Implementation of the New European Health Technology Assessment Regulation (HTAR)

The main challenges in the preparation of the new European Health Technology Assessment Regulation (HTAR) and how ProPharma can help you succeed with your product launch in Europe.

In 2021, the adoption of the legislation for joint European Health Technology Assessment (EU HTA) initiated a new era for HTA assessments at a European level. This new regulation process is potentially the biggest change in the last ten years for European market access.

Background & Timeline for Implementation

The new regulation process is called the HTA Regulation (HTAR), and it aims to enable a joint perspective among EU member states on clinical aspects in the development of medicinal products, in vitro diagnostics (IVDs), and high-risk medical devices. The HTAR incorporates Joint Clinical Assessments (JCA), Joint Scientific Consultations (JSC), horizon scanning activities, and voluntary cooperation in areas outside the scope of mandatory cooperation.

This white paper will only focus on the JCA and JSC, which are crucial components for all companies who plan to submit their Market Authorization Application (MAA) to the European Medicines Agency (EMA). The horizon scanning activities on the other hand, is a work performed by the European Commission (EC), to allow the early identification of emerging health technologies that are likely to have a major impact on patients, public health and healthcare systems. And the voluntary cooperation is a collaboration between the EU member states in areas such as the development and implementation of vaccination programs and the capacity building of national HTA systems.

The HTAR will make it mandatory for companies to submit a JCA to the EC in parallel to their MAA filing to EMA. The JCA will consist of a clinical, epidemiological and safety section and be published by the EC. Subsequently, the JCA will be part of the HTA decision-making at the national level.

> As of 2025, companies with products indicated for the treatment of cancer and/or an Advanced Therapy Medicinal Product (ATMP) will be required to prepare and submit a JCA dossier.

The Time to Begin Preparing for HTAR Implementation Is Now

The implementation of the HTAR will be a staggered process. As of 2025, companies with products indicated for the treatment of cancer and/or an Advanced Therapy Medicinal Product (ATMP) will be required to prepare and submit a JCA dossier. Next in line will be orphan drugs, planned for 2028, and all remaining drugs, as of 2030.

With the HTAR implementation in 2025 drawing ever closer, the initiation of parallel scientific advice meetings has already begun. As such, it is time for companies to begin implementing changes at an EU or global level to meet the needs of the JCA. Currently there are significant uncertainties around the process remaining, and the major concern among companies is that the increased time and necessary resources will hinder patient access to new health technologies.

In this white paper, ProPharma's regulatory and HTA experts discuss the challenges and effects of the HTAR on companies with health technologies in the pipeline, and actions to consider ensuring successful market access and avoid any product launch delays.

Path to Successful European Product Launch

Although the HTAR implementation is looming and parallel scientific advice meetings have already initiated, we have observed that only a small number of companies have started to consider the changes that may be needed at an EU or global level to meet the demands of the JCA. What are the reasons for the apparent lack of engagement from the companies and how can we improve the chances for approval and market access upon the implementation of the HTAR process?

ProPharma can help you ensure your company is ready for the new requirements coming early next year by offering you the following four steps approach to a successful product launch. These four steps are based on what the HTAR requires from the companies in the new procedure.

Step 1: Introductory Training on HTAR Rules & Implications

To begin the process, you must start with an introductory training on the HTAR process and its implications. It Is critical that the Individual conducting the training Is fully versed and completely understands the entire process as well as the consequences of non-compliance.

Step 2: Conduct a Technology-Specific Scoping Study

It Is important to ensure you are well prepared for the assessment scope by conducting a technology-specific scoping study and developing a plan for the JCA preparations including potential budget outcomes and timelines.

Step 3: Workshop Preparation to Define Optimal PICO(s)

The preparation of the technology-specific scoping study and plan for the JCA dossier development will be arranged in more detail as part of this workshop and next steps forward will be agreed and discussed.

Step 4: Implementation of the Plan

The PICO frameworks, and the budget and timelines for the JCA development that have been outlined in Steps 2 and 3 will be implemented.

We support our clients by offering our unique strength in combining our regulatory and market access expertise to optimize a fast and efficient product launch and patient access. Our staff of experienced subject matter experts, including former regulatory and HTA agency employees, are well-informed on the latest evolutions of market access and HTA regulations.

Potential Challenges & Solutions Associated with HTAR Compliance

Uncertainties Around the EU HTA Process

While companies are well aware that the EU HTA process is going to change, significant uncertainties remain surrounding the requirements for placing innovative health technologies on the market in the EU. For example, it is not specified how comparators, endpoints, and subgroups for the different member states (MSs) will be selected for the JCA preparation. Therefore, it is also challenging to estimate the amount of additional work the HTAR will require of the companies despite the communication that has been published on the process and timelines.

Approximately two months after the submission of an MAA to the EMA, each member state will define their assessment scope and PICO [Population, Intervention, Comparator(s), clinical Outcome(s)] framework for the JCA. It is still unclear how extensive this part of the preparation for the JCA dossier will be.

The assessment scope proposal is prepared by the assessors and will be shared with the members of the JCA Subgroup. The EU HTA Coordination Group comprises of four different Subgroups. The JCA Subgroup, the JSC Subgroup, the Methodology Subgroup, and the Identification of emerging health technologies Subgroup.

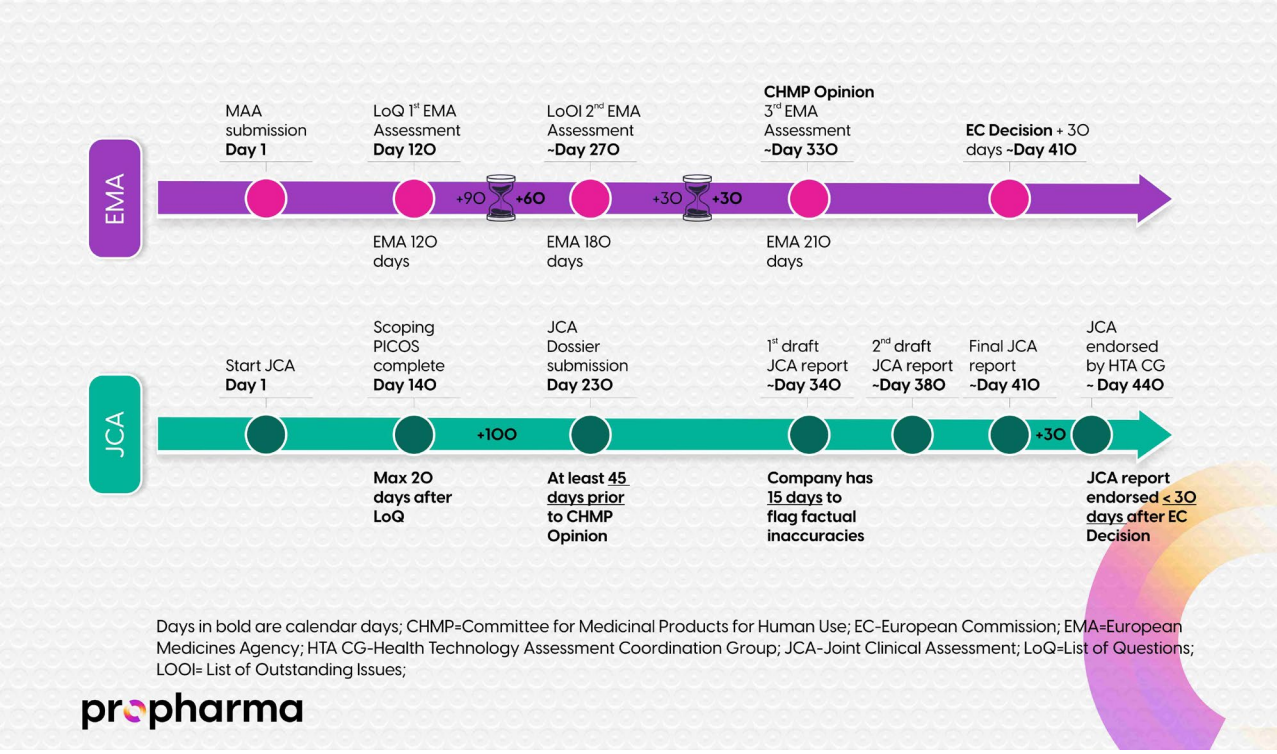
The JCA Subgroup consists of representatives from the member states and is directly responsible for the delivery of the JCA reports. The different PICO frameworks are then presented to the companies, and the companies will have 100 days to develop their JCA dossier.

The JCA steps from the Implementing Act include:

- Start: JCA process starts when the MAA dossier is submitted to EMA
- EU HTA Coordination Group appoints a Subgroup
- Subgroup appoints assessor and co-assessor from 2 different member states
- PICO frameworks are outlined with involvement of 27 member states
- JCA dossier preparation by the company
- JCA dossier submitted by the company 45 days before CHMP opinion
- JCA dossier evaluated by the assessors
- Input stakeholder network
- EU HTA Coordination Group approves the JCA dossier
- Report to the EU HTA Coordination Group
- End: Publication by the European Commission < 30 days since the European Product Assessment Report (EPAR) has been approved by EMA

More details on the timelines for this process are available in Figure 1, on the following page.

Figure 1: Timelines for the parallel JCA and EMA process



At ProPharma, we can support you with proactive planning for the JCA process ahead of your MAA submission to EMA in advance of the mandatory implementation of the JCA process. This will ensure you are well prepared for the assessment scope and PICO frameworks. By conducting a technology-specific scoping study, a PICO workshop, and developing a plan for the JCA preparations promptly, we can outline potential budget outcomes and expected timelines, ensuring that you are fully equipped for the final preparation and submission of the JCA within the defined 100 days.

Concerns of an Increase in Time and Resources Rather Than Faster Patient Access

The aim of a JCA is to enable a joint perspective on clinical aspects of development of health technologies, accelerating the process for patient access, and ensuring consistency in assessing new health technologies. However, many predict the HTAR process will be more time and resource consuming due to the early timing of the JCA relative to the MAA, the very challenging procedural timelines, and the opportunity for the JCA Subgroup to request that additional information is provided at almost any time during the process.

In order to reorganize your internal resources and skills appropriately to accommodate the upcoming requirements in a timely manner, ProPharma can support with the strategic planning and preparatory steps for the regulatory MAA submission to EMA jointly with the upcoming JCA. These steps are based on what the HTAR requires from the companies in the new procedure and will help you create a successful market access plan in Europe.

Complex Requirements and Short Timelines for Compliance

After the PICO frameworks are presented to the companies, organizations will have 100 days to develop their JCA dossier by incorporating safety, clinical, and epidemiological data through performance of systematic literature reviews (SLRs) and indirect treatment comparisons (ITCs) following each PICO framework. The draft template of the JCA report from the EC that was published for review is extensive. Although the national specific HTA sections such as health economic modeling and relative costs-effectiveness are not covered by the JCA, the JCA preparation still requires complex evidence synthesis and comprehensive SLRs which are time consuming and not something that is normally achieved within a 100-day timeframe.

In addition to these proposed tight deadlines, the assessment scope might be subject to change by the JCA Subgroup's appointed assessor with the co-assistance of the co-assessor. For example, his can occur when there is a change to the therapeutic indication(s) initially submitted to the EMA. It is up to the assessors to decide whether that change affects the assessment scope and then inform the JCA Subgroup. These factors add to the complexity of the process and may be expected to substantially impact the progress of the procedure.

Price setting, health economics, and full reimbursement in each market is still performed at a national level and usually commences following Committee for Medicinal Products for Human Use (CHMP) opinion. For transparency, each MS is obliged to report how the JCA was used in national decision making and is not allowed to redo/require analyses already evaluated in the JCA.

Here there is still a risk that data from the JCA are not detailed or accurate enough to allow for national decision-making due to further country-specific data and HTA requirements on each national level. Some examples include sub-populations and specific target populations, which may vary from country to country based on factors such as demographic differences. Moreover, clinical care may be very different among the EU member states depending on national choices for reimbursement, as an example.

Indirect treatment comparisons on subgroups will still need to be tailored to the specifics of the MSs that have different requirements for the health economic aspect of national HTA decision-making. The assessment scope and PICO frameworks that represent all European healthcare systems are therefore a main challenge. There might still be countries which will aim to maintain their own assessments where additional national HTA dossiers with country-specific demands will be expected.

To overcome these issues, ProPharma has a multidisciplinary scientific team of European regulatory and HTA consultants with strong scientific skills and extensive experience in each national clinical and health economic requirements. As such, we are uniquely positioned to guide you through the process, developing a customized development plan and accelerating your product's approval.

Value of Joint Scientific Consultations and Parallel EMA/HTAb Scientific Advice Meetings

Joint scientific consultations (JSC) are an opportunity to engage with HTA bodies (HTAb) representatives either alone or jointly with EMA representatives; this will be implemented at the same time as the JCA in January 2025. However, during the interim period, prior to JSC's implementation, JSC can be conducted in parallel with EMA Scientific Advice meetings, termed Parallel EMA/HTAb Scientific Advice.

ProPharma's Regulatory Sciences team of experts can support you with the preparation and participation in the ongoing Parallel EMA/HTAb Scientific Advice process. EMA/HTAb Scientific Advice is strongly recommended to discuss any issues of concerns from EMA and HTAb to ensure that company's PICO and trial designs are accurate to facilitate the development plans.

Expert European Regulatory Consultants with Extensive HTAR Knowledge

Contact us today and apart from our immediate capability to support you with the preparation steps for the new HTAR implementation, we can also help you with anything from early regulatory and HTA interactions, to full MAA support to EMA, JCA preparations to the EC, and national HTA preparations and submissions. Our unique ability to support your company throughout the full product life cycle enables us to help you achieve a successful product launch across the EU and beyond.