Public Policy Statement | November 2023

European Union Health Technology Assessment Regulation

MSD welcomes the European Union's Health Technology Assessment (EU HTA) Regulation that should have solid Member State commitment to reduce demand for duplication of clinical relative effectiveness assessments at the national level. MSD supports the practice that Member States use the joint clinical assessment report to aid understanding of the clinical value of the health technology. We recognize that Member States will continue to be solely responsible for drawing conclusions on the overall clinical value of the assessed health technology. This should be based on the holistic evaluation of the EU level joint clinical assessment report combined with their country-specific supplementary (but ideally, not duplicative) assessment incorporating local information on socio-economic and financial impact, i.e., the appraisal which will inform the national pricing and reimbursement decision making.

Background

In recent years, patient access for medicines and vaccines in European Union (EU) Member States after marketing authorization has become increasingly complex, with national Health Technology Assessment (HTA) agencies using different methods and criteria to inform national pricing and reimbursement decisions. This current complexity in European HTA is not unlike the regulatory approval environment in the EU before the Centralized Approval mechanism was created through the European Medicines Agency (EMA). With the EMA in place, the requirements for regulatory approval across Europe are now systematically well understood by all stakeholders.

The complexity of HTA requirements across EU Member States has led to the adoption of an EU Regulation on HTA. The adoption recognizes that while regulatory approval addresses the question of whether or not the benefits of a new product outweigh the risks, more could be done to address the questions that remain regarding relative effectiveness that HTA bodies seek to address, and to harmonize the HTA process and reduce undue duplication between national HTA assessments.

Industry has supported the stepwise harmonization of the clinical dimensions of HTA, including development of standards and guidelines. The EU HTA Regulation is the culmination of more than 10 years of collaboration at the EU level on HTA. The Regulation establishes a Coordination Group made

up of Member State representatives who will carry out assessments of clinical effectiveness, starting gradually in 2025 with selected centrally approved medicines, and expanding to assessment of all centrally approved medicines upon full application in 2030. The Regulation presents a unique opportunity to ensure a degree of HTA harmonisation throughout the European Union and is intended to lead to faster patient access to new innovative medicines and to create synergies in clinical evidence generation needs and assessments by Member States.

The Regulation states clearly that a core objective is to remove existing divergences in clinical assessment across Member States through harmonization at EU level. To be effective therefore it is critical to align on methods and the core principles of national application across all Member States. As the details of how the regulation will be applied become clearer, industry is disappointed that these foundational ambitions, set forth by the European Commission in its original proposal, have been diluted and that there continues to be the risk of an unpredictable, duplicative and complex system whereby Member States can decide on a case-by-case basis if and how they commit themselves to use jointly conducted clinical HTA assessments.

The European Commission considers the EU HTA regulation to be the very first output of the EU Pharmaceutical Strategy with the declared objectives to foster patient access to innovative and affordable medicines and to support the competitiveness and innovative capacity of the EU's pharmaceutical industry. As we move forward into the implementation period of the HTA Regulation, we must continue to keep the objective of timely access to innovative treatments in mind and avoid further delaying timelines at national level.

Principles

The overall aim of the future assessment at the pan-European level should be to ensure that there is timely and appropriate access to effective new medications that improve health outcomes for patients. To meet this objective, we believe that several conditions would need to be fulfilled or addressed at EU and/or Member State level during the current three-year implementation phase of the Regulation:

Procedural Principles

- **The regulatory evaluation and assessment must remain a separate process without HTA influence.** The role of the regulator is to focus on benefit-risk balance, not to limit access for any patient that may benefit. However, collaboration and dialogue between regulators and HTA assessors at the Pan-European level is critical to allow for an exchange of information to ensure timely HTA outputs and key learnings on the scientific reasoning for an opinion. The dialogue should be constructed so that it avoids undue influence but supports mutual understanding. At the same time, any Pan-European HTA assessment should not impact the regulatory decision, approval process or timeline. There is also an opportunity to increase dialogue between regulators, HTA assessors and the technology developer.

- **Any follow-on assessment at the Member State level should recognize the clinical assessment made at the Pan-European level.** Member State assessments should build on the joint clinical EU assessment and consider those data for their national appraisals.

- **National adaptation should be ensured and streamlined to be able to use the EU level outputs**; we call on Member States to ensure new processes are put in place in advance and transparently communicated, and that existing templates and national policies are adapted (where needed) to optimize the timing of the overall EU and national full HTA process.

- **Any assessment of economic value (including cost-effectiveness) of a health technology must remain at the Member State level as long as the financing of healthcare is in the remit of Member States** according to TFEU 168. It is critical that any assessment at the Member State level recognize the HTA assessment made at the Pan-European level. At the same time, it is equally important that Member States' assessments take into account country-relevant economic and societal impacts, and the country's own burden of disease and national treatment guidelines.

- The Pan-European HTA process **needs a balanced conflict of interest framework** to ensure that the unique expertise and knowledge of patients, clinicians, and health technology developers (marketing authorization applicants/holders) on disease context and evidence development can be reflected in the joint EU HTA work.

- **Marketing authorization applicants/holders should be meaningfully included in the assessment process.** Experience has shown that HTA assessments are less effective if there is no explicitly defined opportunity for the marketing authorization applicant/holder to consult with assessors and if the assessment plan cannot be "informed" by the knowledge of a marketing authorization applicant/holder about the technology. Insights from marketing authorization applicants/holders throughout the process (e.g., scoping, PICO definition, touchpoints throughout the process, opportunity to comment on evidence interpretation, appeals mechanism etc.) is a key element of a high-quality assessment.

Methodological Principles

- **The HTA assessment at the Pan-European level should employ internationally accepted measures of clinical effectiveness for the therapeutic area in question.** It should be underpinned by 'fit-for-purpose' methodology (not a summation of Member State needs) leading to high quality outputs that can be used by diverse national HTA bodies. Methodological guidelines should be aligned to approaches required for highly innovative portfolios (Cancer, ATMP, OMP, Vaccines, etc.); given that these approaches may change over time, the methodological guidance needs to retain flexibility.

- **The HTA assessment at the Pan-European level should be evidence-based** and reflect the core values of HTA including transparency, good governance, involvement of stakeholders (including scientific leaders and patient representatives), realistic handling of uncertainty, inclusion of a wide range of evidence and outcomes, and reflection of a full societal perspective.

- Methods of clinical assessment, including which PICOs (Population, Intervention, Comparison, Outcomes) are in scope, should be discussed and evaluated by the full range of relevant

stakeholders, including industry. **To prevent unintended consequences, the evaluation of clinical assessment methods should consider the impact on access, outcomes for patients**. The approach to the scope of the assessment should take into account the risks of over-interrogating data which can lead to uninformative or misleading outputs. Over-interrogation of clinical data, using multiple populations/subgroups, comparators, and outcome measures, may lead to situations where patients, providers, and developers of clinical guidelines become overwhelmed with the available information and unable to interpret the evidence appropriately[i] and can also be methodologically questionable.

Implementation Principles

- **Sufficient capacity and appropriate resources for joint scientific consultations should be enabled to allow any marketing authorization applicant/holder access to such a process.** Joint scientific consultations remain a key element in the framework. As well as providing an opportunity to establish evidence requirements for the marketing authorization procedure and joint clinical assessment at an early stage during the drug development process, it is also crucial as a means of allowing companies to plan and carry out studies in a manner that meets the criteria for marketing authorization and HTA specifications.

- **Careful consideration needs to be given to ensuring that both the national HTA agencies and the regional assessors have sufficient time, training, and skills to conduct the joint clinical assessments**. The current proposals point to the need to rapidly evaluate complex information in a limited time, and ensuring availability of well-trained, appropriately skilled assessors representing all Member States to undertake meaningful joint assessment processes is critical to the success of the Regulation. In addition, all involved stakeholders including national HTA agencies, regional assessors, scientific leaders, patient representatives and health technology developers have sufficient time, training, etc.

- **Progress in terms of implementation and specifically the added value of the** implementation of the **regulation needs to be systematically and continuously monitored.** Identified shortcomings should trigger relevant adjustments as early as possible, not just years after its initial application in 2025.

[i] Oddens BJ, Agaku IT, Snyder ES, et al. Exploratory analyses of clinical trial data used for health technology assessments: a retrospective evaluation. BMJ Open 2022; 12:e058146. doi: 10.1136/bmjopen-2021-058146