ISPOR Europe 2023

12 - 15 November

Poster Tour Guide Packet

Poster Session:	**Poster Session 3**
Tour Name:	**EU Joint Clinical Assessment**
Tour Date/Time:	Tuesday, 14 November 2023, 11:30 - 12:15
Tour Location:	Area A, Poster and Exhibit Hall, Hall C

Acceptance Code:	PT25
Board Number:	1A
Abstract Title:	Comparison of Approval Dates of New Substances Between the United States of America (Food and Drug Administration, FDA) and Europe (European Medicines Agency, EMA)
Presenting Author:	Doreen Bonduelle

Abstract Body:

OBJECTIVES: Early access to innovative medications is a key factor for the quality of medical care. We investigated differences in approval dates of new active substances between the United States (US) and Europe.

METHODS: Data of new active substances approved by the US FDA and EMA from 01.01.2018–26.05.2023 were retrieved from FDA and EMA websites. Generic, biosimilar and hybrid approvals were excluded from evaluation. We reviewed whether and when each drug was approved by the other agency. Subsequently, the time difference between the drug approval dates between the agencies was calculated.

RESULTS: In total, n = 353 new active substances were approved since 2018 by FDA or EMA. Of these, 101 (28.6%) were only approved by FDA compared to 31 (8.8%) only by EMA. From the 221 active substances approved by both agencies, 70 (31.7%) were approved with 0.5 years difference. 85 (38.5%) substances were approved by FDA 0.5–1.5 years earlier, 33 (14.9%) 1.5–3 years earlier and 10 (4.5%) >3 years earlier. On the other hand, 7 (3.2%) substances were approved by EMA 0.5–1.5 years earlier, 5 (2.3%) 1.5–3 years earlier and 11 (5.0%) >3 years earlier. Therefore, US patients on average get access to innovative medicines earlier than European patients.

CONCLUSIONS: More than 25% of new active substances approved by the FDA within the last five years are not yet approved in Europe whereas only less than 10% of new active substances approved by EMA are not yet approved by FDA. In total these results lead to later access to innovative medicines in Europe than in the US. Potential reasons for this may be strategic market and pricing decisions of the pharmaceutical industry or differences in data information, evaluation criteria and timelines between the two jurisdictions.

Tour Guide's Questions for Starting Q&A (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

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Tour Location:	Area A, Poster and Exhibit Hall, Hall C

Acceptance Code:	PT26
Board Number:	2A
Abstract Title:	How Aware Are Biotech and Pharmaceutical Companies of the Implementation of the New EU HTA?
Presenting Author:	Graham Foxon

Abstract Body:

OBJECTIVES: To gauge awareness of the new EU HTA process within the pharmaceutical industry; how prepared companies are and the general attitudes and expectations towards it. Also, to identify what challenges and opportunities the pharmaceutical industry envisions when the new regulations come into force.

METHODS: 30 industry executives from biotechnology and pharmaceutical companies were surveyed, 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.

RESULTS: While 2025 is rapidly approaching and even though 97% of respondents are aware of the new process, less than 10% of companies have started implementing changes at an EU or global level to meet the needs of joint clinical assessments. This is potentially explained by the fact that 78% of the respondents felt the new EU HTA process has not been communicated clearly. Some opinions towards the EU HTA process are surprisingly negative, with perceptions that it will increase the time and resource burden on companies and not speed up patient access to new drugs. Many also expect that country-specific dossiers will still be needed. Interestingly, respondents who have had previous engagement with the EUnetHTA, 21 were much more likely to have a negative opinion towards the new EU HTA. However, some did have a positive outlook on the opportunities for alignment on evidence requirements and overall opinion on the EU HTA is relatively evenly split.

CONCLUSIONS: In general awareness of EU HTA is high, however, there is still significant uncertainty as to how pharmaceutical companies will adapt their processes to meet the increased recourses required to deliver an EU HTA dossier, especially considering the overall preparedness is low.

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Acceptance Code:	PT27
Board Number:	3A
Abstract Title:	How Much Does TLV Value Rarity? A Review of Reimbursement Decisions on Orphan Drugs in Sweden from 2017 through 2022
Presenting Author:	Maria Kinderas

Abstract Body:

OBJECTIVES: Reimbursement of orphan drugs continues to pose significant challenges for decision-makers given frequent high costs and limited evidence. Historically, the willingness to pay (WTP) for new treatments appraised by the Swedish Dental and Pharmaceutical Benefits Agency (TLV) has been influenced by disease severity and uncertainty in the documentation but not by the rarity of the condition. However, in 2016, TLV for the first time accepted a higher cost per quality-adjusted life-year gained due to the rarity of the targeted condition. This study aims to explore whether the rarity of the conditions has impacted incremental cost-effectiveness ratios (ICERs) accepted by TLV from 2017 through 2022.

METHODS: Data were extracted from all TLV decisions on reimbursement applications of medicinal products from 2017 through 2022 that had orphan drug status according to European Union regulations at the time of TLV evaluation and included a TLV ICER as a basis for decision. Extracted variables included TLV ICERs, disease severity, uncertainty in the health economic analysis, and reimbursement outcome. Information on the number of patients with the disease conditions were extracted from the European Medicines Agency's orphan drug designation decisions.

RESULTS: 22 positive TLV decisions met the inclusion criteria. The estimated mean number of patients with each condition in Sweden was 1,842 (range, 105-4,209). The mean TLV ICER was 753,628 SEK (range, 96,784-1,450,696 SEK), and only two decisions had ICERs above the previous unofficial WTP threshold for very high disease severity of 1,000,000 SEK, not accounting for the rarity of the condition.

CONCLUSIONS: Although the decision made by TLV in 2016 opened rarity for consideration in determining acceptable ICERs, the current review suggests that there has not been any clear shift in accepted ICERs as a function of rarity.

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Acceptance Code:	PT28
Board Number:	4A
Abstract Title:	Lost in PICO? a Simulation of the EU HTA Scoping Process
Presenting Author:	Matthias Schönermark

Abstract Body:

OBJECTIVES: The joint clinical assessment (JCA) according to Regulation (EU) 2021/2282 (EU HTA) will initially be implemented for oncology drugs and ATMPs from January 2025. All JCA procedures are commenced by the scoping process: The formulation of a member state-specific research question, represented as individual PICO schemes. Patient population, intervention, comparator, and study endpoints to measure the outcome are determined by the authorities as basis for clinical evaluation. Given the diversity of standards of care in Europe, multiple PICOs can be demanded. By simulating an EU HTA-like scoping process as of today, this analysis aims to assess the risk of receiving numerous PICOs. How complex will it be?

METHODS: To determine heterogeneity of expected PICO schemes, completed national HTA assessments from the “EU big 6” member states were compared regarding several oncology drugs of specific indications. Procedures from the voluntary earlier joint clinical evaluation Joint Action 3 were used as supplement.

RESULTS: Complexity of the number and design of PICO schemes for oncologics was identified: chosen patient groups and interventions were largely consistent between HTA assessments, whereas selection of comparators differed and resulted in indication-dependent heterogeneity with up to 5 PICOs for 6 member states. The acceptance of outcomes was consistent, albeit relevance of progression-free survival varied significantly.

CONCLUSIONS: EU HTA is supposed to reduce redundancies and bureaucracy by harmonization. However, the diverse standard of care across member states needs to be reflected in the EU HTA dossier through numerous PICO schemes, especially in dynamic indications. This analysis supports the anticipation of strategic and operational effort for future EU HTA dossiers. Compared to national HTA procedures, this will create complexity and uncertainty in predictability of the statistical analyses required for assessment. It is therefore questionable whether EU HTA can comply with its objective.

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Acceptance Code:	PT29
Board Number:	5A
Abstract Title:	Predicting PICOs for EU Joint Clinical Assessment: Lessons from PICOs in Relative Effectiveness Assessments (REA) from EUnetHTA Joint Action 3 Project
Presenting Author:	Catherine Chamoux

Abstract Body:

OBJECTIVES: To identify how PICOs were determined by EUnetHTA reviewers during the JA3 project (2016-2021), for medicines, in order to anticipate how PICO selection might be done for the forthcoming EU Joint Clinical Assessment.

METHODS: Examination of the lists of PICOs in the REA reports published by EUnetHTA during the JA3 project (2016-2021): 14 medicines were selected from the 18 published, excluding 4 Covid-19 treatments.

RESULTS: The 14 REAs were authored by 9 countries. Six products were Oncology drugs. Most medicines were appraised on the population stated in their label. Only 2 medicines had 2 sets of populations in their REA report: Polatuzumab (JA6) and Ustekinumab (JA07), one corresponding to their label, the other being on a restricted population. The authors of the reports were different, as were the therapeutic areas. The existing comparators (on average, 4 comparators per product) were chosen from EU clinical guidelines. The Outcomes lists were of different structures and lengths (average of 6 for efficacy, average of 9 for safety) some differentiating critical outcomes, others not. Only four of the efficacy outcomes were common for all Oncology drugs (OS, PFS, CR, Progression/relapse free survival). HRQoL requirement was a standard. Safety outcomes were different, some using a grade classification, others not.

CONCLUSIONS: In this analysis, we see that the PICOs reviewed for the 14 medicines selected from the JA3 EUnetHTA project were different in their presentations and content/wording, even for drugs in the same therapeutic area (Oncology). Safety outcomes were not standardized. A minority of drugs were appraised for 2 different populations. EU JCA co-ordinators should consider improving standardization and predictability.

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Acceptance Code:	PT30
Board Number:	6A
Abstract Title:	Will Health Technology Assessment (HTA) Bodies in Europe Accept Evidence from an External Control Arm to Supplement Evidence from Clinical Trials for Chronic Diseases?
Presenting Author:	Nick Nielsen

Abstract Body:

OBJECTIVES: As HTA bodies become increasingly familiar with real-world evidence (RWE), and as indicated in the NICE RWE framework, there is a greater recognition of its value in supplementing the clinical evidence package, primarily from randomized-controlled trials (RCTs). External control arms (ECAs) use historical RCT or RW data, allowing for comparison against relevant therapeutic options. This study examined the acceptance of ECA in HTA for chronic diseases.

METHODS: HTA guidelines for RWE from NICE, HAS, and IQWiG were reviewed to examine the detail of guidance for ECA analysis. Furthermore, six double-blinded payer expert interviews were conducted to explore the acceptance of ECA in the United Kingdom (UK), Germany, France, and Italy.

RESULTS: NICE RWE framework provides guidance on ECA, however insights from HAS and IQWiG are scarce. In the UK, NICE is more open to accept evidence that support the findings from RCTs, whereas in Germany there is a stronger preference for RCT alone. In France and Italy there is an increased interest in ECA, but its acceptance remains low. Acceptance of ECA is higher in the absence of relevant comparator in the RCT, due to evolving treatment landscape or ethical reasons, and in rare diseases and oncology rather than chronic diseases. Overall, ECA is more likely to be accepted in HTA if a strong rationale supporting its use is provided and if data sources are suitable. Moreover, appropriate methodology should be applied to ensure unbiased analysis, especially when ECA is used to show clinical efficacy.

CONCLUSIONS: HTA acceptance of ECA remains low, with UK being the exception. A detailed rationale regarding why ECA is relevant, in combination with the use of appropriate data sources and analytical methods can improve acceptance across therapy areas, ultimately leading to an enriched evidence package and reduced uncertainty.

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