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Access in all areas? A round-up of developments in market access and health technology assessment: part 14

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In this update we examine the selection of 15 drugs for the third cycle of Medicare price negotiations under the Inflation Reduction Act and analyze emerging evidence of the Most-Favored-Nation impact on global pharmaceutical access, including launch delays and market withdrawals. We also review recent research on the tension between US patient values and foreign health technology assessment frameworks and discuss the review of the first year of implementation of the Joint Clinical Assessment procedure in Europe.

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The third cycle of Medicare drug price negotiations under the Inflation Reduction Act is now underway. On 27 January 2026, the Centers for Medicare & Medicaid Services (CMS) announced the selection of 15 drugs for negotiation, with maximum fair prices (MFPs) to take effect on 1 January 2028 [1]. This follows the first cycle, which covered ten drugs for initial price applicability for 2026, and the second cycle, which encompassed 15 drugs for 2027, for which negotiated prices achieving discounts of 38–85% from list prices were announced in November 2025 [2–4]. The third cycle selections came as little surprise. Because drugs are ranked by total Medicare expenditure, with eligibility determined by time since approval and absence of generic or biosimilar competition, there is limited scope for discretion in the selection process. The selected drugs span a wide range of therapeutic areas including cancers (Erleada®, Kisqali®, Verzenio®, Lenvima®), autoimmune conditions (Orencia®, Cosentyx®, Entyvio®, Xeljanz®, Cimzia®), respiratory disease (Anoro® Ellipta®, Xolair®), HIV (Biktarvy®), diabetes (Trulicity®), CNS disorders (Rexulti®), chronic migraine and spasticity (Botox®). Notably, this third cycle includes the first Medicare Part B medicines to be subject to negotiation, as well as the first drug to undergo renegotiation: Tradjenta® (linagliptin), a dipeptidyl peptidase-4 inhibitor for Type 2 diabetes that was negotiated in the second cycle with a price effective from January 2027, but which now qualifies for renegotiation because more than 16 years have elapsed since its original US FDA approval without generic entry. Tradjenta's renegotiation should provide an illuminating test case. Nothing material about the drug has changed since the first negotiation concluded – its list price, competitors and indications remain the same – raising the question of whether the government will arrive at the same price or a different one. Manufacturers have until 28 February 2026 to sign agreements to participate in the negotiation program. CMS will send initial offers of MFPs by 1 June 2026, with a period of counteroffers and meetings through September 2026. Companies must accept or reject a final MFP offer by 31 October 2026, and any agreed-upon prices will be published by 30 November 2026. CMS will also host patient-focused roundtable events and a clinical town hall meeting in April 2026 to gather input on the selected drugs. A drug-by-drug case can be made that the impact of negotiated prices on these 15 products may be manageable for their manufacturers. Trulicity has experienced consistent sales declines as patients migrate to newer GLP-1 agents such as semaglutide (Ozempic®) and tirzepatide (Mounjaro®). Medicare represents only a fraction of Biktarvy's global revenue. Orencia's sales are declining and Medicare accounts for a relatively small share of its US business. Wall Street analysts have broadly

shared this assessment, with analysts noting that the ultimate negotiated prices for each company are expected to be manageable. The absence of major oncology brands from the list is also noteworthy. A year ago, this cycle was anticipated to include blockbuster checkpoint inhibitors such as pembrolizumab (Keytruda®) and nivolumab (Opdivo®). However, the Big Beautiful Bill, passed in the summer of 2025, widened the orphan drug exclusion in a way that delays their eligibility for negotiation. For products first approved as orphan disease drugs but subsequently approved for broader, nonorphan indications, the clock on when they can be selected for negotiation now starts at the time of the later approval rather than the original orphan approval. Keytruda, for example, was first approved in 2014 as an orphan drug for certain types of advanced melanoma and received a nonorphan approval the following year for lung cancer. Under the revised exclusion, the relevant starting point shifts to the 2015 approval, delaying Keytruda's eligibility for Medicare price negotiation by at least 1 year, from 2026 to 2027.

While Inflation Reduction Act negotiations proceed through structured cycles, the broader implications of Most-Favored-Nation (MFN) pricing for global pharmaceutical markets are becoming apparent. One notable early example involves Insmed's Brinsupri® (brensocatib), a first-in-class dipeptidyl peptidase 1 inhibitor for non-cystic fibrosis bronchiectasis. Approved in the US in August 2025, the company projects revenue of $1 billion in 2026, with a US list price of $88,000 per year [5]. The European Commission granted marketing authorization in November 2025, and the UK's Medicines and Healthcare products Regulatory Agency approved the drug in February 2026. However, the company has not initiated health technology assessment (HTA) processes in any major European market and asked NICE to pause its evaluation a week before the UK marketing authorization was granted. A marketing authorization in Japan is expected in 2026, but the company has signaled it will delay launch there as well. In a recent earnings call, Insmed's Chair and CEO stated that the company's strategy remains to launch in Europe and Japan but that it needs clarity on MFN policies before proceeding [6]. A second example comes from Denmark. On 16 February 2026, Amgen announced the withdrawal of Repatha® (evolocumab), a PCSK9 inhibitor for hypercholesterolemia, from the Danish market, citing changed global pricing conditions. Danish media reported that Amgen had effectively won a procurement tender and secured reimbursement for the drug, making the withdrawal particularly striking. Denmark is among the comparator countries in the GENEROUS Model and both the GLOBE and GUARD reference baskets, meaning that Danish prices can directly influence what manufacturers are paid in the US market. Denmark's national pharmaceutical procurement body, Amgros, reports discounts averaging 46% off list prices, and health economists have suggested that the combination of deep local discounts and US reference pricing may have made continued Danish marketing uneconomic [7]. These early cases illustrate a dynamic that was widely anticipated but is now materializing: MFN pricing creates incentives for manufacturers to delay, restrict or withdraw from markets where prices are low relative to the US, because those prices may now establish ceilings for US reimbursement. For manufacturers, the strategic calculus of international launch sequencing has fundamentally shifted. Companies must now weigh the revenue from smaller markets against the risk that prices negotiated in those markets will constrain pricing in the far larger US market.

The MFN framework also raises fundamental questions about value assessment methodology. As Seo, Thorpe and Mattingly recently argued in *Health Affairs Forefront*, there is a paradox at the heart of MFN pricing: Congress has long restricted the use of quality-adjusted life-years (QALYs) in Medicare coverage and reimbursement decisions, reflecting concerns that QALY-based metrics may discriminate against elderly, disabled and chronically ill populations [8]. Yet by anchoring US drug prices to those set by foreign governments – whose HTA agencies frequently rely on QALYs and cost–effectiveness thresholds – MFN policies effectively import QALY-based valuations through the back door of international reference pricing. A complementary perspective is offered by Patterson, Wagner and Nordyke, writing for the National Pharmaceutical Council, who examine the divergence between American patient values and the frameworks used by ex-US HTA bodies [9]. Their analysis highlights that US patients consistently prioritize access to a broad range of treatment options, autonomy in treatment decision-making, and a wide definition of treatment impacts that extend beyond survival and quality of life to encompass effects on caregivers, ability to work and value of hope. The authors debate that ex-US HTA bodies, by contrast, typically operate as government-funded gatekeepers focused on cost-containment, emphasizing population-average clinical benefits and costs quantified through metrics such as QALYs, and offer limited scope for consideration of other elements of value. The authors conclude that if US prices are increasingly determined by reference to countries whose HTA decisions reflect values and priorities that diverge from those of American patients, the resulting price signals may undervalue treatments in ways that are inconsistent with US policy objectives. Patterson and colleagues note that value assessment should be a multistakeholder deliberative process that incorporates patient perspectives and reflects diverse patient needs and local treatment contexts. Manufacturers launching products globally must

now contend with the reality that value determinations made by foreign HTA bodies – using methodologies that Congress has explicitly rejected for domestic use – may nonetheless set the ceiling for US reimbursement. This creates pressure to engage more actively in shaping HTA processes in reference countries and to invest in generating evidence packages that demonstrate value across broader assessment frameworks.

These US pricing developments are unfolding against a backdrop of significant change in Europe, where the EU's own HTA framework has now become operational. Following years of planning by European HTA agencies and coordinated by the Member State Coordination Group on Health Technology Assessment (HTA CG), Regulation (EU) 2021/2282 on HTA entered into application on 12 January 2025 [10]. Joint Clinical Assessment (JCAs) represent a central pillar of the new framework, providing a harmonized scientific evaluation of the relative clinical effectiveness health technologies, which Member States may subsequently use to inform national pricing and reimbursement decisions. The initial scope of JCAs during the 2025–2027 period focuses on new active substances in oncology and advanced therapy medicinal products (ATMPs) submitted through the centralized marketing authorization procedure of the EMA. The HTA CG recently published its first annual report providing a comprehensive account of the framework's inaugural year of operation [11].

By the end of 2025, the JCA subgroup had initiated 13 JCAs [11]. Of these, ten were oncology medicines and three were ATMPs; six products had orphan designation, highlighting the concentration of assessments in rare diseases and areas of high unmet need. The oncology portfolio includes tovorafenib (pediatric low-grade glioma), sasanlimab (bladder cancer), lurbinectedin (maintenance treatment of extensive-stage small cell lung cancer), tarlatamab (small cell lung cancer), camizestrant (advanced or metastatic estrogen receptor-positive breast cancer), catequentinib (synovial sarcoma or leiomyosarcoma), senaparib (advanced epithelial ovarian, fallopian tube or primary peritoneal cancer), relacorilant (platinum-resistant ovarian cancer), ensartinib (ALK-positive non-small cell lung cancer) and sintilimab (non-squamous non-small cell lung cancer). The ATMPs undergoing assessment include autologous melanoma-derived tumor-infiltrating lymphocytes for melanoma, onasemnogene abeparvovec for spinal muscular atrophy and zopapogene imadenovec for respiratory papillomatosis in adults. Operationally, the JCA process runs in parallel with the EMA marketing authorization procedure and follows a structured sequence of scoping, dossier submission, clinical assessment and report endorsement. As of the end of 2025, progress across the 13 assessments remained largely in the early procedural stages. Tovorafenib was the only product for which the dossier had been confirmed by the European Commission. Three additional products (onasemnogene abeparvovec, sasanlimab and lurbinectedin) were undergoing confirmation checks of the dossier, five (autologous melanoma-derived tumor infiltrating lymphocytes, tarlatamab, camizestrant, catequentinib and senaparib) were in dossier preparation awaiting submission following the Commission's first request, and four (relacorilant, ensartinib, zopapogene imadenovec and sintilimab) remained in the scoping phase, during which the assessment framework and PICO parameters are defined. No JCA had yet reached the endorsement stage by the end of the year. These timelines reflect the expected duration of the newly established procedure and suggest that most of the JCAs currently underway are unlikely to conclude in the next quarter. Given that the process requires sequential steps – including scoping consultations, dossier submission, detailed clinical assessment and review by the Coordination Group – the first finalized JCA reports are likely to emerge gradually as the system matures and operational experience accumulates across Member States. Alongside JCAs, the EU HTA framework also launched joint scientific consultations in 2025, providing developers with early scientific advice on evidence requirements for future joint assessments. Two request periods were opened during the year – from 3 February to 3 March and 2 to 30 June – resulting in 17 requests from developers, of which seven consultations were selected. Four of these were conducted as parallel consultations with the EMA, allowing alignment between regulatory and HTA evidence expectations. By the end of 2025, four consultations had been completed, one had been withdrawn by the developer and two remained ongoing. In terms of therapeutic focus, cancer accounted for 42% of consultations, neurodegenerative disorders 28%, while neuromuscular and neurodevelopmental conditions each accounted for 14%. The average duration of the consultation process was approximately 140 days, measured from submission of the initial briefing package to delivery of the final outcome document.

The developments reviewed in this update illustrate the increasing complexity of the global pharmaceutical market access landscape. The MFN pricing framework, while not yet fully operational, is already exerting influence on manufacturer launch strategies. The policy tension between US restrictions on QALY use and the effective importation of QALY-based valuations through international reference pricing remains unresolved, and the divergence between American patient values and the frameworks of foreign HTA bodies raises fundamental questions about whose values should inform pharmaceutical pricing. Meanwhile, the EU's JCA framework has become operational,

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with 13 assessments initiated and supporting methodological infrastructure established, though no assessment has yet reached the endorsement stage. As the initial assessments progress through the procedural pipeline, the coming years will be critical in determining whether the framework delivers on its objective of harmonizing clinical evidence evaluation across Member States and what practical impact EU-level JCA reports will have on national pricing and reimbursement timelines. Taken together, these developments demand that manufacturers adopt more integrated approaches to global pricing strategy, evidence generation, payer engagement and lifecycle management. Companies that treat US and international pricing decisions in isolation risk being caught between conflicting policy pressures with limited room to maneuver.

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