Cross-border collaboration to support pricing and access for high-cost, high-value therapies: a review of initiatives in Europe

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Introduction and objectives

Cross-border collaboration for the evaluation and procurement of medicines can be undertaken to pool expertise, minimise risk and increase bargaining power. This has become increasingly important in Europe to improve affordability and access to innovative therapies in areas of high-unmet need. This research aims to understand the rationale for collaboration across borders, outcomes of joint initiatives (and associated implications) and key success factors.

Methods

A comprehensive review of cross-country collaborations was conducted with a focus on Health Technology Assessment (HTA), pricing, procurement, and patient management. Established collaboration models were prioritised including BeNeLuxA, EUnetHTA, and the Valetta Declaration. Pricing and procurement agreements and cross-border healthcare initiatives in response to the pandemic were also reviewed. All research was conducted between June and October 2021.

Results

Successful collaborations occur primarily at HTA level to pool expertise for evaluation of high-cost, high-value therapies (e.g., Zolgensma by BeNeLuxA). However, to date, influence on access and reimbursement has been minimal and collaborative price negotiations have had limited success. Of the 7 established collaborations that have been identified, EUnetHTA has completed the most assessments since initiation of the rapid effectiveness assessment (REA) programme. Other initiatives have completed only a few assessments, showing that successful outputs may only be seen several years after initiation. Those most recently established (excluding FiNoSe) in 2017, are yet to complete a joint assessment (Table 1).

Table 1. Key characteristics of collaborative initiatives

Initiative	Markets	Process	Drug Candidates	Initiation (and first output)
EUnetHTA	EU member states	Joint HTA REA[1]	Medicines with a new mode of action for the indication; targeting a life-threatening or chronically debilitating disease; and responding to unmet need	2016 (2016)
FiNoSe	Finland, Norway, Sweden	Joint health economic evaluation (not intended for joint access and reimbursement decisions but to support earlier access across the region)[2,3,4]	New innovative therapies based on common interest of Fimea, NoMA and TLV	2018 (2019)
Baltic procurement initiative	Estonia, Latvia, Lithuania	Joint procurement of vaccines and lending of medicines and medical devices to prevent or cover shortages and to ensure continuous access to these products[5]	Medicines and medical devices (lending) and vaccines (joint procurement)	2012 (2017)
BeNeLuxA	Belgium, Netherlands, Luxemburg, Austria, Ireland	Joint HTA and price negotiation (no joint procurement)[6,7]	Orphan drugs and high cost therapies	2015 (2018)
Nordic Pharmaceutical Forum	Norway, Denmark, Finland, Iceland and Sweden	Joint access negotiations (increase purchasing power)[8,9]	Hospital medicines focus – new and old high-cost medicines	2015 (2019)
Valletta Declaration	Cyprus, Greece, Italy, Malta, Portugal, Spain, Croatia, Ireland, Romania, and Slovenia (covering over 30% of the EUs population)	Horizon scanning, information sharing initiatives (focused on increased price transparency), joint price negotiation and HTA (limited participation from some companies who submitted reimbursement applications in individual countries)[7]	Focus on oncology drugs, treatments for autoimmune diseases, orphan drugs, biosimilars and products with a potentially substantial BI	2017
The Visegrád Group – "Fair and Affordable Pricing"	Czechia, Hungary, Poland, and Slovakia	Joint HTA and pricing negotiations[7]	High-cost medicines	2017

BeNeLuxA

In 2015, the BeNeLuxA cooperation was initiated with the aim of sustainable access to, and appropriate use of, medicines in the participating countries. Together, the participating countries aim to enhance patient access to high quality and affordable pharmaceuticals. Besides undertaking HTAs, the partnership collaborates on horizon scanning, joint price negotiations and sharing of expertise on policies and future challenges.

BeNeLuxA HTA and joint price negotiations for Zolgensma

After European Commission (EC) conditional Marketing Authorisation (MA) of Zolgensma (onasemnogene abeparvovec) in spinal muscular atrophy (SMA) in May 2020, the BeNeLuxA initiative opened a dialogue with AveXis/Novartis on affordability and access in each participating country.[14] Belgium, Ireland, and the Netherlands undertook a joint HTA of Zolgensma with Austria acting as an expert reviewer in the Belgian procedure. For the first time Belgium, Ireland and the Netherlands have also collectively negotiated the price of a drug.

Reimbursement

The company obtained reimbursement for SMA patients with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of Type 1, and pre-symptomatic SMA patients with up to three copies of the SMN2 gene.[15] Zolgensma qualified for reimbursement in Ireland with immediate effect and in the Netherlands on 1st November 2021, while Belgium will reportedly follow on 1st December 2021.[16]

EU Covid vaccine conditional authorisation

- Conditional MA is designed to enable MA as soon as sufficient data becomes available (with the EMA assessing data through rolling reviews)
- The EC can proceed with MA if a majority of Member States (MSs) are in favour and no further MA is required for marketing in different MSs
- The average MA process takes 67 day. Under emergency situations the EC can proceed with MA within 3 days following positive recommendation from the EMA[10]

EU vaccine negotiations

- Carried out by the EC together with a joint negotiation team who discussed and reviewed the Advanced Purchase Agreement (APA)
- All MSs endorsed this approach at the European Council in June 2020[11]

What is an APA?

- A legally binding agreement made with individual vaccine manufacturers on behalf of all participating MSs in respect of COVID-19 vaccine procurement[11,12]
- As a part of this, the EC financed part of the upfront costs faced by vaccine producers from the €2.7 billion Emergency Support Instrument[12]

Joint procurement via an APA

- As part of an APA, the EC and MSs agreed that the EC will carry out procurement procedures on behalf-of and in the name of the MSs setting out the terms applicable to such purchases[13]
- As part of the APA, the following criteria were considered: soundness of scientific approach and technology, speed of delivery at scale, capacity and timelines for supply, logistical challenges, costs, liability and global solidarity (i.e., commitment to making vaccine available for lower income countries)[12]

Alignment regarding processes and priorities between countries and active engagement from all stakeholders is correlated with success. In this context, smaller initiatives with fewer countries (i.e., BeNeLuxA) are more likely to achieve cross-market consensus in the absence of an established governing body (such as the EC in the joint procurement of COVID-19 vaccines).

Conclusion

Collaborations to support the evaluation of high-cost, high-value therapies and to provide solutions for emergency medical needs, are occurring more frequently. Joint initiatives have the potential to shorten time to market, increase (geographical) access to innovative therapies by reducing the total number of HTA/pricing applications and can result in more efficient procurement (i.e., vaccine procurement by the EC and the Baltic procurement initiative) when a larger total patient population is considered.

With increasing innovation and support for voluntary collaborations, pooling of resources is likely to increase in future to address shared health priorities. To ensure success, continued consultations between participants to align assessment methodologies in order to reduce submission complexity are important. Consequently, increased collaboration presents an opportunity for further consolidation of evaluation frameworks for high-cost, high-value therapies, potentially reducing HTA duplication, and supporting timely, sustainable patient access to new medicines (e.g., recently introduced EUnetHTA 21).

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Abbreviations. APA: Advanced Purchasing Agreement; BeNeLuxA: Belgium, Netherlands, Luxemburg, Austria, Ireland; BI: Budget Impact; EC: European Commission; EMA: European Medicines Agency; EU: European Union; EUnetHTA: European network for Health Technology Assessment; FaAP: Fair and Affordable Pricing; Fimea (Finnish medicines agency); FiNoSe: Finland, Norway, Sweden; HTA: Health Technology Assessment; IHSI: International Horizon Scanning Initiative; MA: Marketing Authorisation; MS: Member State; NoMA: Norwegian Medicines Agency; REA: Rapid Effectiveness Assessment; SMA: Spinal Muscular Atrophy; TLV: The Dental and Pharmaceutical Benefits Agency

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