EU HTA Regulation: Opportunities and Limitations for Advanced Therapy Medicinal Products

Authors: Marie-Pierre Petitjean[1], Sylvie Bozzi[1], Celine Fernandez[1], Ian Keyzor[3], Christelle Pierrot[3], Christopher Mann[2], Jon Giblin[2].

[1] Sanofi

[2] Asphalion

[3] Astellas

Abstract

The European Union Health Technology Assessment Regulation (EU HTAR), in force since January 2025, represents a major policy milestone and aims at accelerating EU patients' access to innovative therapies across the European Union. Advanced Therapy Medicinal Products (ATMPs) are positioned at the forefront of this regulatory transformation, as they are included in the first wave of mandatory Joint Clinical Assessments (JCAs). This section summarizes the ARDAT consortium's views on the opportunities and limitations of the EU HTAR for ATMPs.

It highlights the regulation's potential to harmonize HTAs and foster collaboration among HTA bodies, regulators, and various stakeholders, while also addressing significant challenges related to uncertainty, timeframe, methodological adaptation, and capacity constraints. Particular attention is given to the relevance of Scientific Consultations (JSCs), evidence generation strategies, and the need for adapted assessment methodologies for ATMPs, especially in contexts of limited long-term data. The paper concludes by outlining key discussion questions relevant for further dialogue, implementation, evidence generation, and conditional early access pathways.

1. Introduction and Objectives

The discussion of EU HTA Regulation within ARDAT reflects the strategic importance of the new regulation for the development, and access of advanced therapies in Europe. Since its entry into force in January 2025, the EU HTAR has aimed at expediting patients' access to innovative medicinal products. These objectives are closely aligned with the ARDAT consortium's mission to accelerate research and development for advanced therapies.

ATMPs occupy a central role in the early implementation of the regulation. They are part of the first wave subject to mandatory Joint Clinical Assessment under the stepwise implementation of the EU HTAR. As such, ATMP developers are among the first stakeholders to experience both the benefits and constraints of this new system. While a formal review of this regulation's implementation is planned under Article 31, with a European Commission report expected in January 2028, this review is still distant, making early feedback and dialogue particularly valuable.

The position paper is designed to present the ARDAT consortium's perspectives on the opportunities and limitations of the EU HTAR and to foster a potential exchange with HTA bodies on key points for consideration.

2. Opportunities Introduced by the EU HTA Regulation

2.1 Harmonization and decreased timelines to access through Joint Clinical Assessment

One of the most significant opportunities offered by the EU HTAR is its role as a key first step toward harmonization of access across the European Union. The introduction of Joint Clinical Assessments creates a harmonized clinical evidence base that can be used by Member States, reducing fragmentation and variability in clinical value evaluation.

By decreasing duplication of clinical assessments at national level, JCAs have the potential to shorten timelines for patient access to therapies. This benefit is particularly relevant for ATMPs, where development pathways are complex and time-sensitive. The regulation′s success in this regard is closely linked to the effective avoidance of duplication of assessments.

2.2 Strengthened Collaboration among HTA Bodies and various Stakeholders

The EU HTAR establishes a structured basis for collaboration across HTA bodies, notably through both JCAs and Joint Scientific Consultations (JSC). This collaborative framework is seen as an opportunity to align expectations, methodologies, and evidence requirements across jurisdictions.

The relevance of the collaboration with other stakeholders is particularly emphasized in the context of JSCs. Engagement with developers and patients provides a forum for addressing scientific and methodological challenges early in development. Collaboration with the European Medicines Agency (EMA) is highlighted as especially important and relevant for ATMPs to address their unique development and access challenges. Parallel and coordinated scientific interactions can support better alignment between regulatory and HTA perspectives.

Systematic patient involvement is identified as a key strength of the EU HTAR framework. Incorporating patient perspectives is essential for capturing outcomes that reflect real-world experiences and unmet medical needs, particularly in rare and severe conditions often targeted by ATMPs.

2.3 Methodological Adaptation

The regulation explicitly recognizes the need for methodological flexibility. Recital 24 and Articles 4(1) and 4(4) specify that assessment methodologies shall consider the specificities of the health technology, when data are not readily available. This provision is particularly relevant for orphan medicinal products, vaccines, and ATMPs, where limited patient populations and evolving evidence bases are common. Such flexibility creates an opportunity to develop adapted and innovative assessment approaches.

3. Limitations and Challenges of the EU HTAR

Despite its promise, the EU HTAR presents several limitations that may affect its effectiveness in practice, particularly during early implementation.

3.1 Uncertainty

Uncertainty remains a central challenge, both in terms of interpretation of regulatory requirements and the outcomes of assessments.

While JCAs are intended to reduce duplication, there is concern that incomplete alignment with national processes could perpetuate parallel assessments rather than eliminate them.

Timeliness is another critical issue. Constraints related to fixed timeframes and procedural timelines may limit the ability of developers and HTA bodies to fully address complex evidence questions, especially for ATMPs with evolving datasets.

There is still uncertainty about national HTA adaptation and national HTA bodies capacity constraints.

The successful implementation of the EU HTAR depends heavily on the adaptation of national HTA processes. Differences in readiness, capacity, and resources across Member States may create bottlenecks and inconsistencies in how JCAs are used at national level.

3.2 Constraints Related to Joint Clinical Assessments – Additional Complexity

For health technology developers (HTD), the introduction of JCAs represents a significant change in ways of working, with substantial implications in workload and resource allocation. The need to address multiple PICOs (Population, Intervention, Comparator, Outcome) within a single JCA adds further complexity.

The JCA timeframe and timelines constraints versus the Marketing Authorization Application assessment by the EMA introduces additional operational challenges such as the need to consider late revisions of the Summary of Product Characteristics (SmPC), which may complicate alignment between regulatory approval and HTA assessment.

3.3 Constraints Related to Joint Scientific Consultations – Predictability and timelines of advice

While JSCs are recognized as valuable, their practical implementation is subject to several limitations. Predictability and timeliness of advice are key concerns, as are the limited number of available consultation slots, based on dedicated request submission periods, also in limited number over the year.

These constraints raise questions about the adequacy of JSC opportunities in relation to clinical development timelines, particularly for ATMPs. The need for sufficient clinical data to support meaningful consultation may limit early engagement, even though early advice would be valuable for shaping registration trial design.

Overall, opportunities for collaboration and interactions between HTA bodies and HTD are still limited.

3.4 ATMP-Specific Challenges

ATMPs present particular challenges for HTA due to uncertainty in assessing long-term clinical added value at the time of launch. Limited long-term data make it difficult to demonstrate sustained benefit, yet timely access remains a priority. ARDAT highlights the need for adapted assessment methodologies that are harmonized across Member States to address this uncertainty in a consistent manner.

4. Key Questions and Areas for Further Discussion

The ARDAT consortium has identified several key points for consideration to support potential future dialogue and best practices.

4.1 Early Implementation of the EU HTAR

With the regulation in force and JCAs mandatory for ATMPs, HTA bodies are invited to share feedback on the EU HTAR early implementation. Key points of interest include what is working well and what requires improvement to build best practices for demonstrating value.

Initial experiences with JSCs were also identified as an important source of learning and ARDAT believes that, while respecting confidentiality aspects, some feedback could be made public.

4.2 Transformation of Evidence Generation

The requirement for Member States to "give due consideration" to JCA outcomes raises important questions about how evidence generation strategies for ATMPs will evolve. ARDAT emphasizes the need to explore collaborative opportunities among stakeholders in the ATMP ecosystem to develop innovative and adapted assessment methodologies, particularly for gene therapies with limited long-term data.

Integrating patient-centred evidence and outcomes was highlighted as a priority for reflecting real-world patient experiences.

In parallel, the alignment of emerging standardization efforts in ATMP development, including tools and standards under development in the ARDAT consortium, with the JCA framework was identified as a means to establish consistent evidence requirements across the EU.

4.3 Conditional Early Access Pathways

Finally, ARDAT would like to raise the potential opportunity within the EU HTAR to consider conditional early access schemes for ATMPs, as proposed in the EFPIA/EUCOPE joint statement. From a general perspective, the definition of roles and responsibilities remains an open question of particular interest. From an ATMP-specific standpoint, the

possibility of elaborating such opportunities during parallel EMA/HTA Coordination Group JSCs was identified as an area for further exploration.

5. Conclusion

The EU HTA Regulation represents a transformative step for HTA in Europe, with ATMPs at the forefront of its implementation. While the regulation offers clear opportunities for harmonization, collaboration, and methodological adaptation, it also introduces significant challenges related to uncertainty, capacity, and operational complexity. Sharing of early experience, continued dialogue, and collaborative development of adapted methodologies will be critical to realizing the regulation's objectives and ensuring timely and equitable access to advanced therapies for patients across the EU.