Commentary

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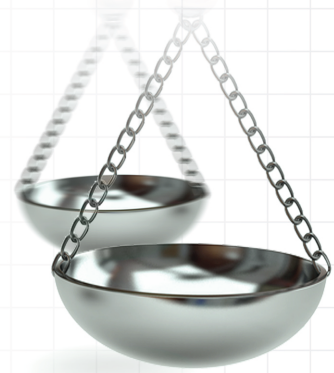

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The evolution of European HTA and access to innovative medicines

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The European Union has a history of emerging pharmaceutical alliances

In recent years, across the European Union (EU), there has been a trend toward consolidating national-level bodies to a single supranational or pan-national authority. The pharmaceutical industry is no exception, and one of the key areas of discussion has been the creation of a unified approach to health technology assessment (HTA) for medicines and medical devices. The European Network for Health Technology Assessment (EUnetHTA) comprises 29 countries and its missions is to "*support collaboration between European HTA organizations that brings added value to healthcare systems at the European, national and regional level*" [1]. The BeNeLuxA Initiative on Pharmaceutical Policy is another example of a collaborative effort, founded by the Benelux countries, Austria and Ireland, with a goal to ensure timely access and affordability of medicines via joint assessments [2].

Earlier this year, the European Commission (EC) published a proposal for a regulation on the EU cooperation on HTA which highlights the need for joint clinical assessments and scientific consultations at the EU level. The proposal has received mixed reviews, both positive and negative, and continues to be a popular topic for debate [3].

> "*This proposal is a starting point for an exchange of views between Member States.*" – Italian HTA expert

In simple terms, the pharmaceutical industry welcomes the joint clinical assessment's potential to expedite patients' access to medicines and reduce the burden of multiple submissions [4]. Conversely, national HTA bodies see hurdles in achieving consensus on assessment criteria.

> "*The EC proposal does not work, it will not be transformed into national legislation. It does not take into account national requirements with regard to end points, comparators and treatment pathways. National assessment bodies and politicians will most likely oppose a more collaborative HTA.*" – German HTA expert

Precision gathered expert opinions on the evolution of European HTA

Precision Xtract conducted surveys with 14 HTA experts to evaluate their expectations for the likely evolution of HTA processes in Europe. Through this research, we sought to understand the drivers for ongoing initiatives for HTA collaboration, identify areas of consensus and forecast the impact of a more collaborative pan-European HTA environment. As a market access consultancy, our goal was to explore the likely impact of these developments on access to innovative treatments and enhance the healthcare community's understanding of the evolving landscape.

HTA alliances: advantageous, but challenging

According to the experts, a collaborative pan-European HTA environment poses many opportunities with the biggest benefit being the potential to save resources by avoiding duplication of work across national HTA bodies. The alliance is also viewed as something that would provide a step toward more equitable and timely access to medicine across the EU.

However, some of the experts note that the risk of losing country-specific expectations and specificities in appraisal criteria is the biggest obstacle. Moreover, they do not anticipate that this alliance will replace the country-level

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economic appraisal step, at least not in the near future. In addition, a unified HTA alliance could potentially introduce an additional step in reimbursement pathways leading to delays in patient access.

> "*Health ministers and governments reluctant to a pan-EU assessment do not want to lose independence, especially when HTA reports can be used as political tools – as a justification for negative decision*." – Polish HTA expert

The added value & the drawbacks of the proposed EC pan-EU clinical assessment

The HTA experts highlight that improved-quality joint clinical assessments can be produced by harmonization and consensus on methods from top experts leading to economies of scale and improved transparency. Particularly in rare diseases, given the novelty of orphan drugs and the absence of real world evidence, a joint clinical assessment produced by a collaboration of top EU experts could better assess the added value of the product and enable quicker access to these medicines [5].

Although a joint assessment will lead to faster evaluation of clinical evidence, many obstacles need to be overcome to prove its value. National or local HTA bodies have the freedom to select the methods they use to evaluate the clinical evidence and guide their reimbursement decisions. A joint assessment will not only require adaptations to local practices, but it will impose misalignment with the economic resources and social values for each member state. The lack of freedom in assessing the evidence and the binding character of the evaluation discourage the payers who view this approach as too ambitious for the time being.

> "*The strengths of the EC proposal lie in a single evaluation of the benefit of the drug and the same quantification of the added value across EU. However, the lowest common denominator will be accepted*." – French HTA expert

The moderate impact of the EC pan-EU clinical assessment proposal on process standardization & quality

Industry stakeholders and European national payer experts are aligned on the potential impact of the pan-EU clinical assessment on quality and process standardization. They agree that it is of moderate importance.

Payers welcome the advantages of efficiency and reduced workload derived from process standardization. The joint assessment provides a sustainable framework allowing payers to pool expertise in their decision making while leaving the economic component of the assessment to national or regional level decision-makers. But, if a joint assessment confers increased quality and cost efficiency, why are payers opposed to a mandatory participation and uptake? Most probably, payers want to maintain the freedom to use their country-specific requirements in appraisal criteria that have been tailored to best suit their country's healthcare system, philosophies, policies and methods for HTA as well as available budget.

It happened with the EMA, could it happen again?

In 1985, the single-market project was launched and it included plans for the creation of the European Medicines Agency (EMA), but the Agency was not formed overnight. It took until 1995, when the Council Regulation (EEC) 2309/93 established the EMA, an agency who grants a centralized, legally binding marketing authorization. This lead to an overhaul of the existing national procedures and created a harmonized European system of medicines approval [6,7].

Today, 25 years after the emergence of the EMA, we believe it is time to work toward a pan-EU HTA assessment and leverage the lessons learned from its creation to allow for a more efficient and transparent EU clinical assessment [6]. However, can the countries agree on the common criteria for a combined clinical assessment and put the differences in their health systems aside?

Variances in clinical practices across countries will need to be resolved to allow for a joint clinical evaluation. We believe it could be viable, but it will be an evolution rather than an overnight transition. It will be particularly welcomed in smaller countries that lack sophisticated HTA assessments and infrastructures in contrast to bigger markets with well-established HTA processes – such as France, Germany and the UK.

ICER independently evaluates drugs on a clinical as well as economic basis

Similarly, the Institute for Clinical and Economic Review (ICER), which was founded in 2006, is a Boston-based nonprofit organization that evaluates prescription drugs and other healthcare innovations [8]. ICER is independent and objectively conducts rigorous analyses of all data. Their end goal is to share the findings which could be

implemented into policy decisions that lead to more effective and efficient healthcare systems [9]. ICER's reports, similar to the reports that would be produced by a pan-European HTA, include a full clinical analysis, the economic value each treatment represents, and other important elements.

ICER is fast becoming very influential on the US healthcare market and is best known as the independent watchdog on drug pricing [8]. Different EU member states could potentially follow this model, joining forces to produce reports following common criteria to evaluate the budget impact of new technologies.

Recommendations & conclusion

A joint EU assessment is a necessary step to address the current healthcare inequalities in the EU. Payers are pronouncing that efficiency and harmonization of criteria are highly important advantages of a joint assessment, while great support is seen from countries with limited infrastructure and those conscious about their resource use. A pan-European clinical assessment would help increase transparency, initiate a discussion between different stakeholders and incorporate clinical and patient input. Both members of industry and payer experts believe that the potential impact of the proposed EU Commission's pan-European clinical assessment approach on the standardization of processes and the quality of the assessment is moderate. However, there is a will to gradually shift toward a common European HTA.

As seen with the creation of the EMA and ICER, the transition from separate to a common body did not materialize overnight – equally, we expect the EC proposal to gradually evolve into a more tangible alliance and finally a supranational body. Given the country differences, trying to reach some form of alignment with mandatory participation and uptake is going to be unachievable in the short-to-medium term. Therefore, the first step toward a joint assessment could begin with voluntary participation and uptake to increase the number of countries participating in such collaborations, like the EUnetHTA and BeNeLuxA agreements. As a second step, countries could be more willing to participate in a joint assessment focusing on orphan drugs given the obstacles they face when evaluating these products (i.e., lack of epidemiology and real-world evidence data). We foresee initial joint assessments focusing on one disease area (e.g., rare diseases) before slowly expanding into other areas. Smaller countries which have limited resources could be more interested in forming this sort of alliance and we envision other countries joining in gradually. Dialogue and consensus will be necessary for bigger markets to recognize that the benefits outweigh the risks and for them to gain trust in following a common approach.

Additionally, a joint clinical assessment will prompt the pharmaceutical industry to ensure that clinical development plans are not too far from the minimum consensus established between the EU countries. The industry will need to form a better understanding of current treatment approaches across jurisdictions to better prepare for a multinational HTA. As regularly mentioned by payers, seeking early scientific advice where feasible to align with HTA criteria is a must-do for the manufacturers in preparation for a pan-European HTA.

> "*The BeNeLuxA evaluations seemed to be more stringent to avoid missing elements of critique which could subsequently be identified by colleagues from the secondary countries. However, joint negotiations on price and volume have the potential of creating more bargaining power.*" – Dutch HTA expert

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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