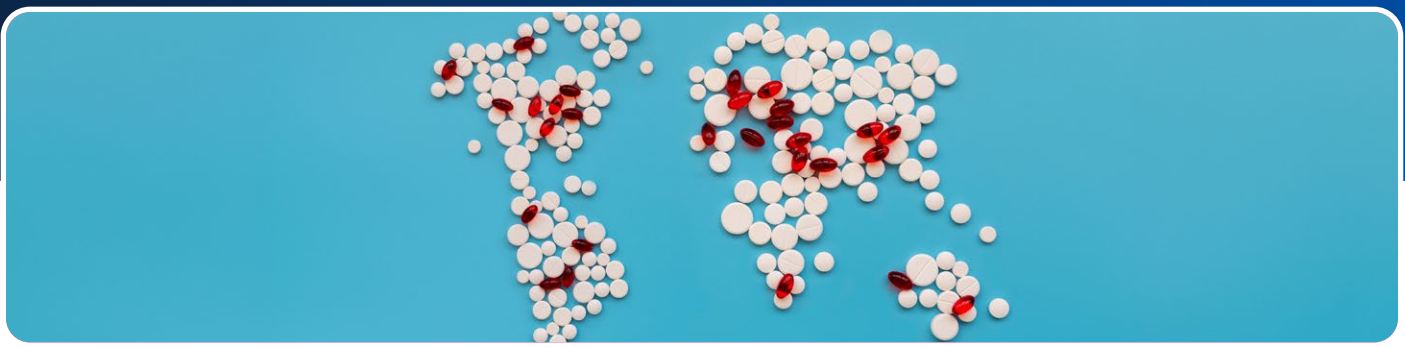
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Global Pricing Under Pressure: Building Most-Favored-Nation-Ready Organizations With Technology

Navigating U.S. drug pricing reforms and mitigating international spillover risks by leveraging technology

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Executive summary

The U.S. pharmaceutical market has long been the primary engine of global drug innovation. As the world's third most populous country, it has historically accounted for more than 50% of industry revenues and roughly 75% of profits. That economic reality is now under direct policy pressure. U.S. list prices for many branded medicines run three times higher than in peer advanced economies, and lawmakers are moving aggressively to close that gap through Most-Favored-Nation (MFN) pricing mechanisms.

The core idea is straightforward: U.S. government programs, and essentially patients and residents in the U.S., should not pay substantially more than other wealthy nations for the same products. What makes the current wave of proposals different is how directly they link domestic pricing and rebate obligations to international benchmarks. A price concession granted in one European market or a Latin American tender can now trigger automatic or near-automatic financial

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consequences in Medicaid, Medicare Part B, or Part D. The old model of managing pricing for the U.S. and internationally in siloes no longer holds.

Real-world experience with international reference pricing (IRP) and earlier MFN proposals already demonstrate the complexity. Manufacturers have responded with launch delays, channel strategies, and in some cases, voluntary agreements. Impacted countries have voiced concerns about access, innovation, and supply.

Most-Favored-Nation in a nutshell

MFN pricing rests on a simple principle: The United States should not pay more for high-cost branded medicines than comparable wealthy nations. Earlier concepts, such as the 2018 International Pricing Index and the 2020 MFN model, sketched the direction. The current legislative landscape has evolved into three specialized programs and models, each targeting a different section of the U.S. government payer system of the Centers for Medicare & Medicaid Services (CMS).

Beyond these core programs, voluntary manufacturer participation agreements under frameworks such as BALANCE (which are tied to expedited reviews) offer an alternative path for companies willing to make broader supply chain and access commitments. Real-world pressure is already evident: GLP-1 therapies have faced demands to reduce net costs of the $1,000 to $1,350 per month range toward international reference levels of around $350, while older products have seen even more dramatic benchmark compression in heavily subsidized channels.

The three main MFN models

Dimension	GENEROUS	GLOBE	GUARD
Target program	**U.S. Medicaid** (state opt-in)	**Medicare Part B** (physician-administered)	**Medicare Part D** (prescription retail)
Mandate level	**Voluntary / state option**	**Mandatory** (Selected regions approx. 25%)	**Mandatory** (Selected regions approx. 25%)
Core pricing mechanism	CMS-negotiated supplemental rebates based on international net price benchmarks. Explicitly excludes best price/340B math	If statutory IRA rebates fall short of international benchmarks, an incremental rebate is triggered on list price (method 1) or net price (method 2)	GUARD rebate applies when the gap between the international benchmark and Medicare net price exceeds standard inflation benchmarks
Reference country basket	Fixed basket of eight advanced economies: UK, Canada, France, Japan, Germany, Denmark, Italy, and Switzerland	Top 19 Organisation for Economic Co-operation and Development (OECD) nations, normalized dynamically via GDP purchasing power parity (PPP) adjustments	Top 19 OECD nations (using method 1 for lowest average list price or method 2 for voluntary net price data)

Risk diagnostic: Where exposure is highest

The fundamental risk is cross-border price spillover. Because U.S. programs now explicitly reference international prices, a local commercial decision in one market can create immediate financial drag in the much larger U.S. business. There are four primary exposure areas that leadership teams need to monitor closely, alongside relevant markets and pricing functions.

1. **Reverse traditional global pricing hierarchies and shift negotiating leverage.** MFN can paradoxically reduce foreign payers' leverage in some negotiations: Manufacturers may resist deeper price concessions abroad because any material lowering of net (or visible list) prices in reference markets now directly pressures high-margin U.S. revenues via MFN-triggered rebates or benchmarks. This can manifest as harder bargaining and greater reliance on confidential net pricing and managed entry agreements (MEAs) that are harder to benchmark.
2. **Net price and gross-to-net volatility.** Regulations that look at international net prices (including confidential rebates and clawbacks) can inadvertently turn those hidden concessions into a benchmark or reference price for a statutory U.S. pricing floor in addition to existing ones (e.g., 340B). The result is less visibility into true net pricing, but nonetheless, it does not prevent a greater risk of retrospective adjustments.
3. **Launch sequencing disruptions.** The traditional approach of launching first in high-price markets, such as the U.S. and Germany, then expanding, breaks down when early entry into a lower-price or heavily referenced market creates an immediate low anchor that pulls down U.S. value before meaningful volume is established.
4. **Access versus margin trade-offs.** To protect U.S. revenues, some companies are delaying or withholding launches in certain lower-income or highly referenced markets. While understandable from a financial standpoint, this approach raises real questions about patient access and long-term reputation.

Regional exposure snapshot

European Union: Highest structural risk due to transparent list pricing and well-established cross-border reference pricing within the EU-27. The practical response so far is to shift concessions away from public list prices toward confidential mechanisms such as MEAs, while tightening launch sequencing discipline and aligning local health technology assessment (HTA) strategies with U.S. revenue forecasts. However, as previously outlined, even confidential MEAs may not prevent the risk of retrospective adjustments to the net price.

Latin America: Characterized by currency volatility, inflation, and large public tenders. A single uncoordinated bid can establish a permanent low benchmark. Companies need clear, centralized oversight of tender exposure, strict price floors, and greater use of non-price-based access tools (patient support programs, diagnostic partnerships, free goods) instead of direct discounts.

Emerging markets (APAC, Middle East, Africa): Lower commercial volumes but still capable of influencing global reference baskets. The priority is usually to sequence launches carefully, decouple early access programs from standard list prices, and manage government disclosure risks so that local pricing data does not leak into public international registries.

Real-world lessons from IRP and MFN pressures

The challenges of cross-border price referencing are not theoretical. Decades of IRP, not just in Europe but globally, combined with manufacturer and governmental reactions to earlier U.S. MFN proposals, offer concrete lessons for companies preparing for the current wave of reforms.

Key implementation challenges of IRP

In practice, IRP systems have proven far more complex than the simple concept suggests. Common difficulties include:

- **Data comparability and transparency gaps.** Countries struggle to align on which price point to use (e.g., manufacturer, pharmacy purchase, or pharmacy selling price), and how to easily calculate the realized net price after all confidential rebates, discounts, and other applicable deductions. This may lead to inconsistent benchmarks and disputes.
- **Ripple effects and launch delays.** Because a price in one market can automatically influence many others, manufacturers frequently delay launches in lower-price or heavily referenced countries to protect the global pricing architecture. European Federation of Pharmaceutical Industries and Associations (EFPIA) and OECD analyses have linked IRP to reduced product availability and launch delays, particularly in lower-income European markets. The same risk can now occur in many more higher-income countries in European markets and beyond.
- **Administrative burden and errors.** Large reference baskets lead to complexity and errors. For example, Greece's IRP system, which references approximately 20 countries, has experienced errors that have disrupted patient access. Currency fluctuations, inflation, and differing pack sizes or indications further complicate calculations.
- **Undermining differential and value-based pricing.** IRP can conflict with tiered pricing strategies that reflect local ability-to-pay or value assessments. It also sits uneasily alongside sophisticated HTA processes used in many European countries.
- **Misalignment with healthcare system differences.** Direct price comparisons ignore variations in HTA methodologies, legal frameworks, disease burden, willingness to pay, and distribution systems. These differences make mechanical referencing prone to unintended consequences on both access and innovation incentives.

Manufacturer reactions and strategic responses

Some companies have already developed clear playbooks in response to existing IRP and new MFN pressure:

Launch sequencing and delays. A well-documented response to European IRP has been to delay or sequence launches, prioritizing high-price markets (Germany, UK, U.S.) and holding back from lower-price Southern or Eastern European countries until global pricing is more secure. This has been very common in recent years, especially in high-cost areas such as oncology (including certain PD-1/PD-L1 inhibitors and other biologics) and rare diseases. This protects revenue but can delay patient access. More recently, in early 2026, U.S. MFN policy uncertainty has led to concrete delays in Europe: Insmed postponed the Germany launch (and broader European rollout) of its newly approved anti-inflammatory lung disease drug BRINSUPRI, with CEO William Lewis citing the need for clarity on MFN policies on an earnings call. Industry reports (including from Reuters) indicate multiple other companies, including Ligand Pharmaceuticals and United Therapeutics, are similarly pausing or reevaluating European launches, with many more evaluating strategies privately. Analysts note that

delayed or staggered rollouts in lower-price reference markets are becoming increasingly common as companies seek to avoid setting low U.S. benchmarks.

Recent voluntary agreements and tactical adjustments (2025–2026). With renewed MFN momentum, including tariff linkages and demonstration models, manufacturers have pursued a mix of cooperation and mitigation. Pfizer reached a landmark voluntary agreement with the Trump Administration involving MFN-aligned pricing for new products, substantial U.S. manufacturing and R&D investment commitments, and tariff relief. Bristol Myers Squibb has indicated plans to align list prices in markets such as the UK with U.S. levels for certain new launches (including in schizophrenia). Manufacturers of high-visibility therapies such as the GLP-1 receptor agonists (Novo Nordisk's Ozempic and Wegovy; Eli Lilly's Mounjaro and Zepbound) have continued to navigate intense international benchmark pressure, which has influenced launch timing, net pricing strategies, and channel decisions. Similar discussions are underway with other companies. Additional tactics observed or discussed include prioritizing private or high-income channels over public tenders in reference countries, selective product withdrawals from certain markets, and in some cases, exploring price rebalancing outside the U.S. UK National Institute for Health and Care Excellence (NICE) leadership has publicly noted uncertainties, including potential reductions in medicines launched, reduced commercial flexibilities, and increased product terminations as companies navigate these pressures. To summarize for the GENEROUS model, as of July 2026, at least 17 major pharmaceutical companies have MFN pricing agreements with the Trump Administration (e.g., Pfizer, AstraZeneca, Lilly, Merck, and others); these companies are expected to participate in GENEROUS once terms are finalized.

Reactions and countermeasures from impacted countries

Countries whose prices are referenced have not remained passive:

European Union and EFPIA. European stakeholders have long expressed concern that U.S. MFN referencing of European prices could accelerate launch delays, discourage investment in European R&D and manufacturing, and undermine confidential pricing and differential pricing arrangements that support access in lower-income markets. EFPIA has published principles for the application of IRP systems, emphasizing the need for fair basket design, adjustments for market differences, transparency where possible, and safeguards to prevent harm to innovation or patient access.

United Kingdom (NICE). NICE has begun systematically tracking baseline data on drug approvals, launches, and discontinuations to monitor potential MFN spillover effects. Its leadership has highlighted the risk of reduced medicines availability and commercial flexibility, underscoring the need for careful policy design on both sides of the Atlantic.

Other reference countries and potential countermeasures. Health authorities in Canada, Japan, Germany, France, and other referenced nations generally view their lower prices as evidence of sustainable systems but worry about supply security and deprioritization by manufacturers. Possible responses include refining national IRP methodologies or reference baskets, strengthening independent value assessments (HTA) to justify prices on clinical and economic grounds rather than relying solely on international benchmarks, exploring regional pooled procurement, and, in the context of U.S. trade measures linked to MFN participation, considering reciprocal trade or regulatory measures. Some countries may also limit further price transparency or adjust policies to reduce their attractiveness as low anchors in U.S. calculations.

These real-world dynamics reinforce why fragmented, manual pricing processes are inadequate. Companies need robust simulation capabilities, clear governance, and real-time data integration precisely because the system is reactive, interconnected, and prone to unintended consequences on all sides.

Conclusion and current state of technology

The real-world experience with the accelerating rollout of U.S. MFN frameworks and IRP demonstrates one unambiguous truth: **Global pharmaceutical pricing has become a single, interconnected system.** A pricing decision, tender outcome, or confidential concession in one market now carries immediate, quantifiable consequences for U.S. gross-to-net performance. The old model of managing pricing in geographic silos with spreadsheets and periodic manual reviews is no longer fit for purpose. Manufacturers have responded with the predictable but costly playbook we have seen play out for years under European IRP and that is now accelerating under MFN pressure: launch sequencing and deliberate delays (evident in recent pauses in Germany and broader European rollouts for high-cost therapies), greater reliance on confidential net pricing and MEAs that are harder but not impossible to benchmark, selective channel prioritization, and, in some cases, product withdrawals or rebalancing. Impacted countries are pushing back through refined IRP methodologies, stronger HTA justification, pooled procurement, and, in some cases, reciprocal policy considerations. The net result is increased volatility, higher administrative burden, and real friction between commercial objectives and patient access.

This environment demands capabilities that manual processes and fragmented systems simply cannot deliver at scale. The current state of technology among most manufacturers remains basic to intermediate: Central databases exist in pockets, but data on net realized prices, reference basket positioning, and cross-market exposure remains incomplete or lagged. Scenario modeling, when it occurs, is often ad hoc, Excel-based, and too slow to support timely decisions. Governance is frequently reactive rather than embedded in daily workflows, creating both leakage risk and compliance exposure.

Leading organizations are moving to purpose-built global pricing management platforms that address exactly these gaps. These systems deliver:

- A governed single source of truth across countries, channels, and net price realizations, with full audit history
- Real-time price intelligence that automatically identifies the lowest global prices, MFN-relevant anchors, and exposure risks (including FX-adjusted views)
- Advanced scenario simulation, the capability that separates leaders from laggards, where teams model "what if we approve this tender price in Country X?" or "what is the optimal launch sequence for Product Y under current MFN constraints?" and instantly see the downstream impact on U.S. rebates, overall net present value (NPV), and access timelines
- Automated governance, workflow enforcement, threshold alerts, and exception management that prevent value leakage while maintaining compliance-ready documentation
- Seamless integration between global commercial decisions and U.S. government pricing engines (average manufacturer price, best price, average selling price, and rebate calculations), ensuring consistency and reducing manual reconciliation

As of July 2026, with the GENEROUS model in active pre-implementation (at least 17 major manufacturers with MFN agreements positioned to participate

once terms are finalized), GLOBE and GUARD advancing toward mandatory application for qualifying high-spend products, and ongoing voluntary MFN commitments, the requirement for these capabilities is no longer theoretical. Companies that treat global pricing management as a "nice-to-have" reporting tool will continue to operate reactively. Those that embed simulation, real-time visibility, and automated governance into their operating model will convert regulatory pressure into a structured decision-making advantage.

The companies that act now, building the data foundation, simulation muscle, and governance discipline while the models are still stabilizing, will be best positioned to protect value and maintain launch momentum. Those that wait will face the same reactive cycle that has already produced launch delays, margin leakage, and access friction in every IRP jurisdiction that preceded today's U.S. reforms.

The mechanics are clear. The risks are material. The technology exists. What remains is disciplined execution:

1. **Conduct a focused MFN exposure diagnostic** on your top 5 to 10 products.
2. **Assess current maturity against the global pricing management capabilities** described previously.
3. **Identify the highest-priority simulation use cases** (launch sequencing, tender response, reference-price sensitivity).
4. **Engage cross-functional stakeholders** (global pricing, U.S. government pricing, market access, finance) to align on a shared roadmap.

Ready to see where your MFN exposure runs deepest?

Talk with the Model N team to pinpoint your highest-risk products and the capabilities you'll need to get ahead of them.

About Marbls

*Marbls partners with pharmaceutical and medical device and diagnostic manufacturers to provide practical, innovative services that address complex pricing, contracting and commercial excellence needs — driving the path of critical drugs, devices, and diagnostics to market. Learn more at **marblsgroup.com** or reach out to **themarblsteam@marblsgroup.com**.*

About Model N

*For more than 25 years, Model N has been the leader in end-to-end commercialization, revenue optimization, and compliance for pharmaceutical and medtech innovators. Our intelligent platform, purpose-built solutions, and advanced analytics and AI automation are trusted by more than 110 of the world's leading companies. For more information, visit **modeln.com**.*