International Reference Pricing and Most-Favored-Nation Arrangements

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Learning Objectives

- Identify and compare various international pharmaceutical reference pricing arrangements in use by foreign governments.
- Discuss how voluntary Most-Favored-Nation arrangements in the United States have reshaped the pharmaceutical supply chain.
- Explain the ongoing legal challenges to the Trump administration's existing Most-Favored-Nation arrangements, as well as barriers to codification.

Financial Relationship Disclosures

Role	Reported Relevant Financial Relationships
Haider Andazola ***Faculty***	Disclosed no relevant financial relationships.
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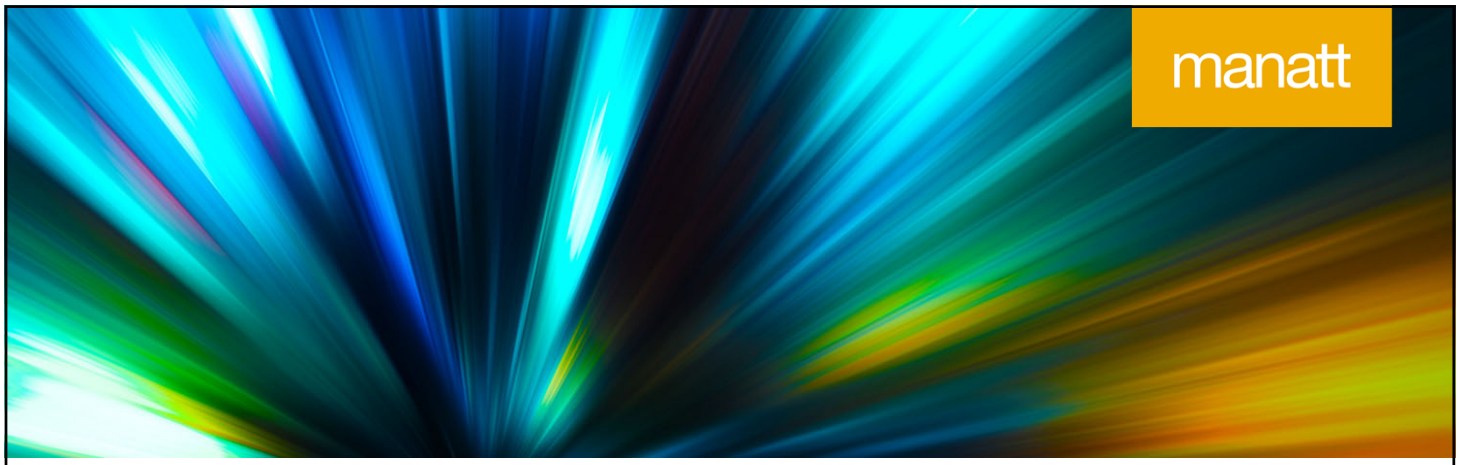
Tyler Thorne ***Staff Reviewer***	Disclosed no relevant financial relationships.

- If applicable, relevant financial relationships have been mitigated and documented.
- Content has undergone a peer review to ensure content validity.



International Reference Pricing and Most-Favored-Nation Arrangements

AGENDA FOR TODAY

01 — International Reference Pricing as the Conceptual Origin of MFN

02 — The Lineage of U.S. MFN Proposals — Trump 1 & Trump 2

03 — The Seventeen Voluntary Deals — Anatomy and Supply-Chain Consequences

04 — Legal Barriers to Codification/Implementation

05 — What Codification Could Actually Look Like

06 — Implications and Outlook

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Section 1
International Reference Pricing as the Conceptual Origin of MFN

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SECTION 1 | REFERENCE PRICING IN FOREIGN SYSTEMS

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Foreign systems pair external reference pricing with HTA authority that U.S. proposals do not replicate, which is why opponents call MFN "price controls without the institutions that justify them."

01 Germany's AMNOG framework couples external reference pricing with G-BA benefit assessment that determines whether a drug receives a price premium over comparators.

02 United Kingdom's VPAG combines a voluntary industry-government rebate scheme with NICE cost-effectiveness review at a published QALY threshold.

03 France's HAS issues SMR and ASMR ratings that determine reimbursement levels before any reference price is calculated.

U.S. proposals borrow the price-setting outputs of these systems while leaving each system's HTA infrastructure behind.

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SECTION 1 | THE FIVE DESIGN VARIABLES

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Every MFN proposal — executive, regulatory, or statutory — generally pulls the same five levers

01 PAYER SCOPE
Who is covered?
Public payers only or commercial reach? Commercial without statute may not be legally available.

02 DRUG SCOPE
What is covered?
Orphan, breakthrough, biosimilar, cell/gene therapy carve-outs determine which trade groups engage.

03 REFERENCE BASKET
Compared to whom?
Country count, GDP threshold, OECD vs. G7—drives more price impact than mechanism choice itself.

04 PRICE MECHANISM
How is price set?
Rebate, ceiling, upfront discount, differential fee—determines who pays when and effectuation mechanism.

05 ANTI-GAMING
How does it hold?
Launch sequencing, foreign-price-manipulation penalties, clawbacks—keeps benchmark from eroding.

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Section 2
The Lineage of U.S. MFN Proposals — Trump 1 & Trump 2

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SECTION 2 | THE 2020 MFN INTERIM FINAL RULE

The IFR would have tied Medicare Part B payment to the lowest-priced peer country and shifted manufacturer rebate liability onto a federally-set benchmark – two district courts enjoined the 2020 IFR on APA notice-and-comment grounds

- The IFR designated the top fifty single-source Part B drugs by spending as "MFN Model drugs," covering an estimated $137 billion in seven-year Medicare expenditures and reaching most physician-administered oncology, ophthalmology, and rheumatology biologics.
- Medicare payment to providers was set at a blended rate phasing from seventy-five percent ASP plus twenty-five percent MFN Price in Year 1 to one hundred percent MFN Price by Year 4, with a separate flat add-on payment per dose to insulate provider margin from the price cut.
- Participation was mandatory for any manufacturer of an MFN Model drug doing business with Medicare, with no opt-out mechanism (except withdrawal from Medicare entirely)
- Maryland and CA enjoined the IFR finding “good cause” exception was not met; Maryland court distinguished established good-cause precedents — national security and life-threatening safety — from a rule aimed at general financial concerns about Part B drug costs.

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SECTION 2 | TRUMP 2'S THREE LAYER CMMI ARCHITECTURE

Three CMMI models work as a coercive sequence — GENEROUS offers a voluntary on-ramp into Medicaid MFN, while GLOBE and GUARD function as mandatory sticks designed to make participation in GENEROUS or a bilateral deal look like the rational choice.

01 GENEROUS is the carrot — a voluntary supplemental-rebate model offering manufacturers a single negotiated track for extending MFN pricing into Medicaid in exchange for predictable benchmark methodology without affecting Best Price and 340B

02 GLOBE and GUARD are the sticks — mandatory MFN rebates against a deeper basket and a more aggressive benchmark, designed to make the economics of declining GENEROUS or a bilateral deal worse than the economics of accepting one.

03 It remains unclear whether GLOBE/GUARD will exclude GENEROUS model participants, but that appears to be the operating assumption from manufacturers with GENEROUS deals.

04 The rollout also addresses the 2020 IFR's procedural defeat as a secondary benefit — front-loaded notice-and-comment rulemaking for GLOBE and GUARD coupled with Section 1115A waiver authority preempting most merits mitigates legal vulnerabilities.

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SECTION 2 | SECTION 1115A VS. SECTION 402

The waiver-authority choice constrains what each model can actually do — Section 1115A shields models from review but cannot waive the Medicaid drug rebate statute.

	Section 1115A (CMMI)	Section 402 (1967 SSA)
Purpose	Test innovative payment/delivery models reducing program expenditures	Experiments to determine if reimbursement changes increase efficiency
Waivable Provisions	Medicare; limited Medicaid (NOT § 1927); fraud/abuse; MDPNP	Medicare and Medicaid (including § 1927)
Judicial Review	Precluded for model elements, parameters, scope, duration	No preclusion — full APA review available
Budget Neutrality	Required (model must be modified/terminated if costly)	Not statutorily required
Mandatory Demos	Yes (existing precedent)	Never used for mandatory demonstration
Current Use	GENEROUS, GLOBE, GUARD; CGT Access Model; 2020 MFN	Medicare Part D Premium Stabilization Demo

Trump relying on Sec. 1115A for its approach

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SECTION 2 | GENEROUS — VOLUNTARY MEDICAID MFN

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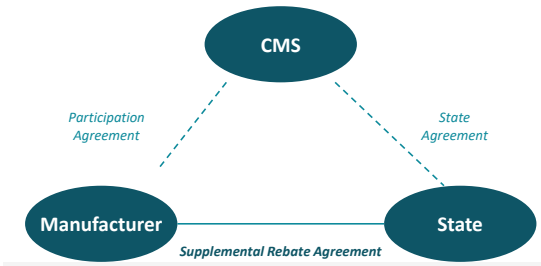
CMS negotiates a Guaranteed Net Unit Price with manufacturers under a three-agreement framework, and the bilateral MFN deals are already funneling into this model.

THREE-AGREEMENT Framework



Supplemental Rebate = WAC − (GNUP + URA)

AUTHORITY

Section 1115A; voluntary participation contingent on existing MDRP participation.

REFERENCE BASKET

8 countries — Canada, Denmark, France, Germany, Italy, Japan, Switzerland, U.K. — second-lowest PPP-adjusted net price.

BEST PRICE & 340B

Supplemental rebates expressly excluded from Medicaid Best Price and 340B ceiling-price calculations.

TIMELINE

Five-year demonstration: Jan. 2026 – Dec. 2030. Manufacturer applications due June 11, 2026. State applications due Sept. 10, 2026.

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SECTION 2 | GENEROUS VS. MFN 1.0 — THE 58 PERCENT DIFFERENCE

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RAND[1] data show that the same drugs benchmarked under MFN 1.0's twenty-country lowest-price rule produce a reference price 58 percent lower than GENEROUS's eight-country second-lowest rule, and the difference is driven entirely by basket design.

MFN 1.0 (2020 IFR)

Aggressive design

14.23

Reference price (U.S. = 100)

- ~20 OECD peers in basket
- Lowest GDP-adjusted price selected
- Anchor: Korea

58%

higher reference price

GENEROUS (2026)

Manufacturer-favorable design

22.47

Reference price (U.S. = 100)

- 8 countries (G7 + Denmark + Switzerland)
- Second-lowest price selected
- Anchor: France

Takeaway: *Identical foreign prices, identical mechanism — only basket size and selection rule differ. In MFN policy design, the basket is a key lever.*

1. Andrew W. Mulcahy et al., RAND Corp., International Prescription Drug Price Comparisons: Estimates Using 2022 Data (2024), https://www.rand.org/pubs/research_reports/RRA788-3.html.

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SECTION 2 | GLOBE — MANDATORY MEDICARE PART B MFN

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GLOBE replaces the IRA's Part B inflation rebate calculation in selected geographies and reaches drugs CMS already covers, making it the most operationally aggressive of the three models.

$11.9B

Projected seven-year savings

$100M/12-Month	19	25%
ANNUAL SPEND THRESHOLD	OECD COUNTRIES IN BASKET	BENEFICIARIES BY GEOGRAPHY

October 2026 – September 2031 performance period; reconciliation continues through September 2033.

MANDATORY SCOPE

All manufacturers of Part B rebatable drugs designated across 7 USP DC Categories — single-source drugs and sole-source biologicals.

BENCHMARK METHODOLOGY

Greater of Method I (fixed pricing-database value) or Method II (manufacturer-submitted, voluntarily updated).

WAIVER VEHICLE

Section 1115A waiver of the IRA Part B inflation rebate calculation, substituting MFN-based rebate when U.S. price exceeds international benchmark.

MDPNP INTERACTION

Drugs subject to Medicare Drug Price Negotiation Program excluded for duration of MFP; pre-negotiation timing creates overlap risk.

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SECTION 2 | GUARD — MANDATORY MEDICARE PART D MFN

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GUARD captures more drugs than GLOBE through a lower threshold and broader scope, but CMS itself acknowledges no direct beneficiary savings and possible premium increases.

$14.1B

Projected seven-year savings — higher than GLOBE

$69M/12-Month	ALL	Jan 2027
ANNUAL SPEND THRESHOLD (updated with inflation)	PROTECTED CLASSES INCLUDED	PERFORMANCE PERIOD START

Lower threshold and broader scope than GLOBE — but CMS acknowledges no direct beneficiary savings.

MANDATORY SCOPE

Manufacturers of high-spend Part D drugs across all protected classes — broader than GLOBE's USP-category-specific scope.

BENEFICIARY IMPACT

CMS acknowledges in proposed rule that GUARD provides no direct beneficiary savings and may increase Part D premiums.

PREMIUM EFFECT

Manufacturers may withdraw rebates that PDP sponsors currently report as DIR — IRA's 6% premium-growth cap shifts cost to government through 2029.

POLITICAL SIGNIFICANCE

The indirect-impact admission complicates Republican messaging that GUARD lowers prices for Medicare beneficiaries themselves.

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Section 3
The Seventeen Voluntary Deals — Anatomy and Supply-Chain Consequences

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Each of the seventeen bilateral contracts bundles Medicaid pricing, new-launch pricing, direct-to-consumer participation, and U.S. manufacturing investment.

1

Medicaid MFN

Flows through GENEROUS supplemental rebates against an 8-country reference basket benchmarked at the second-lowest net price.

2

New-Launch MFN

Future innovative products committed to MFN pricing across payer channels whose precise scope remains confidential.

3

TrumpRx Participation

Designated products listed at 33–93% off list price.

4

U.S. Manufacturing

Lilly $27B,[1] Novo Nordisk $10B[2]; deals anchor to America-First trade policy agenda.[3]

[1] Press Release, Eli Lilly & Co., Lilly Plans to More Than Double U.S. Manufacturing Investment Since 2020 Exceeding $50 Billion (Feb. 26, 2025), https://investor.lilly.com/news-releases/news-release-details/lilly-plans-more-double-us-manufacturing-investment-2020.
[2] Eli Lilly & Co., Schedule 14A, Preliminary Proxy Statement (Mar. 7, 2025), https://www.sec.gov/Archives/edgar/data/0000059478/000005947825000089/lly-20250307.htm.
[3] Fact Sheet, The White House, President Donald J. Trump Announces Major Developments in Bringing Most-Favored-Nation Pricing to American Patients (Nov. 6, 2025), 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/

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SECTION 3 | THE CARROTS BEHIND INDUSTRY PARTICIPATION

The price of a deal is the price of MFN; the value of a deal is tariff suspension and informal exemption from the mandatory MFN models.

01 Three-year suspension of Section 232 tariffs on imported patented pharmaceuticals and pharmaceutical ingredients preserves margins on otherwise-100%-tariffed branded imports — the deal-signers move from a default 100% rate to a zero rate through January 20, 2029.[1]

02 Manufacturers reportedly received informal assurances that GENEROUS participation will exempt them from GLOBE and GUARD mandatory participation, although the proposed rules contain no express carve-out.[2]

[1] Proclamation No. 11020, Adjusting Imports of Pharmaceuticals and Pharmaceutical Ingredients into the United States, 91 Fed. Reg. 18183 (Apr. 9, 2026).
[2] Letter from Hon. Frank Pallone, Jr., Ranking Member, H. Comm. on Energy & Com., et al., to President Donald J. Trump (Mar. 5, 2026).Letter from Hon. Ron Wyden, Ranking Member, S. Comm. on Fin., et al., to Pharmaceutical Manufacturers (Mar. 6, 2026).

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SECTION 3 | SUPPLY-CHAIN DISINTERMEDIATION THROUGH TRUMPRX

Direct-to-consumer platforms create a parallel cash-pay channel — but rebate displacement is narrower than the headlines suggest.

Humira	Ozempic	Repatha
TNF Alfa Inhibitor	*GLP-1 agonists*	*PCSK9 inhibitor*
BEFORE (LIST)	BEFORE (LIST)	BEFORE (LIST)
$6,922.62	$1,000–$1,350	$625.89
VIA TRUMPRX	VIA TRUMPRX	VIA TRUMPRX
$950	**$199**	**$239**

STRUCTURAL CONSEQUENCES

- Eligibility excludes Medicare, Medicaid, TRICARE, and VA enrollees, and requires commercial-plan patients to waive insurance reimbursement and forgo deductible credit.[1]
- The addressable pool is narrow — uninsured patients, plan-excluded drugs (GLP-1s for weight loss, fertility), and high-deductible patients pre-deductible ~15% of Americans are realistic users.[2]
- PBM pressure runs through three channels — visible list-vs.-cash spreads, manufacturer-direct platforms predating TrumpRx (LillyDirect, AmgenNow, BMS Patient Connect), and the FTC-Express Scripts settlement[3] signaling potential future TrumpRx-through-insurance integration.

[1] TrumpRx, White House, https://trumprx.gov/ (last visited May 3, 2026).
[2] Sean D. Sullivan & Ryan N. Hansen, *TrumpRx has a fundamental flaw*, STAT (Feb. 5, 2026), https://www.statnews.com/2026/02/05/trumprx-prescription-drug-costs-flaws/.
[3] Press Release, Fed. Trade Comm'n, FTC Secures Landmark Settlement with Express Scripts to Lower Drug Costs for American Patients (Feb. 19, 2026), https://www.ftc.gov/news-events/news/press-releases/2026/02/ftc-secures-landmark-settlement-express-scripts-lower-drug-costs-american-patients.

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SECTION 3 | THE TRANSPARENCY GAP AND CONGRESSIONAL OVERSIGHT

The bilateral deals' confidentiality has generated FOIA litigation and oversight pressure that will pressure any codification bill to contain explicit transparency provisions.

01 Public Citizen filed FOIA litigation in the District of D.C. in January 2026 seeking the unredacted Pfizer and Lilly agreements after HHS and Commerce declined to produce them.[1]

02 Reuters and 3 Axis Advisors reported that at least five deal-signers raised list prices on more than 350 branded products effective January 1, 2026.[2]

03 Ranking members of four congressional committees demanded unredacted MFN agreements from the President in March 2026, with manufacturer follow-up letters from Senator Wyden and six colleagues to eleven companies.[3]

04 The combination of opacity, post-deal price increases, and oversight pressure places pressure on any codification bill to contain explicit transparency provisions absent from the voluntary deals.

[1] Complaint, Ass'n of Brit. HealthTech Indus. v. United States, No. 1:26-cv-00241 (D.D.C. Jan. 27, 2026), https://www.citizen.org/wp-content/uploads/1-Complaint-1.27.2026.pdf.
[2] Michael Erman, Drugmakers raise US prices on 350 medicines despite pressure from Trump, Reuters (Dec. 31, 2025), https://www.reuters.com/business/healthcare-pharmaceuticals/drugmakers-raise-us-prices-350-medicines-despite-pressure-trump-2025-12-31/.
[3] Letter from Frank Pallone, Jr., Ranking Member, H. Comm. on Energy & Com., et al., to Donald J. Trump, President of the United States (Mar. 5, 2026), https://democrats-energycommerce.house.gov/sites/evo-subsites/democrats-energycommerce.house.gov/files/evo-media-document/wh.2026.03.05.letter-re-mfn-agreements.pdf.

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Section 4
Legal Barriers to Codification/Implementation

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SECTION 4 | THE LITIGATION THEORY MAP

Section 1115A's review preclusion does not reach every theory — four of the five likely litigation theories survive preclusion, and the 2020 MFN litigation already established which theories survive.

LITIGATION THEORY	§ 1115A PRECLUDES?	ANALYSIS
Lack of Notice-and-Comment	✓ NO — survives	Procedural challenges proceed despite § 1115A; preclusion reaches model elements, not rulemaking procedure.
Exceeds Statutory Authority	✓ NO — survives	Challenges to § 1115A's "defined populations" or "payment and service delivery model" limits likely reviewable.
Flawed Model Design	✗ YES — barred	The only theory squarely precluded — and the central reason CMS chose § 1115A over § 402.
Major Questions Doctrine	✓ NO — survives	"Vast economic and political significance" challenges survive preclusion; new traction post-Loper Bright.
Constitutional (Takings, Due Process)	✓ NO — survives	Survive preclusion entirely; *Cedar Point Nursery* provides physical-takings vehicle.

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SECTION 4 | LESSONS FROM THE IRA LITIGATION

Manufacturers have lost on every merits ruling — three appellate courts have now affirmed the voluntariness rationale would be a central defense for GLOBE and GUARD.

01 D.N.J. (Judge Quraishi) granted summary judgment for the government against BMS and Janssen in April 2024, holding that "selling to Medicare may be less profitable... but that does not make Defendants' decision to participate any less voluntary.[1]

02 Second and Third Circuits[3] have rejected Takings, Due Process, and First Amendment challenges across six appellate decisions, all relying on Medicare's voluntariness; Judge Hardiman's Third Circuit dissent argues that the economic reality of Medicare withdrawal makes participation effectively coercive.

03 Fifth Circuit reversed W.D. Texas dismissal on jurisdictional grounds *in National Infusion Center Association v. Becerra* in 2024 but did not reach the merits.[4]

04 Cert petitions await SCOTUS review; if cert is denied or the voluntariness rationale is affirmed, GLOBE and GUARD inherit the same defense — manufacturers can decline Medicare participation rather than accept the rebate.

1 Bristol-Myers Squibb Co. v. Becerra, No. 3:23-cv-3335 (D.N.J. Apr. 29, 2024), https://www.uschamber.com/assets/documents/District-Court-Opinion-Bristol-Myers-Squibb-Co.-v.-Becerra-D.N.J.pdf.
2 Boehringer Ingelheim Pharms., Inc. v. United States Dep't of Health & Hum. Servs., 150 F.4th 76 (2d Cir. 2025).
3 Bristol Myers Squibb Co. v. Sec'y, 155 F.4th 245 (3d Cir. 2025) Hardiman, J., dissenting) .
4 Nat'l Infusion Ctr. Ass'n v. Becerra, 116 F.4th 488 (5th Cir. 2024).

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Section 5
What Codification Could Actually Look Like

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Pending proposals related to MFN cluster into two theories of reform — codify executive authority or impose statutory benchmarks

01
Codify Executive Authority

H.R. 7837 — Most Favored Patient Act
Mandates CMMI to test MFN across Medicaid, Part B, Part D using second-lowest net price; effective Jan. 1, 2029.

Statutory mandate replaces discretionary CMMI authority — addresses APA risk while preserving agency execution discretion.

02
Impose Statutory Benchmark

S. 1587 / H.R. 3375 — Hawley-Welch (R)
All Rx, all markets; benchmark = average G7 retail list price.

S. 1753 / H.R. 3391 — Merkley-Dingell (D)
All brand drugs/biologics/biosimilars; lowest of 12-country list price.

Direct statutory price benchmarks with civil penalties — bipartisan in concept but divides on basket and mechanism.

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SECTION 5 | PATH-OF-LEAST-RESISTANCE CODIFICATION

Statutory ratification of GENEROUS, GLOBE, or GUARD is the most legislatively plausible scenario because it requires no new mechanism design and inherits the administration's existing scoring.

01 Medicaid-anchored: extend GENEROUS to all MDRP participants

Captures manufacturers that declined the bilateral deals and converts a voluntary demonstration into a statutory floor.

02 Medicare-anchored: embed GLOBE and GUARD in permanent statute

Removes the demonstration sunset and the Section 1115A waiver dependence; makes mandatory rebates permanent.

03 CMMI-anchored: H.R. 7837 model

Mandates the demonstrations Congress wants without specifying outcomes — addresses APA risk while preserving agency execution discretion.

WHY THIS PATH

Each path-of-least-resistance variant trades narrower reach for higher likelihood of enactment.

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SECTION 5 | FOUR KEY LEVERS IN ANY FINAL BILL

Payer scope, drug scope, reference-basket composition, and Medicaid Best Price interaction are the levers most likely to be negotiated explicitly in conference rather than left to agency discretion.

01 Payer Scope

Medicaid-only (codifying GENEROUS), Medicare-plus-Medicaid (adding GLOBE/GUARD), or all-payer reach (Hawley-Welch, Merkley-Dingell) — determines whether the bill reaches the 155 million Americans on commercial coverage and whether ERISA preemption and First Amendment challenges become viable.

02 Drug Scope and Carve-Outs

Orphan drugs, cell-and-gene therapies, breakthrough biologics, biosimilars — drive which manufacturer constituencies [reluctantly] accept the bill.

03 Reference-Basket Composition

Country count, GDP threshold, OECD vs. G7, selection rule (lowest vs. second-lowest) — drives the magnitude of price reduction; the GENEROUS-vs.-MFN-1.0 58% price difference shows why the basket matters more than the mechanism.

04 Government Price Reporting Interactions

Whether MFN-driven discounts trigger cascading MDRP rebate liability or are statutorily excluded from Best Price/Average Sales Price calculations

WHY THESE LEVERS

These four together let drafters preserve MFN's political optics while controlling the operational provisions that drive manufacturer revenue impact, stakeholder coalition support, and litigation risk. They are conference-committee currency.

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Section 6
Implications and Outlook

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SECTION 6 | Implications and Forward-Looking Questions

MFN in some form is unlikely to disappear — the operative questions for public policy makers and manufacturers are how it scales into adjacent programs, how spillover into commercial markets is managed, and how manufacturers reposition.

01 **Reference pricing in the IRA Negotiation Program** — whether CMS layers international reference data into the IRA's negotiation methodology would extend MFN logic into a statute already insulated from most constitutional challenges.

02 **Public-to-commercial spillover** — whether codification empowers commercial plans to benefit from international reference pricing, or whether it mitigates spillover potential.

03 **Manufacturer risk mitigation** — portfolio rebalancing toward protected categories, foreign-launch sequencing to manage reference exposure, and selective deal-signing will shape commercial reality.

04 **Innovation-preservation drafting** — whether the bill carries orphan exclusions, small-biotech carve-outs, and post-launch pricing grace periods will determine whether MFN sticks or generates R&D backlash.

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SECTION 6 | THE TWELVE-MONTH OUTLOOK

Final rules, manufacturer compliance, and bipartisan codification each operate on independent timelines, and any one of them can derail the others.

01 Final GLOBE and GUARD rules expected in the middle of 2026 will trigger the first wave of substantive litigation and determine whether the mandatory backstop survives.

02 GENEROUS manufacturer applications close June 11, 2026 and state applications close September 10, 2026 — deadlines have been extended due to challenges in aligning on participation agreements.

03 Supreme Court action on the pending IRA cert petitions will fix whether the voluntariness rationale that defeated manufacturers at Second Circuit and Third Circuit is available to defend GLOBE and GUARD, or whether manufacturers get a fresh merits look.

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