ISPOR EUROPE

2023 REPORT

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Remap

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ISPOR Europe 2023, Copenhagen, Denmark

Remap Consulting joined over 4,100 other delegates in attending the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual International Meeting in Copenhagen, Denmark from 12th - 15th November 2023.

The theme for this year's meeting was "HEOR at the Nexus of Policy and Science". The theme was styled as a "thread" that was woven throughout many of the sessions to bring a fresh and holistic view of the importance of the HEOR community's role in impacting the present and more over the future of innovation, value, and decision-making for health globally.

Our report summarises the plenary sessions and our research that we presented at the conference.

Plenary Sessions Overview

European health data space – RWE put to work for public health

In this keynote panel, a number of panellists providing perspectives from both national level decision-making and the industry discuss the challenges and opportunities faced with the upcoming EU HTA. Interesting points are made on readiness for the EU HTA, and although a number of challenges exist that must be addressed for successful launch in 2025, the panellists also provide positive opinions on how the scheme may be implemented by member states, likening the implementation of the EU HTA to the uptake of the EMA in the 90s.

Overview and Strategic Insights

The discussion commenced with the query of EHDS replacing existing health databases. Andrzej Rys, Principal Scientific Advisor at the European Commission, outlined the three developmental stages: organizing data gathering, defining best practices and the legal framework, and establishing a system for cross-European data sharing. Markus Kalliola, Project Director at the Finnish innovation fund Sitra, emphasized the importance of determining how EHDS data would be processed post-research.

The subsequent discussion revolved around EHDS beneficiaries and access. Dr. Petra Wilson, Managing Director at Health Connect Partners, highlighted the universal benefit for patients, foreseeing enhanced efficiency in healthcare delivery. Panel members affirmed that EHDS would facilitate more efficient care delivery and foster potential for public health research. Trine Pilgaard, Director of Market Access at Pfizer, emphasized EHDS contributing to better decisions and streamlined healthcare.

Addressing EHDS access, the consensus was to involve as many users as possible while maintaining stringent protocols. Key stakeholders include HTA agencies, research centres, hospitals, and doctors, with an emphasis on preventing misuse such as advertising or raising insurance premiums.

Patient privacy emerged as a key challenge, with concerns about the opt-in/opt-out mechanism. While legal processes are being debated, the panel expressed hope that robust procedures could minimize the need for individual patient opt-ins. In the concluding segment, panel members highlighted opportunities and obstacles. Patient privacy and logistical hurdles in building a network for data sharing were identified as challenges. However, the potential to broaden RWE data access for informed decision-making by healthcare providers was seen as a significant opportunity. Patrice Verpillat emphasized the broader perspective on disease states provided by a pan-European database, while Petra Wilson viewed EHDS as an opportunity to advance global acceptance of data usage.

The Key Takeaways

1. The quality of patient care can greatly benefit from the EHDS through both better decision-making by healthcare providers, or government bodies, and improved access to RWE for research and development.

2. The EHDS provides a fantastic opportunity for pan European data usage but there is still concern that patient acceptance and privacy will provide a significant challenge to its implementation.

3. The logistics of EHDS will also require significant attention before implementing the program, requiring pan European cooperation and robust processes for who may have access to the database.

4. Whilst there is considerable ambition for broader cooperation on data usage the question remains; **what are the motivating factors that may persuade key players to take part in the program and how it will benefit them?**

The New Pharma Legislation Proposal: The Good, the Bad or the ...

After extensive negotiations and recent stakeholder consultations, the European Commission has unveiled a **revised proposal for the EU pharmaceutical legislation**. The objective is to establish a future-proof regulatory framework with four core pillars identified back in 2020:

- Ensuring access to affordable medicines for patients, addressing unmet medical needs, such as in the areas of antimicrobial resistance and rare diseases.
- Supporting competitiveness, innovation, and sustainability of the EU's pharmaceutical industry, fostering the development of high-quality, safe, effective, and environmentally friendly medicines.
- Enhancing crisis preparedness and response mechanisms, ensuring diversified and secure supply chains, and addressing medicines shortages.
- Ensuring a robust EU voice globally by promoting high standards of quality, efficacy, and safety.

This panel session critically examines whether these initial intentions are adequately reflected in the latest proposal.

The panel delved into several crucial topics during the session, shedding light on the complexities and challenges within the pharmaceutical landscape.

Medicinal Prices and Evidence Requirements

The discussion kicked off with an exploration of the contradictory trends in medicinal prices, especially for innovative medicines, alongside a diminishing emphasis on evidence requirements. Johan Pontèn from the Medicines Evaluation Committee highlighted the lack of effectiveness evidence, leading to payer ambiguity about the value of these medicines. He emphasized the need for streamlining the pathways for new products to address these challenges. Yannis Natsis, from the European Social Insurance Platform, connected this trend to the post-COVID-19 mindset, where speed trumps evidence, resulting in the current conundrum of low evidence and high prices.

Affordability vs Sustainability

The second focal point revolved around the delicate balance between affordability and sustainability. Gloria Ghequiere, advisor to the Belgian deputy prime minister, noted progress in thinking about medicine shortages but underscored the persistent issue of stakeholders paying significant amounts for innovations while generic prices remain low. Panelists expressed concerns about the proposal lacking measures to address rising prices, despite welcoming initiatives for increased competition through a simplified regulatory framework.

Designations of Unmet Medical Need

The final segment tackled the designations of unmet medical need and high unmet medical need. Panelists, echoing the sentiment of moderator Dr. Anja Schiel, discussed the risk of every new medical product receiving a special designation. Denis Lacomb, CEO of the EORCT, proposed a shift towards evaluating overall public health needs rather than broad designations of unmet need at the patient level. Panelists collectively urged the next set of European Commissioners to define a new strategy on unmet need.

In Conclusion

Throughout the discussion, a recurring theme emphasized the need to revise incentives offered to companies, considering potential negative impacts on access. Additionally, concerns were raised about the misalignment between the Pharma Legislation Proposal and EUHTA, posing potential challenges to HTA timelines.

The Key Takeaways

1. Stakeholders are concerned by the contradictory trends of increasing medicinal prices and the erosion of the evidence requirements for new products.

2. The legislation lacks clarity, with the stakeholders involved being concerned about the unmet medical need designation and the incentives that have been put forward not having the desired effect.

3. There is a lack of alignment between the Pharma Legislation Proposal and EUHTA, where there could potentially be increased pressure on HTA timelines going forward.

4. Overall, there is a **sense of hesitancy among stakeholders** with the title of this talk going unanswered: **The Good, the Bad or the … What?**

The Calm Before the Storm? Delivering the New Reality for EU HTA

Embarking on a journey that spans more than 16 years of planning, the European Union's vision for collaborative Health Technology Assessment (HTA) is now on the verge of becoming a new standard. With the adoption of the EU HTA Regulation in January 2022, a paradigm shift awaits stakeholders, slated to take effect from January 2025. At the heart of this transformative regulation are Joint Clinical Assessments (JCAs), which will soon guide the evaluation of cutting-edge technologies.

In just over 12 months, the inaugural technologies mandated by this regulation will navigate their paths through a JCA. Health Technology Developers and other stakeholders are proactively preparing for these initial assessments.

The plenary discussion delved into the mutual expectations among stakeholders and explored collaborative strategies to overcome anticipated challenges, ensuring a seamless adoption of the new Regulation. Perspectives from the European Commission, EU HTA entities, innovators, Member States, and, notably, the patient community were shared, highlighting the multifaceted nature of this pivotal transformation.

The session commenced with Adrian Griffin, VP of HTA and market access at Johnson & Johnson, highlighting the inescapable significance of the impending changes in HTA that could reshape the way stakeholders operate.

Greg Rossi, SVP and Head of Oncology Europe and Canada at AstraZeneca, set the scene by revealing that European patients, on average, face an additional two-year delay in accessing innovative medicines compared to their U.S. counterparts.

The initial discussion centered around the goal of transforming HTA in Europe, with Jose Valverde from the European Commission emphasizing EUHTA's primary objective: to expedite patient access to medicines within the EU.

Roisin Adams, Head at HTA Strategy National Centre for Pharmacoeconomics, stressed the collaborative spirit among member states, advocating for equitable access and opportunities across the entire bloc. From the industry viewpoint, Greg Rossi viewed it as an excellent avenue for delivering innovative therapies, making Europe not only more accessible to patients but also more attractive for research and development. However, concerns were raised about the potential impact on member states' pricing and reimbursement negotiations.

Bettina Ryll, founder of the Melanoma Patient Network Europe, highlighted the unequal distribution of recent treatment innovations across Europe. Jose Valverde outlined the commission's actions, emphasizing the six acts tasked by the regulations, with a central focus on the Joint Clinical Assessment (JCA). The next steps involve private and public consultations before EUHTA comes into force in 2025.

Preparation for the upcoming changes involves strategic planning and horizon scanning for agencies like the National Centre for Pharmacoeconomics in Ireland. On the industry side, there's a strong focus on education, particularly regarding PICOs, and discussions about cross-departmental teams and internal process adaptations.

The subsequent discussion addressed preparations for EUHTA, with Roisin Adams noting differences based on country archetypes. Greg Rossi stressed the importance of dialogue with countries to understand their system rewiring for faster access but expressed concerns about potential duplications of work.

Throughout the discussion, a recurring theme emphasized the need to revise incentives offered to companies, considering potential negative impacts on access. Additionally, concerns were raised about the misalignment between the Pharma Legislation Proposal and EUHTA, posing potential challenges to HTA timelines.

Audience questions revolved around resource implications, with industry and local HTA agencies expressing concerns. The industry fears increased resource requirements, especially with numerous PICOs per product. The commission acknowledges potential challenges but believes the long-term benefits will outweigh short-term concerns.

In closing statements, Bettina Ryll acknowledged potential short-term access challenges but stressed the necessity of changes for long-term equitable access. Roisin Adams and Greg Rossi believed the changes would resolve ongoing access issues, making decision-making clearer and more aligned across the EU. Jose Valverde expressed a desire for increased transparency, mutual trust, and collaboration, concluding with the exciting announcement that the first JCAs will commence in 14 months.

The Key Takeaways

1. The EUHTA heralds a promising opportunity to address significant access challenges, including the **equitable distribution of innovative medicines, advancing evidence generation**, and **expediting timelines for product access.**

2. In the coming months, crucial details about the implementation of Joint Clinical Assessments (JCA) will be unveiled. This presents a pivotal moment for the industry to contribute insights before the EUHTA takes effect in 2025.

3. Proactive measures are already underway in both industry and local HTA agencies, involving a strategic overhaul of internal structures, comprehensive educational initiatives, collaborative discussions with partners, and strategic planning exercises like horizon scanning.

4. Despite these positive strides, persistent concerns linger. There's **apprehension that the EUHTA may not deliver immediate acceleration of access**, coupled with fears that countries might be reluctant to relinquish local processes. Furthermore, there's a prevailing worry that the resources required for successful market access by industry could experience an unwarranted surge.

Educational Symposias Overview

EUHTA Impact on Innovations: Expectations and Challenges of EUHTA for Germany

The recently introduced EU HTA Regulation marks a significant development as it establishes, for the first time, a standardized approach to the benefit assessment of novel therapies across Europe. This regulation specifically governs a collaborative clinical assessment of new medicinal products on a European scale. The initiation of this process is slated for January 2025, encompassing various products, notably advanced therapy medicinal products (ATMPs) and oncology medicinal products, including orphan drugs. The details and specifics of this framework are set to be further clarified and defined. This session brought together several German stakeholders to discuss the expectations and challenges of EUHTA in Germany.

The Discussion

Eva Dietrich, founder and head of the institute for evidence-based positioning in the healthcare sector, opened the discussion and made several points from the perspective of the AMNOG process:

- EUHTA is unlikely to have an impact on access to innovative medicine in Germany, largely due patients already having very good access through the AMNOG process.
- The German government believes the AMNOG process should continue regardless of EUHTA, at least in the short term, as it is necessary to maintain the equal treatment of companies and drugs over time.
- The G-BA has stressed that the introduction of EUHTA will not delay patient access to innovative medicines in Germany, however, concern from companies and stakeholders remain.
- In conclusion, Eva posed the question of whether EUHTA will be relevant for the G-BA and IQWiG and answered by stating “not from the AMNOG perspective”.

This was followed by a talk from Lutz Herbarth, head of the medical compliance team at the health insurer KKH, who discussed the EUHTA from the perspective of the German Statutory Health insurance association (GKV-SV). He pointed out that the GKV-SV have expressed concerns over the EUHTA procedure and how this will impact the endpoints used in trials, however, health insurers believe that EUHTA will have minimal impact on the on the operation of their businesses.

The final speaker was Julia Rumsch, head of the Brussels office for the Federal Association of the Pharmaceutical Industry (BPI) and focused on the current plan for the implementation of EUHTA. Concerns were raised that details on the timelines for EUHTA processes and how the legislation will be implemented are still lacking, although there was acknowledgment that more information is due to be released in Q4 2023 or Q1 2024. In addition, Julia mirrored the sentiments of Eva Dietrich's talk earlier on the issues of EUHTA hampering the rapid access of patients to innovative medicines in Germany.

Panellists, when probed on the impacts of EUHTA regulations not aligning with the AMNOG process, conceded that the implementation of new legislation will be a stepwise process that is likely to require Germany adopt its procedures. However, it was also pointed out that in the long term there may be further additions to EUHTA regulations such as acceptance of patient reported outcomes.

The Key Takeaway

There is concern among some stakeholders in Germany that EUHTA will interrupt the AMNOG process thereby slowing patient access to innovative medicines, however, over time EUHTA may evolve and reduce these potential issues. Whilst from a health insurers perspective there is expected to be minimal impact from the new legislation.

EU HTA Regulations (HTA-R) in Motion: Italy's Path Forward

Italy's pharmaceutical terrain, known for its meticulous pricing and reimbursement regulations, stands at the threshold of a paradigm shift. In the wake of evolving challenges, notably EUHTA and specifically JCA, a recent forum delved into the intricate dance between EUHTA and the local Italian pricing and reimbursement dynamics for pharmaceuticals and devices.

Here's a glimpse of the transformative landscape:

1. The Rise of CSE:

The introduction of the Scientific and Economic Committee (CSE) marks a pivotal moment, assuming responsibilities previously held by the Technical Scientific Committee (CTS) and the Pricing Committee (CPR). Appointed by decree of the Ministry of Health, the CSE operates autonomously on both technical and healthcare levels, engaging in scientific advisory activities.

2. Unravelling the CSE Process:

While the organization of CSE activities into clinical and economic spheres remains unclear, the implementation of EUHTA holds the promise of streamlining CSE's workload. The synergy between EUHTA and CSE offers potential benefits, providing essential data analysis for scientific appraisal based on pre-agreed PICOs and creating space for pricing and economic negotiations.

3. Positive Impacts and Challenges:

The positive influence of EUHTA on CSE is underscored by its role as a provider of raw material for scientific evaluation. However, challenges arise from the lack of detailed information on the practical functioning of EUHTA, echoing concerns in other markets. Additionally, the willingness of AIFA and CSE to collaborate with the EUHTA process for local PICOs remains uncertain.

The Key Takeaway

Patrizia Berto, Director of P&R at Pharmalex Italy and Director of the Italian chapter of ISPOR, underscored a crucial insight from the session. She emphasized the urgent need for the swift implementation of CSE to alleviate uncertainty in Italy's healthcare landscape. Additionally, Berto highlighted the necessity for the Ministry of Health (MoH) and AIFA to provide clarity on how EUHTA will impact the pricing and reimbursement of pharmaceuticals in the country.

Notably, the prevailing sentiment towards EUHTA in Italy appears positive, in contrast to our earlier insights on its impact in Germany. This divergence in perspectives adds an intriguing dimension to the ongoing narrative, making it a development worth closely monitoring.

Spotlight Session Overview

EU Joint Clinical Assessment – One for All and All for One?

Moderator Anke van Engen (IQVIA, The Netherlands) and panellists Anne Willemsen (Zorginstituut Nederland [ZIN], The Netherlands), James Ryan (AstraZeneca, UK) and Kim Helleberg Madsen (Danish Medicines Agency, Denmark), provided perspectives from industry and regulatory. The speakers discussed how the unique needs of member states from EU Joint Clinical Assessments will likely lead to additional analysis requests to provide all the required PICOs.

The EUnetHTA approach to consolidate EU PICOs is based on a survey of the 27 EU member states, followed by consolidation and validation. Of note, and highlighted by Willemsen, was that PICOs should be based on policy needs, and should not be data driven. Ryan also highlighted the opportunity we now have in Europe to develop a, 'world-class system of HTA across all stakeholders.' However, he did also call out some of the issues that keep him awake at night, including that a lack of evidence-based guidance and engagement reduces predictability, transparency and inclusivity.

The Elephant in the Room: Which Stakeholders Should be Responsible for RWE Generation After Launch?

Discussions revolved around the roles and responsibilities in generating Real-World Evidence (RWE) to address evidence gaps. Specifically, the debate focused on situations where RWE is needed post-launch to fill gaps for payers, questioning whether this responsibility should fall on the industry, Health Technology Assessment (HTA) bodies/payers, or other entities.

Pall Jonsson, from NICE, UK, expressed thoughts on LinkedIn, stating, "Who should be responsible for post-launch evidence generation? It is a big question without a simple answer, but the data infrastructure in healthcare is becoming mature enough for us to start thinking about this on a larger scale. We at NICE are certainly interested!".

Ashley Jaksa from Aetion, MA, USA, served as the moderator, and the panel included perspectives from Solange Corriol-Rohou (AstraZeneca, France) and Jesper Kjær (Danish Medicines Agency, Denmark).

Real-World Impact of Real-World Evidence Guidelines: Monitoring the Influence of International Regulator and HTA Guidance With Key Case Studies

Moderator Stephene Duffield from NICE, UK, highlighted the abundance of RWE guidance from regulatory and HTA bodies compared to a year ago. A case study (TA850) showcased the use of the NICE RWE Framework to enhance a submission and strengthen the evidence base.

Juan Jose Abellan from the European Medicines Agency, The Netherlands, outlined the EMA's vision for using RWE and discussed current and planned guidance. Hwee-Lin Wee from the National University of Singapore discussed RWE to support reimbursement decisions in Asia, sharing insights from the REALISE Working Group. Tanja Podkonjak from Takeda Pharmaceuticals International AG provided the industry viewpoint, addressing challenges in navigating global regulators' diverse guidance on RWE.

As the session concluded, each panelist shared their priorities for the future. Abellan called for pilots, Podkonjak emphasized alignment, and Wee looked forward to the EMA's upcoming publication of the final metadata list in early 2024 for improved data discoverability.

Remap Consulting Research Posters

We're pleased to have presented five pieces of research at the conference, with two posters being awarded a poster-tour presentation.

If you would like any further information on the plenaries or research presented below, please contact Paul, Graham or Janice at contact@remapconsulting.com

Are acute therapies and curative drugs more affordable than chronic treatments in rare diseases?

EE700

An analysis of the top 10 most expensive drugs in the US compared with Germany

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INTRODUCTION

Recently there has been focus on acute treatments being 'the most expensive drugs in the world'. In 2019, we compared the costs of the most expensive gene/acute therapies and chronic treatments for rare diseases in the US on an annual and lifetime basis to contrast short- and long-term costs

That research suggested that acute and curative drugs may be more affordable than chronic treatments over a patient's lifetime.

This is an updated analysis to identify any changes since 2019

OBJECTIVES

1. To compare the annual and lifetime treatment costs of the 10 most expensive drugs in the US
2. To compare the costs from Objective 1, between the US and Germany

METHODS

Figure 1. Methods flow diagram

- A literature review of PubMed and grey databases was conducted. This included the following search terms: high cost, most expensive treatment, therapy, annual, lifetime
- The most expensive 25 drugs were assessed and prices and dosing data were identified and analysed to calculate annual treatment costs. Dosing assumptions were based on a product's SmPC, average weight or body surface area where applicable
- Age of onset and life-expectancy data were used to estimate lifetime treatment costs. The top 10 most expensive products on an annual treatment basis were selected based on US WAC price for the first year of treatment
- The annual and lifetime cost of the top 10 most expensive products between US and Germany was compared

RESULTS

- The top 10 most expensive drugs are a combination of acute therapies and chronic-use treatments, compared with 2019 where the top 10 were all acute therapies
- Of the top 10 most costly treatments, 3 acute treatments (Zolgensma, Luxterna, Folotyn) remain with the new addition of Spinraza since 2019 (Chart 1)
- Considering the lifetime costs of the top 10 products, based on US ex-factory price, the acute treatments are ranked #7-10 (Chart 2). Based on the German ex-factory price the most highly ranked acute treatment is #4 for Zolgensma
- Takhzyro, accrues the highest lifetime costs in both the US and Germany on a chronic basis.
- The average annual (first year) ex-factory price for the acute treatments remains higher than for the chronic treatments (Table 1). The average lifetime costs of the 6 drugs used chronically is far higher than the lifetime cost of the acute therapies with an average of $14.7m/€2.6m compared to $1.4m/€707k for acute treatments
- Furthermore, the annual and lifetime costs of the top 10 most expensive drugs has increased since 2019

Chart 1. Annual cost of the 10 most expensive drugs in the US compared to Germany (based on ex-factory price in EUR)

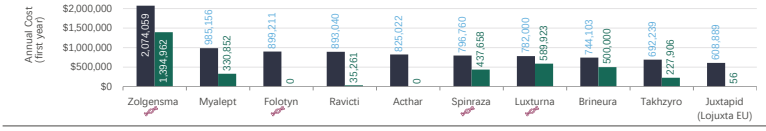

Chart 2. Lifetime cost of the 10 most expensive drugs in the US compared to Germany (based on ex-factory price in EUR)

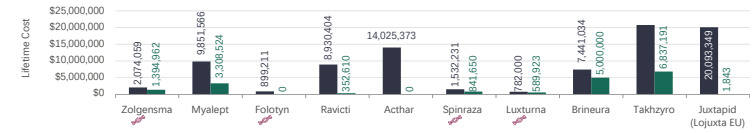

Table 1. Comparison of annual and lifetime costs of the 10 most expensive drugs globally, based on ex-factory price

	ACUTE TREATMENTS	ACUTE TREATMENTS 2019	CHRONIC TREATMENTS	CHRONIC TREATMENTS 2019
	us$		us$	
Most expensive annual cost	$2.3m €1.4m	$2.1m	$1.1m €331k	$840k
Average annual cost	$1.2m €606k	$833k	$860k €156k	$586k
Most expensive lifetime cost	$2.3m €1.4m	$2.1m	$22m €6.8m	>$18.0m
Average lifetime cost	$1.4m €707K	$0.9m	$14.7m €2.6M	$9.3m

CONCLUSIONS

Overall, the research continues to suggest that acute and curative drugs may be more affordable than chronic treatments over a patient's lifetime.

1. **Existing pricing models tend to focus on short-term affordability.** Innovative assessment frameworks need to focus on the long-term, taking into consideration comparative lifetime costs and overall budget impact to assist payer decision-making and mitigate concerns relating to high 'one-off' prices
2. **The development of novel payment agreements to assist with short-term budget concerns by payers is necessary** to reduce high up-front costs and also uncertainties over long-term clinical benefits of gene-therapies in particular in the real-world setting.
3. **The study highlights the difference in drug prices between Europe and the US.** The Inflation Reduction Act IRA aims to make innovative medicines more affordable by providing greater negotiating power to Medicare and will require manufacturers to pay a rebate for drug list prices that exceed the rate of inflation
4. **Limitations of this research should be noted:** our analysis is based on publicly available pricing information and does not consider confidential discounts. Further, lifetime costs do not account for patients discontinuing treatment prior to death, or any survival benefits associated with the treatment if the analysis is based on historic life expectancy figures

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Abbreviations: APU=Manufacturer Sales Price; CADTH=Canadian Agency for Drugs and Technologies in Health; CE=Cost-effectiveness; EMA: European Medicines Agency; EU=Europe; HTA=Health technology assessment; ICER=Institute for Clinical and Economic Review; NICE=National Institute for Clinical Excellence; US=United States; USD=United States Dollars; WAC=Wholesale Acquisition Cost

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Evaluation and reimbursement of digital therapeutics in Germany, France, Belgium and England

PT21

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INTRODUCTION

- Digital Health Therapeutics (DTx) aim to treat, prevent or manage specific conditions through mobile-based software
- Payers are increasingly acknowledging DTx's potential in healthcare delivery, resulting in the development of country-specific reimbursement frameworks
- The objective of this analysis is to compare and contrast the objectives, methodology and eligibility of four established DTx reimbursement frameworks: German DiGA fast track, French PECAN fast track, Belgium mHealth Pyramid, and English Early Value Assessment (EVA)

METHODS

Scientific publications and web pages of DiGA, PECAN, mHealth Pyramid and the EVA were reviewed to extract data on the assessed processes

Figure 1. Methodology used in this research

Data extraction cutoff date: 1st October 2023

RESULTS

Analysis shows that the assessed frameworks differ in objectives, requirements and methodologies.

Figure 2. Comparison of DTx assessment frameworks across Germany, France, Belgium, and the UK

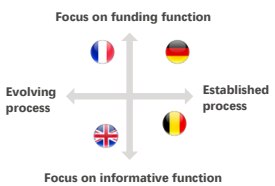
	DiGA	PECAN	mHealth validation pyramid	EVA
Overview	**Categorizes DTx based on criteria level**	**Aim to accelerate reimbursement foreligibleDTxduring functionality andcompliance, offering evidence generation phasefunding only to those reaching highest**		**Evaluates selected by NICE medical technologies to provide recommendations for use within NHSwhile evidence is generated**
	CE mark mandatory, country-specific safety and interoperability criteria must be met			
Eligibility criteria	•Basic level: DTx that enables sharing information with HCPon DTx - MD risk class I and IIa •Telemonitoring solutions	Technologies are selected by NICE based •DTx - all MDrisk classes; •Reimbursement level: DTx that enables remote diagnosis,therapy, or monitoring in an area of national unmet need byhealthcare providers•Need of further data collection	•Potential for patient and system benefit	
What is reviewed to inform funding	Medical benefit orpatient-relevant Innovation in structure and organization of the process	Benefit to patients, and/or the socio-economic value healthcaresystem		
Required evidence type	Comparativestudy (may be Clinicaltrial**ongoing duringthe time of assessment)	Various accepted: RCT, RWE, expert opinions,etcundefined)	Evidence in a publishedformat (type	
Evidence generation support	12-month conditional reimbursement Identifies key gaps in evidence and assists No support offered	supporting completion of studyin RWE collection planning		
Pricing considerations	•12-month free pricing•Negotiated price after	•12-month fixed price**•Does not impact price but states whether it is good use of healthcare resources•Negotiated price aftercare process	•Price determined as a part of the health	
Evaluations conducted to date	•40 DTx reimbursed, including:•Process only introduced in 114 recommended (only DTx focused o rehabilitation)mental health assessed)	•37 DTx in the validation pyramid •Mental health – 182023•22 DTx evaluated, •DTx temporarily reimbursed (orthopedic n •Musculoskeletal disorders – 5•1 DTx reimbursed •Oncology - 4(oncology)		
Other assessment Routes	Yes (direct LPPR route to Yes (full NICE MTG on national level, local NoNo national reimbursement)reimb.assessments)			

*Inclusion of IIb class planned;** Details to be announced

CONCLUSION

- Countries are taking diverse approaches with varying evidence requirements for assessing the value of DTx, in contrast to the unified EU HTA initiative
- This divergence forces companies to invest substantial local resources to facilitate patient access to DTx solutions

Figure 3. Comparison of DTx framework function with the establishment of the process



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All web sources accessed 13th October 2023

Abbreviations: DTAC: Digital Technology Assessment Criteria; DiGA: Digital Health Applications;EVA: Early Value Assessment; DTx: Digital therapeutic; HCP: Healthcareprofessional; LPPR: List of products and services; MD: Medical device; MTG:Medical technologies guidance;NICE: The National Institute for Health and Care Excellence

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How has NICE's severity modifier been implemented?

HTA122

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INTRODUCTION AND OBJECTIVE

- In January 2022, the National Institute for Health and Care Excellence (NICE) published its updated manual on methods and processes for health technology evaluations. As part of this update, NICE introduced a quantitative decision modifier based on disease severity[1]
- NICE defines disease severity as the future health lost by people living with the condition having standard care in the NHS. This is assessed through absolute and proportional quality-adjusted life year (QALY) shortfall, as defined below:
  - Absolute shortfall: difference between potential future QALYs and QALYs with current standard of care (i.e. Areas A+B+C+D minus area D in Figure 1)[1,2]
  - Proportional shortfall: ratio of QALYs lost over the QALYs remaining (i.e., Areas A+B+C as a proportion of Areas A+B+C+D in Figure 1)[1,2]
- For conditions that qualify for the severity modifier, a QALY weight of 1.2 to 1.7 is applied, depending on the shortfall (Table 1)

This study aims to understand how the severity modifier has been implemented so far and its impact on committee decision making

Figure 1. Overview of QALYs taken into account for proportional and absolute shortfall calculations (adapted from OHE[2])

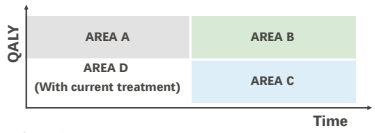

Table 1. QALY weightings for severity

QALY WEIGHT	PROPORTIONAL QALY SHORTFALL	ABSOLUTE QALY SHORTFALL
1	Less than 0.85	Less than 12
x1.2	0.85 to 0.95	12 to 18
x1.7	At least 0.95	At least 18

METHODS

- NICE health technology evaluations for which the updated methods applied (with final scopes from February 2022 onwards, cut-off date July 2023), were identified from publicly available information. As the severity modifier does not apply to the highly specialised technologies (HST) process, only topics undergoing NICE's single technology evaluation process were identified
- Evaluation documents were analysed to collect data on indication, cost-effectiveness results, recommendations, and mention of the severity modifier
  - For relevant evaluations, details on the company's approach to the severity modifier, NICE's critique of the severity modifier and the impact on the outcome of the appraisal were assessed

RESULTS

- 27 relevant evaluations were identified with draft or final guidance. The company made the case for the severity modifier in 3 evaluations: TA862, TA866, TA896 (Table 2)
- Of these 3 appraisals, a severity weighting was applied by the NICE committee in only 2, including a 1.2 weighting in TA896 and a 1.7 weighting to a subgroup in TA866. Both these technologies were recommended for use in routine commissioning. In contrast, the NICE committee concluded that there was high uncertainty on severity being met in TA862. The technology (trastuzumab deruxtecan) was recommended for use only within the Cancer Drugs Fund
- Unlike TA862 and TA866, TA896 was for a non-cancer therapy area and had a relatively young patient population. In each of the 3 appraisals, the manufacturer used the online Schneider tool to calculate proportional and absolute shortfall

Figure 2. Overview of number of company submission including a case for the severity modifier

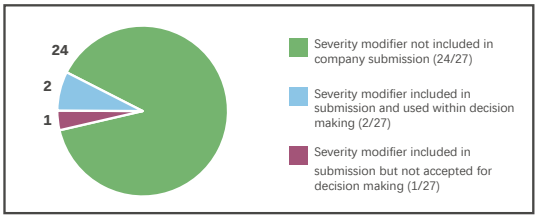

Table 2. Overview of appraisals including a case for the severity modifier

APPRAISAL	INTERVENTION	INDICATION	AVERAGE POPULATION AGE	PROPORTIONAL SHORTFALL	ABSOLUTE SHORTFALL	WEIGHTING APPLIED IN DECISION-MAKING?	EVALUATION OUTCOME
TA8623	Trastuzumab deruxtecan	HER2-positive unresectable or metastatic breast cancer	53 years	Not met for EAG or company	Met for 1.2 weighting in company scenario	No	Recommended for use in CDF
TA8664	Regorafenib	Previously treated metastatic colorectal cancer	60 years	Met for 1.7 weighting (for one subgroup)	Not discussed in final evaluation document	Yes 1.7 to one subgroup	Recommended for routine commissioning
TA8965	Bulevirtide	Chronic hepatitis D	35 years	Not discussed in final evaluation document	Met for 1.2 in all but 1 of the company's scenario analyses	Yes 1.2	Recommended for routine commissioning

CONCLUSION

- The severity modifier has been proposed in few evaluations so far, less than the proportion that NICE's analysis suggested would have applied for evaluations from 2011 to 2019 (~39%)[6].
- The NICE committee has generally needed convincing evidence to apply the modifier, although recognised the need to accept greater uncertainty in rare diseases in TA896
- Despite not officially recommending the Schneider tool, NICE has referred to it as a potential "helpful resource" and manufacturers have notably been using this within appraisals[7]
- During development of the severity modifier, some consultees suggested that older populations may have difficulty in qualifying for it[6]. NICE considered this unlikely to be an issue and it is interesting to note that in TA866, where proportional shortfall was met, the average population age was 60 years old
- Future research after further implementation of the severity modifier will enable greater insights

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How aware are biotech and pharmaceutical companies of the implementation of the new EU HTA?

PT26

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INTRODUCTION

After being ratified in early 2022, the Regulation (EU) 2021/2282 will bring joint EU HTA into effect in 2025 for selected products, establishing an EU-wide joint assessment of clinical effectiveness (JCA)1.

This will have wide-reaching changes on how HTA and early scientific advice is conducted in Europe and aims to replace the simultaneous evaluations of clinical data conducted by multiple country-specific HTA bodies.

METHODS

An online survey was distributed to 30 industry executives from biotechnology and pharmaceutical companies, with most respondents being from medium to large companies across a range of internal teams including health economics and outcomes research (HEOR), pricing, market access and global market strategy.

OBJECTIVES

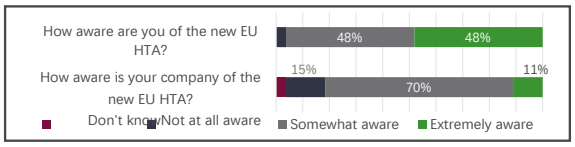
1.Gauge the current awareness of the new EU HTA process within the pharmaceutical industry
2.Understand the levels of preparation within the industry for EUHTA
3.What is the perceived impact of EUHTA on companies and why?

We also identified what challenges and opportunities the pharmaceutical industry envisions when the new regulations come into force then understand the reasons why companies have taken a particular approach

RESULTS

WHAT ARE THE CURRENT LEVELS OF AWARENESS OF EUHTA?

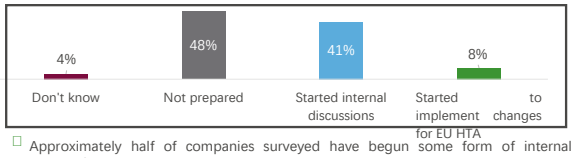
Figure 1: Awareness of the biotechnology and pharmaceutical industry of EU HTA



Only 22% of the respondents felt that the process has been clearly communicated, with respondents unclear as to what will be required in the EU HTA submission

HOW PREPARED ARE COMPANIES FOR THE START OF EUHTA?

Figure 2: Levels of preparedness for EU HTA among pharmaceutical companies

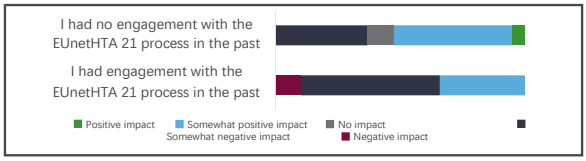


Approximately half of companies surveyed have begun some form of internal preparation

Reasons for not preparing yet include lack of time/resources, insufficient information on EU HTA and those without products launching soon enough warrant discussions

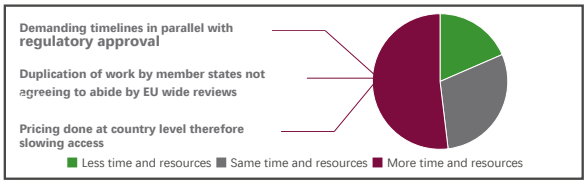
WHAT'S THE IMPACT ON COMPANIES, NEW PRODUCTS, AND GENERAL ATTITUDES TOWARD THE LEGISLATION?

Figure 3: The perception of the impact of EUHTA between those that were/were not engaged with EUnetHTA 21



48% of respondents believe the new EU HTA process will have a negative impact on their company, and this rises to 75% in respondents who have experience with EUnetHTA21

Figure 4: Perception of how the new EU HTA will impact time and resourcing



Over half of respondents thought EUHTA would increase the burden on companies

Although, 48% thought it would reduce time to market by requiring only a single dossier

DISCUSSION AND CONCLUSIONS

Whilst overall awareness of EU HTA is high there is uncertainty as to how pharmaceutical companies will adapt their processes to meet the increased resources required to deliver an EU HTA dossier. This is partly due to the perception among the majority of respondents that the detailed processes of EUHTA have not been clearly communicated

We anticipate that companies with orphan products in the pipeline are waiting to see how the first phase of JCAs (for oncology products) proceed before beginning to implement internal changes ahead of the second phase of the EUHTA in 2028

Opinions towards the EU HTA process are largely negative, with concerns about an increased resource burden required for successful market access, a sentiment that is the antithesis of the original purpose of the EUHTA. However, respondents acknowledge that the JCA provides an opportunity for better alignment on evidence requirements across countries and could speed up patient access in countries willing to use the JCA to form the basis of price negotiations. The general negative feeling towards the EU HTA shown in this survey also mirrors industry statements

Joint EU HTA is fast approaching realisation and with less than two years until products start to enter the process in 2025 manufacturers need to start thinking about what impact the new process could have for them and what plans they could action to navigate in these changing waters

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Can just three PICOs be feasible for oncology assessments with the Joint EU HTA Framework, whilst considering all 27 member states specificities?

HTA228

Authors Chirico, G.1; Boland, L.1; Craddy, P.2; Foxon, G.1

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INTRODUCTION

- From 2025, oncology treatments will be the first therapy area to be mandated to be assessed using the Joint EU Health Technology Assessment (HTA) process for clinical evaluation
- Prior to the manufacturer submission, each member state (MS) will define PICOs (Population, Intervention, Comparator, Outcomes) using a survey
- PICOs help specify the assessment framework and will be consolidated by the assessor and co-assessor from the Member State coordination group into as few PICOs as possible1. Though no official upper number of PICOs have been reported, anecdotally it has been assumed to aim for 2-3
- Different MS often have different views on the comparators depending on available products and clinical practice in their market, on the populations they are willing to treat and the types of endpoints that they deem to be relevant; leading to uncertainty over whether PICO's can be condensed to just 2-3

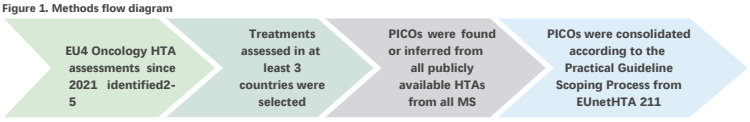
OBJECTIVE

To understand the number of PICOs that may be proposed by EU Member States for inclusion in oncology EU HTA assessments

METHODS

EU4 Oncology HTA assessments since 2021 were identified using HTA agency databases2-5. Treatments assessed in at least 3 countries were selected and PICOs were found or inferred from all publicly available HTA assessments from all MS. PICOs were consolidated according to the Practical Guideline Scoping Process from EUnetHTA 21

Figure 1. Methods flow diagram



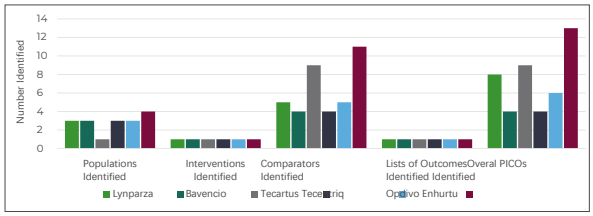
RESULTS

- Six were the oncology treatments assessed in at least 3 of the EU4 countries and for which all publicly available HTAs from all the MS were identified and analysedto extract the PICOs
- All 6 oncology products from 4 EU countries had a higher number of PICOs than what has been estimated

DRUG	THERAPY AREA	EU COUNTRIES WITH PUBLIC HTA	PICOS IDENTIFIED	POPULATIONS IDENTIFIED	INTERVENTIONS IDENTIFIED	COMPARATORS IDENTIFIED	LISTS OF OUTCOMES IDENTIFIED
Bavencio (avelumab)	Urotelial carcinoma	DE FR IT ES DK IE	**4**	3	1	4	1
Lynparza (olaparib with bevacizumab)	Ovarian cancer	DE FR IT ES DK IE	**8**	3	1	5	1
Tecentriq (atezolizumab with bevacizumab)	Hepato-cellular carcinoma	DE FR IT ES DK IE PT	**4**	3	1	4	1
Tecartus (brexucabtagene autoleucel)	Mantel cell lymphoma	DE FR IT ES SE FI	**9**	1	1	9	1
Opdivo (nivolumab)	Squamous cell carcinoma of the oesophagus	DE FR IT ES SE	**6**	3	1	5	1
Enhertu (trastuzumab deruxtecan)	Breast cancer	DE FR ES DK SE NL FI	**13**	4	1	11	1

- The high number of PICOs was due either to subpopulations or differences in the comparator

Figure 2. Comparison of the PICO breakdown across the recently assessed oncology therapies in the EU



CONCLUSION

- None of the investigated treatments were found to have 2-3 PICOs, following consolidation as per the Joint EU HTA guidelines1
- Similarly, a recent EUnetHTA PICO exercise found 9 PICOs for Pombliti, where 10 MS were surveyed6
- We can speculate that the number of PICOs will grow significantly higher once all EU27 MS PICOs taken into account
- MS-specific heterogeneity in population and treatment practices, exemplified by the number of PICOs, may make the Joint EU HTA's aim to harmonise assessments challenging
- Moreover, if the MS feels the Joint Assessment has not addressed their needs it may lead to duplication due to additional national submissions
- For manufacturers, this means that additional data collection and work on the affiliate level will likely remain necessary
- For patients, this may mean delayed access in countries needing additional data.
- Germany, typically one of the first markets in Europe for products launches, is also one of the country that will likely require additional data and, because of this, may see it-self being pushed down the launch order

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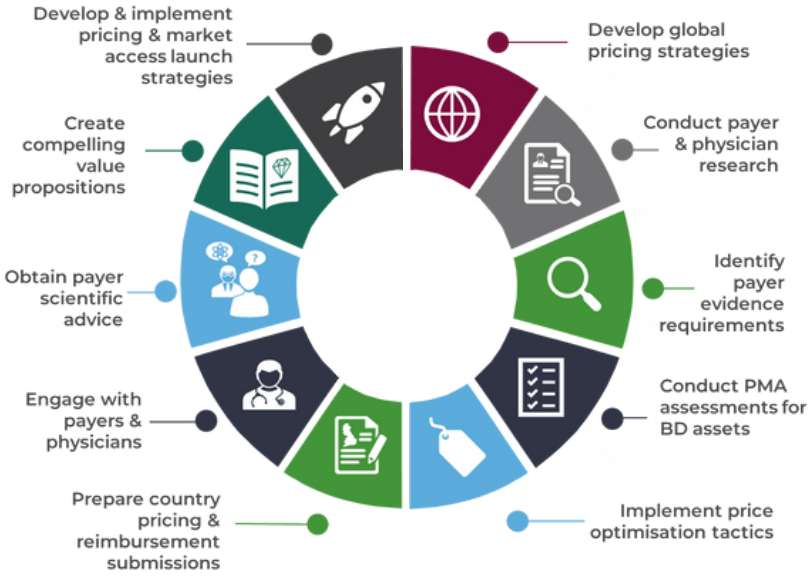

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