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Access in all areas? A round-up of developments in market access and health technology assessment: part 13

Sreeram V Ramagopalan*,[1] & Annie Jullien Pannelay[2]

[1]Centre for Pharmaceutical Medicine Research, King's College London, SE1 9NH, UK

[2]Université Paris Saclay, UFR Pharmacie, Orsay, France

*Author for correspondence: sreeram@ramagopalan.net

In this update we cover the US–UK Economic Prosperity Deal announced in December 2025, which includes NICE's first major cost-effectiveness threshold increase in over two decades. We also analyze the latest developments in US pharmaceutical pricing policy, including the second cycle of Inflation Reduction Act drug price negotiations and the implementation of the GENEROUS, GUARD and GLOBE Models for Most-Favored-Nation pricing.

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Englands' health technology assessment (HTA) infrastructure has long been regarded as a gold standard for evidence-based healthcare decision-making, with the National Institute for Health and Care Excellence (NICE) serving as the primary arbiter of value for medicines and medical technologies since its establishment in 1999 [1]. Central to NICE's evaluation framework has been the cost-effectiveness threshold, traditionally set at £20,000–30,000 per quality-adjusted life year (QALY) gained [2]. This threshold, which has remained largely unchanged for over two decades, determines whether a new treatment represents sufficient value to warrant public funding through the National Health Service (NHS).

The stability of this threshold has increasingly attracted scrutiny from multiple stakeholders. Pharmaceutical manufacturers have argued that the threshold fails to reflect contemporary healthcare economics, particularly the rising costs of innovative therapeutic modalities such as cell and gene therapies [3]. Patient advocacy groups have highlighted instances where promising treatments remain inaccessible to UK patients due to unfavorable cost-effectiveness determinations, creating disparities compared with other developed healthcare systems [4]. Simultaneously, the life sciences sector, representing a significant component of the UK economy with substantial research, development, and manufacturing infrastructure, has emerged as a priority area for trade negotiations [5]. The convergence of domestic pressure for HTA reform and international trade objectives created conditions conducive to comprehensive policy change.

In December 2025, the UK and USA announced a landmark agreement as part of the broader UK–US Economic Prosperity Deal, with pharmaceutical provisions representing a central component of the arrangement [6,7]. The deal establishes the UK as the only country globally to secure zero percent tariff treatment on pharmaceutical exports to the USA, representing a substantial competitive advantage for UK-based pharmaceutical manufacturing. Crucially, the pharmaceutical provisions directly link trade concessions to domestic health policy reforms, specifically addressing NICE's cost-effectiveness methodology. This linkage represents an unusual integration of trade policy with HTA procedures, reflecting the strategic importance both governments attach to pharmaceutical market access and the economic implications of HTA decision-making. NICE's standard cost-effectiveness threshold range will increase from £20,000–30,000 per QALY gained to £25,000–35,000 per QALY gained, representing increases of 17–25% depending on the specific threshold point considered [8]. This adjustment constitutes the first major

increase in NICE's base threshold in over two decades and brings UK thresholds into closer alignment with international comparators, though they remain below thresholds employed in several other developed healthcare systems. For technologies assessed as not being cost-effective using current thresholds but potentially cost-effective under revised thresholds, NICE will pause assessments until the new thresholds can be applied, avoiding premature negative determinations that could subsequently be reversed. Importantly, the new thresholds will not be applied retroactively [9]. Technologies previously rejected due to unfavorable cost-effectiveness determinations will not be automatically reappraised unless substantial new evidence emerges that would typically trigger reassessment under NICE's standard procedures. This approach maintains stability for prior decisions and resource allocation commitments while preventing potentially overwhelming administrative burden from systematic reassessment of historical determinations. Complementing the threshold adjustments, the agreement stipulates adoption of a revised instrument for measuring health-related quality of life, transitioning from the established EQ-5D-3L to the EQ-5D-5L. This methodological change addresses long-standing technical concerns about the sensitivity and granularity of quality-of-life measurement in health economic evaluations, particularly for conditions where health state changes may be subtle or multidimensional. The pharmaceutical agreement also incorporates adjustments to the Voluntary Pricing and Access Scheme (VPAG), which governs pricing relationships between the UK government and pharmaceutical manufacturers. The VPAG clawback rate, representing the percentage of sales revenue above agreed growth thresholds that manufacturers must repay to the government, will decrease from its current level to 15% in 2026, with provisions maintaining this rate at or below 15% for the scheme's duration.

Critics have raised concerns about whether the threshold increases represent optimal use of finite NHS resources and whether the linkage to trade negotiations compromises the integrity of HTA processes [10]. Supporters argue that the threshold adjustment corrects a longstanding undervaluation of health benefits that has denied UK patients access to beneficial treatments available elsewhere, and that the trade benefits provide tangible economic returns that partially offset increased NHS pharmaceutical expenditure [11].

The UK–US pharmaceutical agreement and associated modifications to NICE's cost-effectiveness assessment framework represent the most significant changes to UK pharmaceutical market access conditions in decades. Manufacturers developing products with anticipated cost-effectiveness ratios in the £25,000–35,000 per QALY range face improved prospects for UK market access. Products that would have required price concessions or risked negative NICE determinations under previous thresholds may now achieve positive recommendations at commercially viable prices. The combination of increased cost-effectiveness thresholds and reduced VPAG clawback rates may influence global portfolio strategies and market sequencing decisions. Manufacturers might prioritize UK market entry for certain products, leveraging positive NICE determinations to support subsequent submissions in other markets. The UK's established reputation for rigorous, evidence-based assessment means that NICE recommendations carry significant weight with other HTA bodies, potentially creating strategic value beyond direct UK market revenues. However, while the threshold increases offer improved market access prospects, UK pricing decisions now carry implications that extend well beyond domestic NHS spending, potentially influencing global pricing strategies and US market access conditions through international reference pricing mechanisms discussed below.

The landscape of US pharmaceutical pricing has undergone unprecedented transformation in recent years. The Inflation Reduction Act of 2022 (IRA) established Medicare's authority to directly negotiate prices for high-expenditure drugs, marking the first time in Medicare Part D's history that the federal government could engage in price negotiations with pharmaceutical manufacturers [12,13]. The program operates through structured cycles, with the first cycle covering ten drugs for initial price applicability year 2026, and the second cycle encompassing 15 drugs for 2027 [14]. On 25 November 2025, CMS announced negotiated prices for the 15 selected drugs in the second cycle. The negotiated prices achieved significant discounts from 2024 list prices, ranging from 38 to 85%. Novo Nordisk's semaglutide used for diabetes and obesity had a negotiated price of approximately $274 for a 30-day supply. The other major US pharmaceutical pricing policy was President Trump's executive order in May 2025 directing alignment of American drug prices with the lowest prices paid by comparable nations through a Most-Favored-Nation (MFN) pricing framework [15]. Through an agreement with the Trump administration announced on 6 November 2025, Novo Nordisk offered Ozempic® and Wegovy® for $245 [16]. However, as CMS has clarified, MFN prices are 'expected to supersede' IRA prices, particularly if MFN prices fall below IRA negotiated prices in future cycles. More recently, the Trump administration has introduced three distinct MFN drug pricing models, each targeting different segments of the US pharmaceutical market: GENEROUS for Medicaid, GLOBE for Medicare Part B and GUARD for Medicare Part D.

The GENEROUS Model (GENErating cost Reductions fOr U.S. Medicaid), launched 1 January 2026 and represents the only voluntary MFN framework [17]. It defines the MFN price as the second-lowest country-specific manufacturer-reported net price across eight reference countries: Canada, Denmark, France, Germany, Italy, Japan, Switzerland and the UK. The model covers all single-source and innovator multiple-source outpatient drugs across all Medicaid therapeutic categories except cell and gene therapy products, running through 31 December 2030. These international net prices, calculated at the NDC-9 level (active ingredient, dosage form and strength) as the average net price over the previous 12-month period after all rebates, discounts and price concessions, are then adjusted by gross domestic product per capita using purchasing power parity methodology to account for economic differences between countries.

The GLOBE Model (Global Benchmark for Efficient Drug Pricing Model) [18], launching 1 October 2026, applies MFN pricing to Medicare Part B drugs. Unlike GENEROUS, GLOBE imposes mandatory participation on all manufacturers supplying qualifying drugs. The program utilizes a substantially broader reference basket of 19 OECD countries: Australia, Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Ireland, Israel, Italy, Japan, Netherlands, Norway, South Korea, Spain, Sweden, Switzerland and the UK. GLOBE targets single-source drugs and sole-source biologics within seven specific therapeutic categories (antigout agents, antineoplastics, blood products/modifiers, CNS agents, immunological agents, metabolic bone disease agents and ophthalmic agents) that have driven Medicare Part B spending exceeding $100 million annually. The model applies to approximately 25% of Medicare Part B fee-for-service beneficiaries in randomly selected geographic areas, functioning as a structured demonstration project running through 30 September 2031.

The GUARD Model (Guarding U.S. Medicare Against Rising Drug Costs) [19], launching 1 January 2027, extends MFN pricing to Medicare Part D outpatient prescription drugs. GUARD also mandates manufacturer participation and employs the same 19-country OECD reference basket as GLOBE. The program targets sole-source drugs with gross Part D spending exceeding $69 million in 2027 (adjusted annually by the Consumer Price Index) across 17 therapeutic categories, including analgesics, anticonvulsants, antidepressants, antimigraine agents, antineoplastics, antipsychotics, antivirals, bipolar agents, blood glucose regulators, cardiovascular agents, CNS agents, gastrointestinal agents, genetic or enzyme or protein disorder replacement or modifiers or treatment, immunological agents, metabolic bone disease agents, ophthalmic agents and respiratory tract/pulmonary agents. GUARD applies to approximately 25% of Part D beneficiaries in randomly selected geographic areas, including both standalone Prescription Drug Plans and Medicare Advantage with Part D coverage, running through 31 December 2031.

The three programs employ divergent approaches to establishing reference prices. GENEROUS uses the second-lowest net price to minimize outlier effects while maintaining realistic market anchoring. In contrast, both GLOBE and GUARD offer two calculation methods. Method I (the default) identifies the lowest country-level average price across reference countries, adjusted by GDP PPP. Method II (optional) allows manufacturers to submit volume-weighted average net prices from international markets, with GLOBE applying a 105% adjustment plus the Medicare Part B add-on payment (currently 6% updated quarterly), while GUARD applies only a 105% adjustment (updated annually). These upward adjustments reflect policy decisions to maintain adequate provider reimbursement and encourage manufacturer participation while still achieving net price reductions compared with current US levels.

GENEROUS's voluntary structure fundamentally distinguishes it from its Medicare counterparts. Manufacturers can choose enrollment for standardized negotiation and potential volume benefits, with prices determined at the national rather than state-by-state level. GLOBE and GUARD impose mandatory participation for all manufacturers supplying qualifying drugs, ensuring comprehensive coverage but potentially facing greater industry resistance and legal challenges. Notably, companies that have negotiated bilateral MFN agreements directly with the Trump administration reportedly expect exemption from both GUARD and GLOBE, potentially creating a two-tier system where direct negotiations may offer more favorable terms than the standardized models.

The inclusion of the United Kingdom in all three reference baskets creates direct linkage between the recent UK–US Economic Prosperity Deal's NICE threshold increases and US MFN pricing calculations. Despite the recent increase in NICE's cost-effectiveness thresholds, UK net prices frequently remain among the lowest internationally. Consequently, UK pricing decisions may disproportionately influence US MFN prices. This creates an unusual dynamic where the UK–US trade agreement's threshold increases, designed partially to support higher UK pharmaceutical revenues, could paradoxically establish lower US price ceilings through the reference pricing mechanism. The dual framework of IRA negotiations and MFN pricing fundamentally reshapes manufacturer

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strategy across multiple dimensions. Manufacturers must now approach US market access with recognition that prices are no longer determined primarily by US-specific factors but rather by their global pricing strategies and the lowest prices they offer internationally. This creates several strategic imperatives: first, manufacturers must carefully consider how prices offered in reference countries will establish US price ceilings. Second, manufacturers face increased complexity in managing multiple pricing frameworks simultaneously. Products subject to both IRA negotiations and MFN pricing must navigate two distinct assessment processes – the IRA's multifactorial negotiation framework and the MFN international reference pricing methodology – while recognizing that the lower price ultimately governs. Looking ahead, the long-term implications of this dual framework remain uncertain but potentially transformative. As more manufacturers participate in MFN pricing additional drugs enter IRA negotiations, the historical price differentials that have characterized US drug pricing may be reduced, with significant implications for manufacturer revenue, research and development investment, and ultimately innovation incentives. The pharmaceutical industry's response to these challenges – whether through more conservative global pricing, strategic sequencing of market entries or novel pricing structures that segment markets more effectively – will determine not only individual product success but the broader trajectory of pharmaceutical innovation and patient access.

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References

1. Zhang X, Tikhonovsky N, Ramagopalan SV. A review of 25 years of National Institute of Health and Care Excellence decision making. *J. Comp. Eff. Res.* 13(9), e240063 (2024).
2. Paulden M, O'Mahony JF, Culyer AJ, McCabe C. Some inconsistencies in NICE's consideration of social values. *Pharmacoeconomics* 32(11), 1043–1053 (2014).
3. Why the government must urgently raise the NICE cost-effectiveness threshold. (2025). Available from: https://www.abpi.org.uk/media/blogs/2025/october/why-the-government-must-urgently-raise-the-nice-cost-effectiveness-threshold/
4. Breast cancer drug blocked for NHS use as price talks break down. *The Independent* (2024). Available from: https://www.independent.co.uk/news/health/breast-cancer-drug-enhertu-nhs-b2650091.html
5. Life Sciences Sector Plan. (2025). Available from: https://www.gov.uk/government/publications/life-sciences-sector-plan/life-sciences-sector-plan
6. Landmark UK–US pharmaceuticals deal to safeguard medicines access and drive vital investment for UK patients and businesses. (2025). Available from: https://www.gov.uk/government/news/landmark-uk-us-pharmaceuticals-deal-to-safeguard-medicines-access-and-drive-vital-investmentfor-uk-patients-and-businesses
7. U.S. Government Announces Agreement in Principle with the United Kingdom on Pharmaceutical Pricing. (2025). Available from: https://ustr.gov/about/policy-offices/press-office/press-releases/2025/december/us-government-announces-agreement-principle-united-kingdom-pharmaceutical-pricing
8. Changes to NICE's cost-effectiveness thresholds confirmed. (2025). Available from: https://www.nice.org.uk/news/articles/changes-to-nice-s-cost-effectiveness-thresholds-confirmed
9. Changes to NICE's cost-effectiveness thresholds. Available from: https://indepth.nice.org.uk/changes-to-nices-cost-effectiveness-thresholds/index.html
10. Paulden M. Economic consequences of increasing the NICE cost-effectiveness threshold. *Pharmacoeconomics* 44(1), 5–8 (2026).

11. UK–US deal is good news for NHS patients and will help to support UK life sciences competitiveness, says ABPI. (2025). Available from: https://www.abpi.org.uk/media/news/2025/december/uk-us-deal-is-good-news-for-nhs-patients-and-will-help-to-support-uk-life-sciences-competitiveness-says-abpi/
12. Beattie A, Treharne C, Mardiguian S, Ramagopalan SV. Access in all areas? A round up of developments in market access and health technology assessment: part 2. *J. Comp. Eff. Res.* 12(12), e230162 (2023).
13. Ramagopalan SV, Pannelay AJ. Access in all areas? A round up of developments in market access and health technology assessment: part 7. *J. Comp. Eff. Res.* 14(6), e250043 (2025).
14. CMS delivers savings for seniors on 15 major drugs for cancer and chronic disease. (2025). Available from: https://www.cms.gov/newsroom/press-releases/cms-delivers-savings-seniors-15-major-drugs-cancer-chronic-disease
15. Ramagopalan SV, Pannelay AJ. Access in all areas? A round up of developments in market access and health technology assessment: part 9. *J. Comp. Eff. Res.* 14(10), e250120 (2025).
16. President Donald J. Trump announces major developments in bringing most-Favored-Nation Pricing to American patients. (2025). Available from: https://www.whitehouse.gov/fact-sheets/2025/11/fact-sheet-president-donald-j-trump-announces-major-developments-in-bringing-most-favored-nation-pricing-to-american-patients/
17. GENEROUS (GENErating cost Reductions fOr U.S. Medicaid) model. Available from: https://www.cms.gov/priorities/innovation/innovation-models/generous
18. GLOBE (Global Benchmark for Efficient Drug Pricing) model. Available from: https://www.cms.gov/priorities/innovation/innovation-models/globe
19. GUARD (Guarding U.S. Medicare Against Rising Drug Costs) model. Available from: https://www.cms.gov/priorities/innovation/innovation-models/guard

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