What You Need to Know as the European Union Embarks on Joint Health Technology Assessment (HTA)

Outlining the implications for biotech companies

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Facing the "Fourth Hurdle"

Member states of the European Union benefit from a centralised marketing authorisation process for medicinal products. Also, since its implementation in 1993, the European Medicines Agency (EMA) has assured pharmaceutical companies the right to commercialise products that underwent a centralised marketing authorisation in the second largest (and most diverse) single pharma market.

However, it remains "the responsibilities of the Member States [to define] their health policy and for the organisation and delivery of health services and medical care. The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them" (Art. 168, "Treaty on the Functioning of the European Union" (Lisbon treaty)). According to the subsidiarity principle, reimbursement decisions are made at a national level, and EU-wide collaboration around pharmaceutical pricing is seen only in terms of international reference pricing (IRP). That leaves companies that have proven the safety, efficacy and quality of their product in a situation in which they have the right to commercialise in the European Union but still face the "fourth hurdle" of a multitude of national pricing and reimbursement processes with an unclear outcome. Simultaneously, EU citizens have delayed or no access at all, depending on their home country, simply as companies may follow a Pareto, or 80/20, approach, focusing their efforts on major markets. That is particularly evident for small to mid-size corporations that do not have local affiliates in all European markets.

Since 2006, the European Network for Health Technology Assessment (EUnetHTA) has attempted to orchestrate a more efficient pan-European approach to HTA. Some small and mid-size EU countries have joint forces in regional alliances (BeNeLuxA, FiNoSe), but it is only now that major change is coming to Europe.

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Change Is Coming to Europe

We at EVERSANA addressed the recently announced "European Health Union" and its future pharma strategy earlier. The joint European COVID-19 vaccines procurement was not only a breach of the above-mentioned art. 168 of the Lisbon treaty; it is probably also the start of the "progress toward an ever-closer union" in the healthcare sector. In the future, health technology assessments will be carried out centrally in the European Union. On 9 November 2021, the European Council agreed to the adoption of a regulation on health technology assessment. The plenum of the European parliament accepted the regulation during its assembly in December, meaning it would enter into force three weeks later, in January 2022.

Q1 2022		**Entry Into Force**
		Committee Procedure For adopting detailed procedural rules
Q1 2025		**Entry Into Application** Cancer medicines, ATMPs, medical devices/in vitro diagnostics (IVD)
2028		**1st Extension** Orphan medicinal products
2030		**2nd Extension** All centrally authorised medicinal products

The implementation of the EU HTA regulation is characterised by a staged approach, starting with the joint assessment of oncology products, advanced therapy medicinal products and medical devices as of 2025. In 2028, orphan drugs should also be assessed jointly before, in 2030, all centrally approved medicinal products are supposed to fall under the new regulation.

Within the first three years, a committee called The **Coordination Group** will be dedicated to set up procedural rules and the methodology, especially taking into consideration specific methods for medicinal products, medical devices and IVDs.

This Coordination Group will govern the EU HTA procedures, and it will consist of all member states with the EU Commission acting as its secretariat. It is at the Coordination Group's discretion to designate a specific medicinal product to the joint HTA earlier based on the unmet need of the underlying condition and the expected therapeutic value of the new technology. Based on a list of priority criteria, the Coordination Group can select technologies for a joint scientific advice. Finally, the Coordination Group is the body endorsing a joint report no later than 30 days after European Commission (EC) Marketing Authorisation for a certain technology is granted.

Also, as of 2022, certain **sub-groups**, as operating bodies next to the Coordination Group, will be established. These sub-groups will consist of experts from national and regional HTA agencies, and they shall be mandated with the following tasks: joint clinical assessment, scientific consultation, horizon scanning and methodology/procedural guidance. Of these activities, the joint scientific advice and the joint clinical assessment are of most interest for biotech and pharma companies that consider commercialising their products in Europe.

The **joint scientific advice** is foreseen for technologies that are still in the stage of clinical study planning and that will likely undergo a joint clinical assessment after finishing the development phase. The manufacturer can request that the joint scientific advice take place together with the EMA scientific advice (for regulatory purposes). Should the applications for joint scientific advice exceed the planned number of meetings, the Coordination Group will select based on prioritisation criteria.

The **joint clinical assessment** will start with a scoping process that involves the member states and will contain information provided by the developer with input from clinical and other experts and patients. The Commission aims to establish a **stakeholder network** and opens a call to support the Coordination Group. This stakeholder network should be operational as of 2023 and will provide comments on joint scientific consultations and draft joint clinical assessment reports.

The manufacturer has to submit the actual dossier no later than 45 days prior to the expected Committee for Medicinal Products for Human Use (CHMP) opinion date, and it is important that evidence submitted for the joint clinical assessment cannot be part of an evidence body subsequently submitted to national HTA authorities, except for early access purposes. The sub-group will draft a report on which, notably, the manufacturer can comment only on technical and factual inaccuracies. No later than 30 days after EC approval, the Coordination Group has to endorse the joint clinical assessment report.

Predicating the Future of New European Legislation

It will now be interesting to see how the new European legislation will change HTA requirements for biotech and pharma companies. Will pharmaceutical companies have to prepare for a new era of benefit assessments as the basis for pricing and reimbursement? Will we face relief in current national HTA processes, or will they become shortened in a negative way so that companies have fewer possibilities to make their case? The latter is certainly a risk given that the dossier for the joint clinical assessment has to be submitted prior to CHMP opinion and the final EPAR (European Public Assessment Report, issued by EMA after EC approval). Or will the new process come on top of all else and add complexity and bureaucracy?

For all these arguments it cannot be expected that national HTA processes in European countries will be entirely replaced by a pan-European HTA any time soon. Instead, we should focus on how and to which extent the newly generated EU joint clinical assessments will be incorporated into national HTAs.

First of all, it is important that the joint clinical assessment obviously can take into account only clinical aspects of the technology appraisal; i.e., important aspects of the multi-disciplinary HTA approach (ethical, legal, social, and economic implications of a new health technology) are not taken into consideration. Second, even when focussing on clinical aspects, it will remain interesting to see how different standards of care or varying treatment pathways in European member states will be taken into consideration in a joint clinical assessment. Further, the already mentioned subsidiarity principle and the legal foundation hinder a more prescriptive approach to countries: Member states are obliged to "give due consideration" to the joint clinical assessment in their own, national assessment to which EU reports shall be annexed, and they must make it transparent how joint reports have been taken into consideration.

For all these arguments, it cannot be expected that national HTA processes in European countries will be entirely replaced by a pan-European HTA any time soon. Instead, we should focus on how and to which extent the newly generated EU joint clinical assessments will be incorporated into national HTAs. Member states must not require evidence, data, and analyses that have already been taken into consideration at a European level; however, they may carry out national updates.

Conclusion

Clearly, as part of the new European pharma strategy, the European Commission is committed to bolster the attractiveness of the European pharma market and reduce inequalities and time to access for EU citizens at the same time. This is to be welcomed and will shorten the companies' time for EU market penetration. As a flipside, it will increase pressure on pharma to launch simultaneously in more European markets – requiring related resources that start-up and smaller biotechs may not have in place. Further, as HTA outcomes build the basis for price negotiations, it can be expected that these negotiations must be performed in a shorter time span. Again, a stretch on resources and the risk for negative pricing implications from international price referencing (IRP) rules increases. In a compressed launch span, the launch sequence will become even more important.

The time for opportunistic, half-hearted European launch attempts is over; you must address it in a fully committed manner.

Due to the reduced time to peak sales, a highly attractive pharmaceutical market (in our view) is becoming even more attractive. However, the risk for first-launch companies to fail with lukewarm attempts to cherry-pick some EU markets will increase. Certainly, the time for opportunistic, half-hearted European launch attempts is over; you must address it in a fully committed manner. This includes robust upfront planning, starting with including the right endpoints in the development program and ending with a commercial launch readiness assessment.