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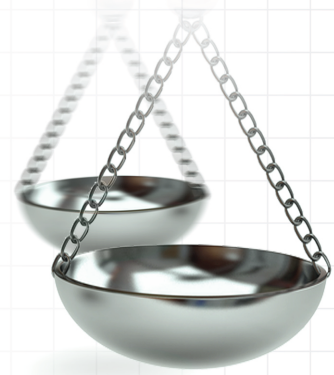

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Access in all areas? A round up of developments in market access and health technology assessment: part 9

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In this update, we examine Spain's comprehensive pharmaceutical legislation reform; France's refined health economic evaluation approach; and the US' proposed Most Favored Nation pricing mechanism.

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In April this year, the Spanish Minister of Health announced a comprehensive reform of Spain's pharmaceutical legislation, marking the first structural overhaul since the 1990s. The announcement is the most recent development of a process started by a court ruling in 2023, which declared void the Spanish medicines evaluation process based on the therapeutic positioning report (in Spanish: informe de posicionamiento terapuetico [IPT]). Multiple objectives are included in this reform, and first it aims to accelerate access to medicines through shortening funding decision making and through the creation of a direct access pathway. Broader objectives also include promoting competition through a reference pricing system, expanding prescription rights to nurses and physiotherapists and enhancing supply chain resilience. It is important to understand the reasons for these changes. As per the 2023 court ruling, despite health technology assessment (HTA) being considered an evidence-based tool and having an established process in Spain, its real impact in informing final funding decisions is unclear. Pinilla-Dominguez and colleagues conducted a comprehensive analysis of 477 therapeutic indications between May 2019 and December 2022 [1], revealing striking disconnects between HTA assessments and reimbursement decisions. Their findings revealed that only 9.5% of reimbursement reports mentioned HTA conclusions, and a mere 21.7% of HTAs included keywords aligned with specific decision-making criteria. The analysis identified different criteria influencing reimbursement decisions depending on the outcome, with positive recommendations being associated with disease severity and therapeutic value, including clinical and cost–effectiveness, while negative recommendations were linked to budget impact and the availability of cheaper alternatives. The innovation criterion was not utilized to support any decision analyzed. To address these challenges, the Spanish government is crafting a new governance structure for HTA, separating the functions for assessment, therapeutic positioning of medicines and final decision making. This includes establishing two Offices for the Evaluation of the Efficiency of Health Technologies, one for medicines and another for other health technologies – and a Health Technology Positioning Group to facilitate stakeholder participation and ensure transparency. The new framework is developed in an integrated manner with the European Union's Joint Clinical Assessment process, which means creating a more transparent, rigorous and inclusive appraisal framework, ensuring that HTA assessments effectively inform pricing and reimbursement decisions, ultimately enhancing patient access to innovative treatments while maintaining the sustainability of Spain's healthcare system. For pharmaceutical manufacturers, this comprehensive reform potentially means companies should prepare for a more complex but more transparent process.

Beyond the reform in Spain, France's Commission d'évaluation économique et de santé publique (CEESP) has successfully implemented a more focused approach to health economic evaluation (HEE) following criteria changes introduced in early 2023. The 2024 activity report [2] confirms that the revised inclusion criteria – raising

the sales threshold to €20 million in the second year post-commercialization and mandating evaluation for all advanced therapy medical products – achieved their intended streamlining effect. Economic evaluations decreased from 30 to 32 dossiers annually in 2021–2022 to 22 in 2023 and 19 in 2024, but review timelines (189–191 days median) were similar. This refinement represents a deliberate effort to concentrate evaluation resources on health technologies with the most significant economic impact and reducing administrative burden. Economic analyses must comply with Haute Autorité de santé (HAS) evaluation guidance. Following technical review, the CEESP may raise concerns about methodology regarding efficacy, safety, utility scores and costs. Reservations are noted when methodological choices deviate from recommendations, with severity determined by the rationale's acceptability and impact on results, particularly regarding uncertainty. The significance varies by product and context – for example, noncompliance in quality-of-life methods has greater impact when health-related quality of life is a key outcome. Reservations are classified into three levels: minor reservations deviate from recommendations with minimal impact; important reservations are justifiable but significantly affect findings; and major reservations invalidate the economic evaluation, rendering it unreliable despite any justifications. Sadeuk-Benabbas *et al.* analyzed all 27 rare disease CEESP opinions from 2014 to 2021 and found that 17 (63%) were classed as having important methodological reservations, and 10 (37%) having major reservations [3]. Fifty-two percent (14 assessments) had significant utility measurement concerns, and major reservations were often due to use of inappropriate data sources such as expert opinion, disease-specific questionnaires or vignettes. Caregiver utilities were rarely considered, despite their potential relevance in rare disease, particularly those affecting children. For the 19 assessments where CEESP had conclusions on efficiency, the average ICER was approximately €827,000 per quality-adjusted life year (QALY), with some evaluations reaching up to €2.7 million per QALY. The average ICER for all innovative medicines subjected to economic evaluation by the CEESP between 2014 and 2020 was €287,821/QALY and therefore 50% of the rare disease ICERs considered extremely high by CEESP. These developments create both opportunities and challenges for pharmaceutical manufacturers operating in the French market. The €20 million threshold means fewer products will undergo HEE. However, the mandatory inclusion of all advanced therapy medical products regardless of sales projections necessitates early HEE planning for cell and gene therapies. Critically, CEESP applies standard methodological frameworks without specific adaptations for rare diseases. With HAS indicating plans to give greater weight to economic evaluation in future decision-making, manufacturers must prepare for an environment where economic arguments require greater sophistication and broader value demonstration [4,5].

The European experience with HTA refinement and economic evaluation takes on added significance in light of recent US policy developments that could fundamentally reshape global pharmaceutical pricing dynamics. The Trump Administration issued an Executive Order on 12 May 2025, proposing a "Most Favored Nation" (MFN) approach to equalize US drug pricing with other developed countries through international reference pricing (IRP) [6]. The President's Executive Order directs the secretary of the US Department of Health and Human Services (HHS) to communicate MFN price targets to pharmaceutical manufacturers and the secretary is directed to propose rulemaking to establish such pricing. On 20 May 2025, the HHS defined its price target as the lowest among countries in the Organization for Economic Co-operation and Development with a gross domestic product per capita of at least 60% of the US, and clarified that its price targets would apply to all brand-name drugs without generic or biosimilar competition [7]. Following the Executive Order, recent developments have escalated the administration's approach significantly. On 31 July 2025, President Trump sent letters to leading pharmaceutical manufacturers including AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, EMD Serono, Genentech, Gilead, GSK, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Regeneron, and Sanofi, outlining specific steps they must take to bring down prescription drug prices in the US to match the lowest prices offered in other developed nations. The letters represent a significant escalation from policy proposal to direct manufacturer engagement, with the administration stating that "industry proposals have fallen short" and warning that the federal government "*will deploy every tool in our arsenal to protect American families from continued abusive drug pricing practices*" if manufacturers refuse to comply. The letters outline four key requirements: calling on manufacturers to provide MFN prices to every single Medicaid patient; requiring manufacturers to stipulate that they will not offer other developed nations better prices for new drugs than prices offered in the US; providing manufacturers with an avenue to cut out middlemen and sell medicines directly to patients at prices no higher than the best price available in developed nations; and using trade policy to support manufacturers in raising prices internationally, provided that increased revenues abroad are reinvested directly into lowering prices for American patients and taxpayers [8]. A recent article discusses the experience with IRP in the European Union, which ultimately resulted in price convergence anchored to high-income countries like Germany and France,

without evidence of sustained price reductions across Europe [9]. The article also provides some scenarios as to how MFN play out. One suggestion is that US implementation of MFN pricing would position America as the global anchor country for price referencing, similar to Germany and France in Europe. This fundamental shift would create immediate strategic challenges for pharmaceutical manufacturers, who would likely seek to achieve list prices in designated reference countries within range of US prices. This approach would necessitate extensive use of confidential net price agreements to maintain market access in countries unable to afford reference prices, while companies may simultaneously consider delisting products in select markets or withdrawing from Europe entirely when concerned about commercial implications in the US market. The authors also suggest that manufacturers might respond with higher US launch prices to compensate for global revenue losses from IRP implementation. The proposed MFN pricing mechanism represents a potential paradigm shift in global pharmaceutical economics, with implications extending far beyond US borders. The success of such a policy will largely depend on implementation details that remain unclear, but the European experience with IRP suggests that achieving sustained price reductions while maintaining innovation incentives and broad market access will prove challenging. Pharmaceutical manufacturers will need to develop sophisticated global pricing strategies that account for the interconnected nature of international markets, potentially requiring fundamental changes to launch sequencing, pricing strategy and market access approaches worldwide.

These developments across Spain, France and the USA illustrate the dynamic nature of market access landscapes and the varying approaches to balancing healthcare sustainability with innovation. The common thread across all three markets is the growing emphasis on demonstrating value that will be important for successful market access regardless of specific policy mechanisms adopted by individual countries.

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References

1. Pinilla-Dominguez P, Pinilla-Dominguez J. Challenges and reforms in Spain's health technology assessment system: analysis of criteria influencing medicines' reimbursement decisions between 2019 and 2022 in Spain. *Eur. J. Health Econ.*, doi: 10.1007/s10198-025-01790-7 (2025). (Epub ahead of print).
2. Rapports d'activité 2024 des commissions et conseil de la HAS. *Haute Autorité De Santé*, Available at: https://www.has-sante.fr/jcms/p_3349687/fr/rapports-d-activite-2024-des-commissions-et-conseil-de-la-has
3. Sadeuk-Benabbas S, Autin E, Couillerot A-L, Clément V. Are there specificities for assessing quality of life and utilities in rare diseases for economic evaluation in France: a case study of published CEESP (Health Economic and Public Health Committee) opinions. *Value Outcomes Spotlight*, (2025). Available at: https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/heor-in-oncology-care/are-there-specificities-for-assessing-quality-of-life-and-utilities-in-rare-diseases-for-economic-evaluation-in-france--a-case-study-of-published-ceesp-(health-economic-and-public-health-committee)-opinions
4. Shafrin J, Kim J, Cohen JT *et al.* Valuing the societal impact of medicines and other health technologies: a user guide to current best practices. *Forum Health Econ. Policy* 27(1), 29–116 (2024).
5. Pannelay AJ, Gilardino RE, Ramagopalan SV. Access in all areas? A roundup of developments in market access and health technology assessment: part 6. *J. Comp. Eff. Res.* 14(3), e240239 (2025).

6. The White House. Delivering most-favored-nation prescription drug pricing to American patients. Available at: https://www.whitehouse.gov/presidential-actions/2025/05/delivering-most-favored-nation-prescription-drug-pricing-to-american-patients/ (2025).
7. US Department of Health and Human Services. HHS, CMS set most-favored-nation pricing targets to end global freeloading on American patients. Available at: https://www.hhs.gov/press-room/cms-mfn-lower-us-drug-prices.html (2025).
8. The White House Fact sheet: President Donald J. Trump Announces Actions to Get Americans the Best Prices in the World for Prescription Drugs. Available at: https://www.whitehouse.gov/fact-sheets/2025/07/fact-sheet-president-donald-j-trump-announces-actions-to-get-americans-the-best-prices-in-the-world-for-prescription-drugs/
9. Grueger J, Martin K, Sullivan SD. Referencing drug prices of other countries may not sustainably lower prices in the United States: lessons from Europe. *Value Health*, doi: 10.1016/j.jval.2025.06.010 (2025) (Epub ahead of print).