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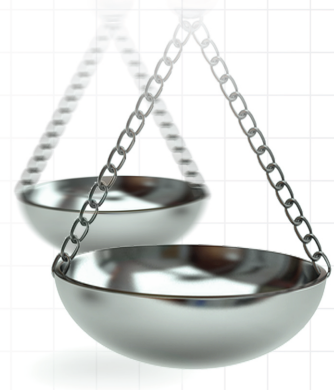

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Access in all areas? A round-up of developments in market access and health technology assessment: part 10

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In this update, we examine the US' Food and Drug Administration (FDA) Commissioner's National Priority Voucher pilot program; The Netherlands' Zorginstituut Nederland (ZIN) implementation framework for the EU HTA Regulation; and Italy's Agenzia Italiana del Farmaco (AIFA) refined criteria for assessing therapeutic innovativeness.

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Announced in June 2025, the FDA's Commissioner's National Priority Voucher (CNPV) pilot program represents an unprecedented initiative to reduce drug and biologic review times from the standard 10–12 months to just 1–2 months [1]. The program employs a collaborative tumor board-style review process led by the US FDA's Office of the Chief Medical and Scientific Officer, rather than the traditional sequential review across multiple offices. The program identifies five key priority areas for treatments: those that address US public health crises (such as developing universal flu vaccines); transformative cures that exceed breakthrough therapy thresholds; therapies that address large unmet medical needs; companies that onshore drug development to support generalizability for the US and manufacturing to strengthen US supply chain resilience; and finally increasing affordability, where companies lower US drug pricing consistent with Most Favored Nation pricing or the treatment reduces downstream medical utilization costs. Unlike existing priority review vouchers, CNPVs are nontransferable and must be commenced within 2 years of receipt. The FDA retains discretion to extend review timelines if data is insufficient or results are ambiguous. For pharmaceutical manufacturers, the CNPV program presents both opportunities and strategic considerations. The dramatic timeline reduction offers first-mover advantages in critical therapeutic areas, potentially providing substantial market exclusivity benefits. Companies with existing US manufacturing infrastructure or willingness to relocate production may find themselves better positioned for CNPV consideration. The CNPV program's incorporation of pricing considerations into regulatory review represents a paradigm shift that blurs traditional boundaries between regulatory approval and market access. By explicitly linking 'increasing affordability' to expedited review benefits, the FDA is establishing a novel precedent where drug pricing becomes a factor in regulatory decision-making rather than remaining separate commercial considerations. For manufacturers, this creates complex strategic considerations around global launch sequencing and pricing strategies. The program may incentivize companies to focus on US-only launches or fundamentally restructure their global pricing models to capture the significant first-mover advantages offered by 1–2 month review timelines.

While the US focuses on accelerating specific priority programs, Europe has embarked on a comprehensive harmonization of HTA processes across member states. The European HTA Regulation (HTAR), which came into effect in January 2025, mandates Joint Clinical Assessments (JCAs) that member states must give 'due consideration' in their national HTA processes [2]. The Netherlands' Zorginstituut Nederland (ZIN) recently published on how they are adapting to this new paradigm [3]. The national HTA report currently prepared by ZIN is based on a submission

by manufacturers and typically includes a pharmacotherapeutic assessment report, often accompanied by budget impact analyses, and may also include a pharmacoeconomic report. ZIN's implementation strategy for the HTAR centers on two major process modifications: earlier scoping phases that align with EMA regulatory timelines, and the adoption of JCA reports as starting points for national assessments. ZIN established a comprehensive governance structure involving project teams, steering committees and advisory groups to manage the transition. Their gap analysis identified challenges across six domains: legal compliance, information and knowledge management, IT infrastructure, communication and stakeholder engagement, capacity and resources and financial sustainability. Notably, ZIN found that no changes to Dutch legislation were required, as European regulations automatically apply and the Dutch Health Insurance Act provides sufficient flexibility. ZIN decided that manufacturers can start the preliminary dossier procedure once the submission dossier at EU level is declared complete and before the JCA report is finalized; however, ZIN's formal National assessment process will only start once the JCA is complete. It was noted that availability of JCAs might impact the way of working of Beneluxa, a collaboration with Belgium, Luxemburg, Austria and Ireland [4] and this needs further discussion with the Beneluxa task force. ZIN needs to clarify the type of additional information beyond the JCA that manufacturers will need to submit to them, information not shared at EU level; for example, a pharmacoeconomic dossier and budget impact analysis. The gap analysis identified the need for enhanced training in advanced statistical methods, particularly indirect treatment comparisons and network meta-analysis, reflecting the anticipated increase in complex evidence synthesis, and especially needed when The Netherlands takes on an assessor or co-assessor role for JCA. ZIN redesigned dossier templates to incorporate JCA findings while maintaining Dutch-language reporting for transparency to national stakeholders. ZIN recognizes the need to develop a process to quickly gather input from relevant patient and physician stakeholder organizations for national scoping of population–intervention–comparator–outcomes (PICOs), because the time to respond to PICO requests is short. The Dutch implementation experience reveals that successful HTAR adaptation requires substantial organizational transformation beyond mere procedural adjustments. For manufacturers, The Netherlands' approach signals that while clinical assessment harmonization may reduce some regulatory burden, national appraisal processes mean companies must still navigate 27 distinct value assessment frameworks across EU member states. ZIN's emphasis on indirect comparison methodologies signals how important this likely will be in the JCA process to address PICOs coming from all member states and suggests manufacturers should prepare for robust comparative effectiveness research in their evidence generation strategies.

The Italian experience provides another perspective on evolving HTA frameworks, particularly regarding how countries define and reward innovation. Italy's Agenzia Italiana del Farmaco (AIFA) has operated an innovativeness designation system since 2017 [5]. The system emerged from a need to balance innovation incentives with cost-containment imperatives in the Italian pharmaceutical market, where spending on medicines is subject to strict budget ceilings. The Italian approach differs significantly from other European countries in that innovativeness status directly impacts market access through dedicated funding and immediate regional access, rather than merely influencing pricing negotiations. Innovative medicines are also exempt from payback mechanisms if the national pharmaceutical expense cap is exceeded. The system underwent significant restructuring when the originally separate funds for cancer medicines and other therapeutic areas, established in 2017, were consolidated into a single fund in 2022 to optimize resource allocation and prevent the inefficiencies that arose from the lack of communication between the two previous funding streams. The assessment framework employs three primary criteria: unmet medical need and added therapeutic value, both evaluated on five-level scales ranging from maximum to absent, and quality of evidence, assessed using the four-level Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology spanning high to very low-quality ratings. Two distinct categories of innovation status exist within this framework. Full innovation status, granted for three years, requires at least moderate ratings for both unmet need and therapeutic value alongside high-quality evidence, providing access to dedicated funding and immediate regional market entry. The other status, conditional innovation, offers an 18-month designation that facilitates accelerated market access without dedicated funding, although it may be upgraded to full status based on post-marketing data. Until now, the policy restricted innovation status to medicines addressing serious medical conditions; specifically, life-threatening diseases, conditions necessitating frequent hospitalization, or disorders causing significant disability that substantially compromises quality of life. Therapeutic value must be substantiated through validated clinical end points, with overall survival for example recognized as the gold standard for oncological indications. Importantly, improvements in patient convenience, such as more manageable administration routes, are not considered sufficient for demonstrating added therapeutic value. A notable exception exists for rare disease therapies, which may qualify for innovation status despite lower evidence quality provided that

maximum or important ratings are achieved for unmet need and therapeutic value. AIFA's updated criteria, published in July 2025, maintain the three-dimensional assessment framework of therapeutic need, added therapeutic value and quality of evidence [6]. The new approach explicitly targets "*serious diseases or pathological conditions with medium-low epidemiological impact*", explicitly ruling out treatments for diseases with high prevalence. The updated criteria exclude certain categories from innovativeness evaluation: medicines based on active ingredients that have lost patent protection, applications for new indications submitted more than 10 years after initial innovativeness designation, and most notably, anti-infective agents targeting multidrug-resistant pathogens. This latter category now has a specific pathway, automatically qualifying for the innovative medicines fund, provided they retain patent protection and target multidrug-resistant infections. The special treatment of antimicrobial agents represents a significant policy innovation that recognizes market failures in antibiotic development. The 2025 budget allocates €900 million for fully innovative medicines, €300 million for conditional innovations and €100 million specifically for antibiotics. Manufacturers are permitted to request therapeutic innovativeness status per indication for products that can 'induce [a] cure or reduce the risk of lethal or potentially lethal complications, slow down the progression of the disease, [or] improve the quality of life of patients', according to the AIFA criteria. Research analyzing 141 medicines evaluated between 2017 and 2021 showed that 31.9, 29.8 and 38.3% were evaluated as fully innovative, conditionally innovative and non-innovative, respectively. Added therapeutic value and the quality of the evidence were associated with receiving innovative status, and full compared with conditional innovativeness. For manufacturers, the Italian model represents a clear framework where innovation status directly translates to tangible commercial benefits – dedicated funding, immediate regional access and exemption from payback mechanisms – making it a critical pathway for companies developing treatments in targeted therapeutic areas. The requirement for high-quality evidence alongside at least moderate ratings for therapeutic value means companies cannot rely on promising but preliminary data to secure full innovation benefits. This emphasis on evidence quality necessitates strategic planning around clinical trial design, with particular attention to head-to-head comparisons where feasible and validated surrogate end points where longer term data may be premature.

Success in the evolving access landscape requires strategic alignment with public health priorities, robust evidence generation capabilities and adaptive approaches to global market access planning. The common thread across all three initiatives discussed is the emphasis on demonstrating genuine value as the foundation for market access success.

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