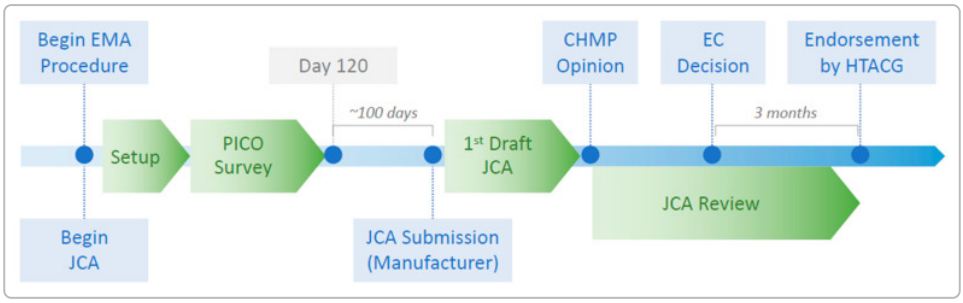
Under the traditional paradigm, pharmaceutical companies often pursued **sequential launches** in Europe – seeking reimbursement in one country at a time, learning from each HTA outcome and gradually adapting their value demonstration for subsequent markets. This approach allowed iteration (for example, adding an analysis for a new comparator or collecting additional data if an early HTA review identified a gap). With the introduction of the JCA, that paradigm is changing dramatically. Now, for the first time, EU member states will collaborate on a **single clinical assessment** of a new medicine's therapeutic value, to be conducted in parallel with EMA's regulatory review [10]. Once a JCA

report is published, **every country must consider it** in their national HTA decisions – they are even required to annex the JCA report to their own assessment report and explain how they used it [11] [12]. The intent is to eliminate duplicate efforts and align countries on the core clinical evidence, thereby *streamlining* the path to reimbursement [7]. In effect, Europe is moving toward "**one clinical voice**" on the efficacy and safety of new therapies.

However, this streamlined JCA does **not** replace national HTA altogether – it supports it. Importantly, the JCA will **not** issue any conclusions on cost-effectiveness, budget impact, or pricing; those remain squarely under each member state's purview [4]. Even on clinical matters, national HTA bodies may still perform additional analyses and apply their own judgment. The HTA regulation mandates that countries give "due consideration" to the JCA's findings, but it does not force them to adopt the JCA's conclusions wholesale [11] [13]. In practice, if a national agency finds that certain patient subgroups, comparators, or outcomes particularly relevant to their setting were not fully addressed by the JCA, they are **within their rights to request further data or conduct complementary analyses** to fill those gaps [13]. What the regulation does require, though, is *transparency*: any divergence of a national HTA's conclusions from the JCA's findings must be scientifically justified and reported publicly [12] [14]. This marks a new era of accountability – if a country decides a drug's benefit is substantially different from what the JCA concluded, they must provide robust evidence or reasoning (e.g. different locally-relevant comparators or clinical practice patterns) to back that stance. Over time, this transparency could exert pressure toward greater consistency in HTA outcomes, at least regarding the interpretation of clinical evidence. But in the near term, **HTA divergence will not disappear** entirely; rather, the nature of divergence will shift to areas like economic evaluation and context-specific considerations, while the *common core* of clinical data interpretation becomes more aligned across Europe [14].

The Imperative for Integrated Evidence Generation Planning (IEGP)

In this new landscape, **integrated evidence generation planning** moves from a "nice-to-have" to a necessity. IEGP means planning *from the outset* how a development program will generate all the evidence needed for regulatory approval, *and* for a positive HTA outcome in multiple markets, *all at once*. The JCA process itself exemplifies why this is essential. Under JCA, a *single* dossier must address the clinical data requirements of **all EU HTA bodies simultaneously**, which is a far broader scope than any one country's HTA. Manufacturers are confronted with a consolidated list of PICO (Population, Intervention, Comparator, Outcomes) criteria covering **multiple comparators, patient sub-populations, and endpoints** requested across Europe [15]. For example, one country's HTA might require comparison against the local standard of care, another might insist on data in an elderly subpopulation, and others might care about different outcome measures (overall survival, quality of life, functional status, etc.). The JCA will aggregate these into a comprehensive assessment scope – and **all those evidence needs must be met in the initial submission** [15] [16]. This is a profound change from the past, when a company could focus on the first few launch countries' requirements and deal with other countries' demands in later years. As one analysis noted, *"the new demand is for all these PICOs to be accounted for even before launch. Before the JCA, manufacturers typically only needed to worry about the PICOs of a select few first-launch countries… and had months or years to address the remaining countries' evidence gaps. Now all must be done by time of launch."* [17]. In other words, there is no "later" – you either have the comparator data or analysis ready in your JCA dossier, or you face potentially critical evidence gaps in the eyes of some HTA agencies.



Timeline of the Joint Clinical Assessment (JCA) process relative to EMA's regulatory review. The JCA scoping survey consolidates EU-wide HTA evidence needs by about Day 120 of the EMA procedure; manufacturers then have roughly 100 days to submit a dossier addressing all required PICOs [18]. A draft JCA report is usually available by the time of EMA's CHMP opinion, and the final JCA report is endorsed within ~30 days of EU marketing authorisation [19]. This parallel timeline compresses the evidence generation and submission process for manufacturers [10].

Meeting this challenge calls for **early and proactive planning**. Companies must forecast likely HTA requirements well in advance – often *before* pivotal trials are even finished – and initiate evidence generation activities "at risk" to ensure nothing is missing in the final dossier [20]. For instance, if you can predict that some countries will expect an indirect comparison versus a certain comparator (because no head-to-head trial exists against it), you need to start assembling that indirect comparison analysis as soon as possible, even while regulatory review is ongoing [21] [16]. If real-world evidence or registry data will be needed to demonstrate outcomes in a specific subpopulation or over a longer term, those studies should be designed and launched early so results can feed into HTA submissions [22]. An effective IEGP process engages all internal experts – clinical developers, biostatisticians, HEOR modelers, RWE specialists, medical and commercial teams – to **map out every evidence requirement** across EMA, JCA, and key national HTA frameworks [9]. Best-practice IEGP involves steps like: (1) defining the target evidentiary requirements (regulatory endpoints, comparative effectiveness, safety, patient-reported outcomes, etc.) in light of future reimbursement goals; (2) assessing how the landscape is evolving (e.g. new HTA guidelines, emerging comparators); (3) auditing what evidence currently exists or will come from ongoing trials; and (4) identifying the new studies or analyses needed to fill gaps [23]. Crucially, these plans must be made early enough to actually execute – the **JCA dossier submission typically occurs only ~3 months after trial data readouts**, leaving no time to start major new studies after seeing HTA demands [10]. As one consultancy bluntly warned, *"Without starting early, manufacturers will struggle to address all PICOs effectively and risk public 'no evidence' statements in the JCA report."* [20] In an era where a "no evidence" finding in a pan-European report could instantly be visible to all payers, that is a risk no company wants to take.

IEGP also means being prepared for the **compressed timelines** that JCA brings. The coordination group conducting JCA gives manufacturers just 100 days to compile and submit the joint dossier once the consolidated scope (PICO list) is communicated [10] [24]. (In fact, if the product is under an accelerated EMA review, the JCA timeline shrinks further – the HTD may get only 60 days to submit the dossier in those cases [25].) These tight deadlines demand a high level of operational readiness: writing teams, statisticians, health economists, and others must work in parallel on different evidence pieces, often before knowing final regulatory outcomes. **Cross-functional coordination** is vital. Many organizations are establishing internal "war rooms" or task forces to manage JCA preparations, ensuring regulatory affairs, clinical, and market access teams work hand-in-hand. As the PharmaExec magazine noted, regulatory affairs teams in particular need to *"be fully engaged in the JCA and ready for new collaborative working models with their market access and HEOR colleagues."* [26] The JCA is not just a technical submission; it effectively combines what used to be separate regulatory and HTA submission processes

into one concurrent effort. IEGP helps teams anticipate this crunch and allocate resources accordingly (sometimes bringing in external experts or CRO support for rapid evidence synthesis [27]).

Adapting Trial Designs and Development Programs

One of the biggest implications of the JCA era is the need to **adapt clinical trial designs and development programs** to generate more broadly applicable evidence. In the past, a Phase III trial program might have been designed primarily to satisfy regulators (EMA/FDA), with a focus on demonstrating efficacy versus placebo or a single comparator, and safety. Considerations of what each European HTA would want were often secondary, addressed later via additional trials or post-hoc analyses. Now, because the JCA will scrutinize relative effectiveness through the eyes of *all* member states at once, trial programs must be designed with a *wider lens*.

Comparator selection is a prime example. Companies need to think beyond one main comparator and anticipate the different standards of care across Europe. The JCA's consolidated PICO process explicitly asks each country what comparators they require; the outcome is that a manufacturer might have to provide evidence against multiple comparators (some of which were not included in the pivotal trials) [28] [15]. To address this, trial sponsors are considering **multi-arm trials or platform trials** that include more than one active comparator where feasible, or at least ensuring that their single-comparator trial is supplemented by robust **indirect treatment comparisons (ITCs)** for other relevant comparators [29] [16]. The use of network meta-analyses and other indirect comparison techniques isn't new, but under JCA it becomes even more critical – it's expected that head-to-head evidence will *not* be available for many of the comparisons demanded, so manufacturers must plan early how they will perform credible ITCs within the short timeframe [21] [16]. This includes scouting data sources (published trials, real-world datasets) well in advance and even initiating indirect comparison analyses **"earlier than ever before,"** sometimes before the official HTA scope is finalized [21] [30]. Without such preparation, there's a risk of scrambling to conduct complex analyses in a matter of weeks, leading to **poor-quality comparisons that could be challenged** by assessors [31].

Trial **endpoints** and outcomes measurement is another area of adaptation. To support both EMA approval and diverse HTA requirements, developers are building trials that capture a more holistic set of outcomes. For instance, **patient-reported outcomes (PROs)** and quality-of-life measures are increasingly included in pivotal trials for diseases where HTAs value these outcomes for assessing patient benefit [32]. The JCA framework explicitly allows inclusion of such outcomes in the assessment of relative effectiveness, and it provides an opportunity for HTAs to consider patient-centric impact more uniformly [33]. A recent EU analysis noted that aligning on meaningful endpoints is crucial for the JCA to provide a *"meaningful evaluation of the drug's value across different member states."* [34] Thus, sponsors are wise to include endpoints like long-term survival, quality of life, functional status, and other relevant metrics in their trials, even if these go beyond what regulators strictly require. This ensures that when the JCA (and later national HTAs) ask, for example, "Does this treatment improve not just clinical markers but also patients' quality of life compared to existing therapy?", the data is on hand.

Broader patient population considerations are also key. While a trial has specific inclusion criteria, HTAs often want to know how the drug works in subpopulations (e.g. elderly patients, patients with comorbidities, different genetic subtypes, etc.). The JCA will aggregate subpopulation requests from many countries [15], meaning a dossier might need to present subgroup analyses for a variety of patient segments. Forward-thinking development teams are stratifying their trial data or ensuring sample sizes allow for meaningful subgroup analysis where they foresee such needs (for example, ensuring adequate representation of both pre-treated and treatment-naïve patients if different countries are interested in different lines of therapy). In some cases, **real-world evidence** can

complement trial data here: for subgroups under-represented in trials, real-world studies or registries can provide additional effectiveness data by the time of launch. An integrated plan might involve running an RWE study in parallel with Phase III – for instance, a compassionate use or early access program data collection – to have extra evidence on how the drug performs in routine practice. Health authorities are increasingly receptive to RWE as part of the evidence package, especially for **external control comparisons** (when a randomized comparator is not ethical or feasible) or long-term outcomes that extend beyond trial duration. Under the new EU HTA regime, leveraging RWE "without borders" – i.e. generating real-world data that can be used across multiple markets – is a way to bolster the transferability of evidence [35]. For example, if a trial only compared the new treatment to placebo, but a certain EU country requires comparison to an active drug, the manufacturer might gather observational data of patients on that active drug from a real-world database to use in an indirect comparison versus the trial data. In short, **every data source is on the table** in the JCA era: RCTs, indirect comparisons, network meta-analyses, observational studies, and modeling all have to be marshaled together to demonstrate the full picture of a therapy's value.

Finally, companies must also adapt their **internal processes and capabilities**. The breadth and technical complexity of a JCA dossier (which has been likened to an expanded version of a German AMNOG dossier covering many more analyses [36] [37]) requires skilled personnel and efficient processes. Companies are investing in training and hiring for roles like evidence synthesis specialists, health economists, and medical writers with HTA experience. Internal governance is being set up to ensure all evidence components (clinical, economic, patient evidence) are developed in sync. Many organizations are treating the JCA preparation as a project on par with the regulatory submission – with its own workstreams, project managers, and dry-run rehearsals to identify gaps. This kind of preparation is necessary to confidently meet the JCA's stringent requirements within the tight timeline. Those who fail to adapt may find themselves unable to **compile a complete, high-quality dossier in time**, which could lead to delays in market access or even decisions to postpone EU launches. In fact, analysts have cautioned that smaller biotech companies, with limited resources, might decide *"not to launch within the EU because they may not be able to handle the workload within the ~3-month timeline"* for JCA dossier submission [38]. All these adaptations underscore a common theme: **never start from a blank page** when approaching evidence generation – start with the end (HTA success) in mind, and design your development program backward from that.

National HTA Bodies Post-JCA: What to Expect

With the JCA handling the heavy lifting of clinical evidence appraisal at the pan-European level, a natural question is: *how will national HTA bodies evaluate new treatments once this joint assessment is in place?* The optimistic view is that much of the clinical debate – about the magnitude of benefit, which trials are relevant, how the new treatment compares to alternatives on clinical endpoints – will already be settled (or at least laid out) in the JCA report. In theory, this allows national authorities to focus on **country-specific elements** like cost-effectiveness, budget impact, and implementation considerations, using a common core of clinical facts. Indeed, the HTA Regulation explicitly states that JCA reports will *"focus on clinical domains only, without any value judgments or conclusions on reimbursement,"* and that member states will add their own analyses of **"cost-effectiveness" and other factors at national level** [4].

In practice, what we can expect is a **hybrid approach** in each country's HTA post-JCA. National agencies will take the JCA report (which will be published around the time of EMA approval) as a key input into their process. They are obliged to *"give due consideration"* to it and **cannot ignore it** [11]. They also cannot ask the manufacturer to re-submit data that were already provided in the JCA dossier [39], which should reduce redundant requests. The **speed** of national evaluations could improve – some countries may initiate certain steps of their HTA as soon as the draft JCA is available, rather than waiting to do everything from scratch after EMA approval. For example, if the JCA concludes that a drug has a

clinically significant improvement in a particular outcome versus standard care, a national body might accept that and move on to evaluating cost-effectiveness with that assumption. In several countries, HTA authorities have indicated they plan to integrate the JCA findings into their assessments immediately, essentially appending a local economic analysis to the JCA's clinical analysis.

However, national HTA bodies will still **apply their own lenses**. They may perform additional analyses on the clinical data if needed for their context. The regulation allows that *"member states are allowed to perform complementary clinical analyses… and apply a different methodology than that of the JCA report, consider different populations, comparators, or endpoints, and request the respective information"* [13]. In other words, if the JCA did not fully address something vital to a country's decision, the country can pursue it. For example, if in Country X the accepted standard of care is markedly different from those considered in the JCA (perhaps a locally used therapy wasn't included among JCA comparators), the HTA body in Country X might request an analysis comparing the new drug to that local therapy – either from the company or by performing an indirect comparison themselves. Or if a country's HTA methodology for interpreting uncertainty (say, handling of surrogate endpoints or survival extrapolation) differs from the approach used in the JCA, they might re-analyze the data according to their own standards.

The crucial point is that any **deviation** a country makes from the JCA's findings must be justified and documented. Member states must *"report on how the joint clinical assessment report has been considered when carrying out the national HTA"* and publicly explain differences [12]. If a national HTA comes to a different conclusion on clinical effectiveness than the JCA did, they need to provide a robust scientific rationale, and that rationale is subject to scrutiny by peers and stakeholders [40]. This is where transparent data sharing could indeed reduce unwarranted divergence: knowing that any inconsistency will be exposed, HTA agencies will likely only deviate if there is a **legitimate reason** (for instance, a relevant study for their population that wasn't included in JCA, or methodological disagreements that can be scientifically defended). If a country cannot adequately justify why their interpretation of the same evidence is different, they risk reputational damage or even legal challenge [14]. In extreme cases, if a manufacturer believes a member state's HTA decision contradicts the JCA without sound scientific justification, the company might have grounds to appeal that decision, pointing to the JCA as evidence [41].

Thus, we likely won't see JCA completely eliminate HTA outcome differences – **national decisions on pricing and reimbursement will still vary**, because countries have different health system priorities and willingness-to-pay thresholds. But we may see a narrowing of differences in the **clinical assessment** portion. For example, it may become less common to see one country declare "no added clinical benefit" while another declares "major clinical benefit" for the same drug (a situation that has occurred in the past). With a common review, there will at least be a shared baseline of evidence interpretation. Divergence may instead manifest in how that benefit is valued or what price is deemed acceptable. Over time, if JCA reports are consistently high quality and encompass the range of national perspectives, they could foster a more convergent view of clinical value across Europe – essentially bringing HTA agencies closer in agreement on the science, even if their policy decisions differ. But achieving this will depend on **continued coordination and trust** among the member state agencies as they use the JCA.

From the manufacturer's side, the post-JCA national phase means HTDs must still be prepared to **engage with each country** on their specific needs. The JCA is not a one-and-done ticket to reimbursement. Companies will need to support affiliates in tailoring the economic models with local cost data, addressing any remaining data needs (perhaps through additional sensitivity analyses or providing local epidemiology), and negotiating outcomes-based agreements if uncertainty remains. In some cases, despite a JCA, a country might request further real-world evidence collection as a condition of coverage (for instance, a managed entry agreement where the drug is reimbursed only with ongoing

data collection on its real-world effectiveness). **Simultaneous launches** across Europe, which JCA encourages, mean that companies will be handling multiple reimbursement negotiations at once – a logistical challenge that requires strong coordination and resource allocation in-country. There may be less staggered learning, but there is also an opportunity: success (or failure) in one market can no longer heavily influence another, since all are moving in parallel off the same JCA. Instead, the critical work happens *upfront* (the integrated evidence planning and JCA submission) and then in a synchronized fashion across markets.

To summarize, national HTA bodies post-JCA will likely operate as follows: use the JCA for the clinical evidence foundation, augment as needed for local context, concentrate analysis on cost-effectiveness and budget impact, and ensure any deviations from the JCA's conclusions are scientifically defendable. HTDs should anticipate remaining **evidence transferability questions** – i.e. "does the JCA evidence apply to my country's population and practice?" – and be ready to address them through additional data or analyses. By doing so, and by engaging collaboratively with each HTA, companies can help the JCA fulfill its promise of *accelerating access* rather than becoming a bureaucratic extra step.

Will JCA End HTA Divergence?

One of the key questions stakeholders are asking is whether having a **joint clinical assessment** will finally resolve the long-standing issue of divergent HTA decisions across Europe. It's a complex question, and the answer is nuanced. **Transparent data sharing** via the JCA will certainly shine a light on differences. When every country is looking at the same core report, it becomes immediately apparent if one country's assessment of the clinical evidence is unusually positive or negative compared to others. This transparency, as discussed, forces agencies to articulate clear reasons for any divergence [40]. It may also facilitate cross-country learning: HTA bodies could adopt insights from each other's comments during the JCA (since many will be involved in the JCA process via the assessor/co-assessor or during peer review). Over time, this collaborative assessment might lead to more **consensus on clinical efficacy**. In areas like defining the appropriate comparator or the clinically relevant endpoints, one could envision convergence – for instance, agreement that a certain trial endpoint truly reflects patient benefit, or consensus that a particular comparator is outdated and can be ignored. If the **HTA Coordination Group** managing JCA works well, it could become an engine for harmonizing methodological standards in clinical evaluation across Europe.

That said, **HTA divergence will not vanish overnight**, and perhaps never entirely. There are several reasons:

- **Different HTA Value Frameworks:** Even with identical clinical evidence, agencies may weigh that evidence differently. For example, some HTA bodies have a higher bar for what they consider a "clinically relevant" improvement (one country might require a larger survival gain to call something a major benefit). JCA will present the data, but the *interpretation* in terms of added clinical value may still differ. Notably, the JCA report itself will **not assign an "added benefit" rating or a clinical score** – it provides the analysis, but avoids value-laden conclusions [4] [42]. Thus, countries will still apply their own grading systems to that analysis (e.g., France's ASMR level, Germany's added benefit categories), which could lead to differing conclusions.

- **Local Context and Priorities:** Health systems have unique priorities and patient demographics. If a country has an alternative domestic therapy or a different standard of care, they might inherently view the new technology's role differently. JCA might include multiple comparators to appease all, but a given country could still focus only on the comparison relevant to them and might disregard others. They could also place different emphasis on certain outcomes (for

instance, a country facing budget pressures might be more concerned with cost offsets from improved quality of life, whereas another might focus on clinical outcomes alone). These contextual factors can create divergence in how the same evidence is valued.

- **Economic and Implementation Factors:** Ultimately, reimbursement decisions hinge on more than clinical efficacy. JCA won't directly resolve differences in willingness-to-pay thresholds or budget impact tolerance. Countries with stricter cost-effectiveness thresholds might still reject or restrict a drug that another country, with a more lenient threshold or higher healthcare budget, is willing to cover fully – even if both agree on the clinical data. These kinds of divergence (access gaps due to economics) are outside the scope of JCA to fix.

However, it is reasonable to expect divergence to **diminish in the clinical realm**. The days of one HTA body saying "we think the trial's results are not relevant" while another says "this trial is robust evidence" should be fewer. All parties will see the same trial critiques and strengths laid out in one document. If JCA works as intended, it could reduce duplicative evidence requests – e.g., multiple countries asking for similar subgroup analyses independently. Instead, those analyses get done once (for JCA) and shared. In that sense, JCA will tackle the *process* divergence (everyone doing their own review) by centralizing it.

Moreover, as mentioned earlier, the requirement for **scientific rationale for differences** is a game-changer [40]. It introduces a mild form of accountability; agencies might hesitate to deviate without strong justification. If, for example, 26 countries accept that Drug A has a mortality benefit based on the evidence in the JCA, the one outlier agency that claims no mortality benefit will come under pressure to explain its position. This could spur more dialogue and perhaps alignment in future assessments.

In conclusion, **JCA will not entirely end HTA divergence – especially on reimbursement decisions – but it is poised to reduce unscientific or avoidable differences in clinical assessments**. Divergence will likely shift to areas outside JCA's scope (economic evaluation, local policy decisions). Success in minimizing divergence will also depend on how well member states collaborate beyond the JCA – for instance, in developing more unified economic evaluation guidelines or sharing best practices for using JCA results. The first few years of JCA implementation (from 2025 onward) will be a learning period, and stakeholders are aware that confidence will build gradually [43]. Like the German AMNOG system in its early days, there may be iterative improvements to the process. Over time, if trust grows that the JCA is rigorous and fair, one could foresee national agencies feeling comfortable placing more weight on it and less on their own duplicate analysis, thereby organically harmonizing outcomes. Until then, HTDs must plan for a scenario where **JCA is a critical foundation but not the final word** – and be ready to navigate a patchwork of national requirements layered on top of the joint assessment.

Handling Evidence Transferability Across Europe

A core challenge in any multi-country assessment is **evidence transferability**: the extent to which clinical data from trials (often global trials) are applicable to each specific country's patient population and healthcare setting. The JCA will produce a single clinical evaluation for all of Europe, but Europe is not monolithic – there are variations in epidemiology, medical practice, and patient characteristics that can affect how relevant the evidence is locally. How will HTA agencies handle this in a post-JCA world? Largely, they will handle it the way they do now, but within the JCA framework's constraints: by looking for **contextualization of evidence** either within the JCA report or via supplemental national analyses.

The JCA process itself attempts to improve transferability by **broadening the evidence base**. As noted, it requires more comparators and subgroups to be addressed than a typical single-country submission

[15]. The idea is that by casting a wide net (covering multiple scenarios), the joint assessment provides each country at least some of the pieces it needs. For example, if Southern European countries tend to use a different comparator than Northern ones, the JCA might include data for both comparators in respective analyses, so each region finds their context addressed. Similarly, if healthcare delivery differs (hospital vs outpatient setting), the JCA might include studies or data relevant to both contexts (when available). The involvement of *all member states in scoping* ensures that **no major perspective is omitted upfront**. In theory, this should improve the "fit" of the evidence to each country compared to a one-size-fits-all analysis.

Nevertheless, perfect transferability is unattainable. Thus, HTA agencies will scrutinize the JCA report for any **mismatches with their local context**. Common questions include: *Are the patient populations in trials similar to those in our country (in terms of demographics, disease severity, comorbidities)? Is the comparator used in trials/JCA reflective of what patients get here? Do differences in healthcare infrastructure affect outcomes (for instance, is the follow-up or concomitant care in trials reflective of local practice)?* If an agency finds discrepancies, they may adjust their appraisal accordingly. They could apply qualitative judgments (e.g., "the benefit might be smaller in our older population") or quantitative adjustments (e.g., using an indirect comparison between the trial comparator and the local standard if those differ).

One approach to addressing transferability is through **additional real-world evidence**. Real-world data from local or regional sources can help validate whether trial results hold true in a given population. For example, if trials were mostly in Western Europe and a CEE (Central and Eastern Europe) country is unsure if those outcomes apply to their patients, data from an observational study in that country could be invaluable. We may see HTA bodies increasingly asking for such data or using registry information in their assessments. The JCA itself may include some real-world evidence, especially for relative effectiveness when RCT evidence is limited or absent. The use of external control arms or indirect comparisons via RWE might become part of joint assessments for areas like rare diseases or certain oncology indications where single-arm trials are common.

Another tool is **statistical adjustment for heterogeneity**. If patient populations differ, techniques like subgroup meta-analysis or meta-regression can be used (for instance, adjusting for a population's baseline risk or certain characteristics). HTA analysts might take data from the JCA and re-analyze subsets more relevant to their country. Because all data submitted in the JCA will be accessible, countries could pluck out what they need (say, outcomes in the subset of patients over 75 years old) to inform their local model. This is still more efficient than each country collecting new data, since the underlying trials are the same; it's more about slicing the data appropriately.

The **HTA Coordination Group** is also providing methodological guidance on how to handle evidence synthesis in a JCA context [44] – for example, guidelines on indirect comparisons and on handling heterogeneity. These guidelines, if adopted widely, could standardize how transferability issues are addressed (so that one country doesn't, for example, reject an indirect comparison that another accepts; ideally they all follow a consistent quality standard).

Critically, the regulation's stance is *not* to force one-size-fits-all. It explicitly acknowledges that member states can consider "different patient populations, comparators, or endpoints" if needed [45]. So the system's flexibility for local context is preserved. The burden is on manufacturers to anticipate these needs: they should **map each PICO in the JCA to the countries that demanded it** [46]. If a certain PICO (e.g. a specific subpopulation vs a specific comparator) is only relevant to a few countries, the manufacturer might plan additional **supplementary evidence** for those markets (perhaps not needed in the core JCA dossier, but ready for local use). For instance, a company might know that only Country Y cares about quality-of-life improvement in patients above a certain age – this might not change the JCA conclusions, but the company could prepare a targeted analysis for Country Y's decision-makers

showing the QoL data in that subgroup. An integrated plan would have identified that requirement early and ensured data were collected to support it [47].

In summary, HTA agencies will handle evidence transferability post-JCA by leveraging the broader evidence included in the JCA, and then addressing any remaining gaps through local analyses or data. **Health technology developers can facilitate this by designing evidence generation to be as transferable as possible** – including diverse patient groups, relevant comparators, and multiple outcome measures – and by engaging with local affiliates to provide any needed additional information. The better the upfront evidence accounts for variability across Europe, the fewer "adjustments" HTA bodies will need to make for transferability. The ultimate goal is that the JCA provides a solid common foundation, and any local tailoring is modest and scientifically straightforward.

Engaging Stakeholders to Build Comprehensive Access Strategies

The scope and pace of the new EU HTA process make one thing abundantly clear: success will require **early and ongoing engagement with stakeholders** beyond the manufacturer's four walls. "Stakeholders" in this context range from regulators and HTA bodies to patients, clinicians, and payers. Engaging these groups throughout the product lifecycle can greatly enhance the relevance and credibility of the evidence generated, and ensure that no major expectation is missed.

A key avenue for engagement is the **Joint Scientific Consultation (JSC)** process (also known as parallel EMA-HTA scientific advice). Alongside the HTA Regulation's rollout of JCAs, a framework for JSCs is being established where sponsors can seek simultaneous advice from regulators and HTA representatives on their development plans [48]. This is an invaluable opportunity to de-risk the evidence strategy: by presenting your planned trial design, comparators, and endpoints to both EMA and HTA experts beforehand, you can obtain feedback on whether those plans will satisfy both sets of requirements. For example, an oncology company might ask in a JSC if a progression-free survival endpoint will be acceptable to demonstrate benefit, or if overall survival (or another outcome) will be needed by HTAs. They can learn if a certain comparator arm is strongly advised to be included to meet HTA needs. The **output of a JSC is advice** (not binding, but highly informative) that can guide protocol adjustments or supplemental data collection long before pivotal trials are locked in. Companies that take advantage of these consultations are effectively doing a "preview" of JCA expectations, which aligns perfectly with the IEGP philosophy – no surprises at the end. HTA bodies have indicated that the parallel consultation mechanism is where they expect companies to bring questions about evidence generation choices, and in return, companies get a clearer picture of the *future landscape* into which their product will launch [49].

Beyond formal consultations, **ongoing dialogue with national HTA agencies** (where possible) and payers remains important. Even with JCA, each country's decision-makers appreciate early engagement. In some countries, there are early dialogue or advice forums at national level (for instance, France's Haute Autorité de Santé offers scientific advice; NICE in England has an Office for Market Access to discuss evidence plans). Engaging in these can provide local insights – such as country-specific preferences for health economic modeling or data on resource use – which can be incorporated into the evidence plan. Moreover, as the Phastar blog suggests, staying *"informed about the latest developments in HTA regulations and participating in consultations, workshops, and forums"* is crucial [50]. The HTA landscape is evolving, and being part of that conversation (e.g. through industry associations or public consultations on HTA methods) allows companies to anticipate changes and help shape practical solutions.

Patient and clinical expert engagement is another pillar of a comprehensive market access strategy. The JCA process itself builds in patient and clinical expert input – patients and clinicians will be involved in scoping and assessing the evidence alongside the assessors [51]. This reflects a broader trend of including patient perspectives in HTA to ensure that what is measured truly matters to those affected. HTDs should likewise involve patients and treating physicians early on: for example, conducting patient preference studies, advisory boards, or incorporating patient-reported outcome measures that capture quality of life or symptom burden that patients prioritize. These insights can not only shape a more patient-centered evidence package but also strengthen the narrative in HTA submissions about the value of the new treatment. If a patient advocacy group can say, "This new therapy addresses an outcome that patients care deeply about, which previous studies overlooked," that can be compelling in an HTA context. Clinician engagement helps ensure that trial endpoints and comparators are clinically relevant and that any assumptions in economic models (like treatment pathways) reflect real practice. Essentially, external stakeholder input makes the eventual **value story** more robust and credible.

Finally, an often overlooked but critical aspect is **internal stakeholder alignment** – ensuring all parts of the organization are on board with the new way of working. As Ruairi O'Donnell notes in *Pharmaceutical Executive*, companies need to invest in *"employee education and engagement… market access and HEOR functions, as well as commercial, medical, regulatory, and others, all need to understand the changes and participate in preparation."* [52] [26]. A comprehensive strategy means the clinical development team isn't just aiming for regulatory success, but is equally accountable for HTA success; the commercial team understands the evidence and can communicate it to payers; the affiliates in each country are prepared to execute the strategy concurrently. This internal alignment, underpinned by strong communication, is what allows the external stakeholder engagement to be effective. When a company shows up to a scientific advice meeting or an HTA negotiation with a unified voice and a deep understanding of the evidence, it builds confidence with the stakeholders on the other side of the table.

In summary, **external stakeholder engagement** in the JCA era involves: leveraging formal advice processes (JSCs and national consultations) to align on evidence needs; collaborating with patients and clinicians to ensure the evidence generated is meaningful and resonant; and maintaining open channels with HTA bodies and payers throughout development to preempt issues. Together, these efforts help build a *comprehensive market access strategy* that leaves as little to chance as possible. In a world where you no longer have the luxury of learning country-by-country, these stakeholder insights become the surrogate for that sequential learning – you gather the learnings upfront, from those who will eventually judge your product, and integrate them into your plan.

Conclusion

The advent of Joint Clinical Assessments in Europe is transforming how we approach market access. No longer is the launch of a new health technology a stepwise march through individual countries' hoops; it is now a **unified sprint**, demanding thorough preparation and coordination. To succeed in this environment, pharmaceutical and biotech companies must **"never start from scratch"** – meaning, never start a trial, a submission, or a value dossier without a clear, integrated view of the end goal. By adopting an Integrated Evidence Generation Planning approach, HTDs can ensure that every study and data point serves multiple masters: the regulator, the joint assessor, and the national payer. This approach turns evidence generation from a reactive, fragmented process into a **strategic accelerator** for market access [53].

Europe's experiment with JCA holds great promise. If implemented well, it can **accelerate access** to important new treatments by streamlining evidence review and pushing all stakeholders to higher standards of rigor and transparency [7] [54]. But the promise of faster approvals and reimbursement

will only be realized if developers rise to the occasion and **navigate the new landscape thoughtfully** [7]. That means investing early in the right evidence, engaging in cross-border scientific dialogues, and staying agile as we learn from the first JCA cases. The initial roll-out (limited to certain product classes) gives everyone a chance to adapt. HTA bodies, too, will be on a learning curve – they will need to collaborate like never before, align on methodologies, and communicate clearly with one another and with industry. In time, trust and efficiency should build.

For now, companies preparing for simultaneous launches in Europe should heed the key lessons emerging: *Plan globally, execute locally.* Ensure your development program is globally informed (by diverse stakeholder input) and yields evidence that can be localized. *Build in redundancy and robustness.* With uncertainty around how each country will ultimately use the JCA, having extra data (say, an additional comparator or longer follow-up) could be the difference between a smooth national HTA and a contentious one. *Stay human-led even as processes speed up.* The use of AI tools and systematic "deep research" methods (like GPT-driven literature reviews or evidence mapping) can greatly aid in handling the technical groundwork of these complex submissions – structuring large volumes of data and scanning for gaps – but human expertise remains irreplaceable for interpretation, strategy, and ethical judgment. As we embrace new technology and new regulations, keeping the human perspective in control is vital, especially in healthcare decisions.

In conclusion, the post-JCA European market access scene is one of **"faster, smarter, but still human-led"** decision-making. Health technology developers that embrace integrated planning, foster stakeholder partnerships, and commit to scientific excellence will find that they *no longer need to start from zero* in each market – instead, they will be positioned to launch across many markets with a strong, consistent value demonstration from day one. The end of sequential launch learnings need not be a liability; with the right approach, it becomes an opportunity to **think broader and act faster**, delivering innovations to patients across Europe in a more unified and timely way than ever before. The roadmap is new and undoubtedly challenging, but it leads toward a more efficient and equitable healthcare future – one where valuable therapies reach those in need with less delay and uncertainty. Achieving that is a shared responsibility, and the journey has just begun. [55] [56]

Sources: The insights and data points in this paper are drawn from a range of official and expert sources, including the European Commission's HTA Regulation and guidance documents [4] [2], peer-reviewed analyses of the new EU HTA system [13] [12], industry white papers and thought-leadership pieces on evidence planning [8] [9], and commentary from HTA experts and consultancies who are at the forefront of JCA preparation [15] [57]. These references collectively underscore the message that **early, integrated evidence generation and collaborative engagement** are keys to thriving in the post-JCA landscape.

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