Whitepaper

Ingenious Brain
Future-Proofing Businesses

MFN Pricing:

Reshaping Global Drug Pricing and Market Access

Abstract

The practice of Most Favoured Nation (MFN) pricing has proven to be controversial but a promising tool for health policy in the pharmaceutical industry. The mechanism ensures that the prices of drugs in one market are aligned with the lowest price available in a comparable market. In this white paper, we aim to explore the principles of MFN pricing, its history and different approaches to implementation around the world. This will also include economic and legal considerations associated with this practice, effects on behavior of manufacturers, payers, and patients, as well as its impact on External Reference Pricing, Managed Entry Agreements, and Value-Based Pricing. Lastly, we will outline current knowledge gaps in terms of availability of data, incorporation of real-world evidence, alignment of policies between countries, as well as contract design. We will also describe how our business and technology consultancy could help to address those gaps.

Introduction

The issue of drug pricing is becoming a key health policy challenge. Precise medicines, cell and gene therapies, and biosimilar products deliver significant clinical value for certain groups of patients but have list prices far more than conventional therapies. To payers and governments, such prices are difficult to afford, while for manufacturers price discrimination among countries becomes critical to recover R&D investment and continue innovating. Against this background, MFN pricing emerged as an option to bring prices in line through leveraging the most favourable conditions internationally.

The concept of MFN originates from international trade, in which countries commit to treating other trading parties no less favourably than the most favoured party. As applied to pharmaceuticals, the MFN principle suggests that the buyer should not pay higher price than the lowest price charged somewhere else in a defined market set. Thus, it makes pricing fairer and speeds up access to affordable prices. But it may also lead to global price convergence, with negative consequences such as delaying launch, limited access, and even product withdrawal from various markets.

In this paper, we present a comprehensive and practical analysis of MFN pricing. We will be explaining its basic principles, and we will be comparing it to external reference pricing and internal reference pricing. We will also be looking into how MFN pricing could relate to confidential discounts and managed entry agreements along with identifying risks and potential benefits for each stakeholder involved to develop an implementation approach that minimizes any adverse effects.

Overview of MFN Pricing principles

Pharma MFN pricing

The pricing mechanism by which the price of the drug within one jurisdiction or segment will not be higher than the minimum price of that drug in the comparator market(s), usually net of all discount and rebate programs.

Relationship to pricing tools

- **External reference pricing (ERP):** Sets a price based on an average or basket of international prices. Usually less strict than MFN, which locks to the minimum.
- **Internal reference pricing:** Sets reimbursement caps based on class comparators domestically.
- **Managed entry/ value based agreements**: Tie price or reimbursement to performance outcomes, confidential.
- **Tendering and price-volume agreements**: Drive discounts via competition or volume commitments.

Impacts on stakeholders

Stakeholders	Impact/Benefits	Dangers
Patients	Quicker increases in affordability in high-priced markets Increased access if the savings are plowed back into expanded coverage.	Delayed launches in smaller or poorer markets Less expansive formularies Step-throughs due to budget constraints
Payers and HTA organizations	Stronger negotiating power Ceilings and budget savings	Erosion of manufacturers' interest in deep confidential discounts SKU manipulation and/or reformulation of products to complicate comparability Allocation issues if prices converge close to marginal costs
Manufacturer	Clarity on payer requirements and possible market stability when combining MFN with multi-year certainty	Global revenue squeeze Low ROI on risky R&D projects Need for restructuring global price governance model Threat of parallel trade if prices are equalized, but currency volatility remains
Hospitals and Providers	Possible cost parity for hospitals in procurement of products	Limited access channels Difficulties in securing supply of margin-lean specialty treatments
Policymakers and Trade Officials	Clear reaction to public opinion on drug pricing	Legal implications Accusation of extraterritorial price control Retaliation by price or launch delays

Jurisdictions that set precedent: Deep Explore High-Importance Geographies

The next few chapters will examine a very few jurisdictions in excessive detail. The excess is deliberate. **Germany, France, Italy, Spain, the United Kingdom, Japan** and **Australia** together account for a small fraction of global revenue -- but they set the observable prices that appear in most international reference baskets and, under most proposed MFN designs, the **U.S. calculation itself**. Importance here is a function of structural influence not revenue generation. Each jurisdiction is based on a different logic: **Germany** exports a particular, published net price; **France** exports confidentiality; Italy exports un-attestability; **Spain** exports statutory transparency; the **United Kingdom** exports a scheme-level rebate away from the product; **Japan** exports scheduled, rules-based erosion; **Australia** exports a threshold judgment captured in a contract. These are no local variants of a common model. The market is either a shield for the global corridor or the floor of the basket, and none of them can be captured in a blended country discount. A generic approach to any one of them will misprice all of them – and, once those prices are read in Washington, misprice the portfolio everyplace else. The depth that follows is the minimum needed to tell the mechanisms apart, and to know which are working for the portfolio, and which are working against it**.**

USA 

Executive Summary

Most-favoured-nation (MFN) pricing is not a discounting mechanism. This is a change in the logic of global price formation: from many independent national negotiations to a single interdependent global price system with one binding constraint: the lowest observable ex-U.S. price.

The following five conclusions are:

1. MFN obtained without legislation in US. The current framework has been delivered thru a failed rulemaking (2018-21), a legislated domestic precedent (IRA, 2022-25), and bilateral, executive-led deal-making underpinned by tariff

and regulatory leverage. Some 17 of the largest manufacturers have signed voluntary MFN-referenced agreements, and the Administration estimates ~$64bn in Medicaid savings over 10 years from the framework.

2. 80% of commercial impact derives from design detail, not the headline principle. Four parameters (comparator basket, gross-vs-net basis, population scope, refresh cadence) swing modeled U.S. net price change from ~10 percentage points to a portfolio-level revenue reset.

3. Price level is irrelevant, but price dispersion is not. The asset most at-risk is the one with the biggest difference between the U.S. net realization and its lowest transacted ex-U.S. price, independent of absolute revenue.

4. Exportability of the mechanism. Any government with a trade instrument now has a working template. The U.S. precedent increases the likelihood of reciprocal reference-pricing and anti-referencing defenses in the EU, Japan, Canada and the Gulf – covered in subsequent chapters.

5. Clients need to respond at the organizational level, not the tactical level. Launch sequencing, capital allocation, manufacturing footprint and pricing governance cannot be stand-alone functions any more.

Why All Serious MFN Analysis Must Start with the United States

The U.S. is the natural place to start not only because it is the world's largest pharmaceutical market – accounting for about 45-50% of global branded pharmaceutical revenue on about 25% of high-income-market volume – but because it is the only large market trying to import a pricing mechanism that the rest of the developed world built decades ago from a position of structural disadvantage.

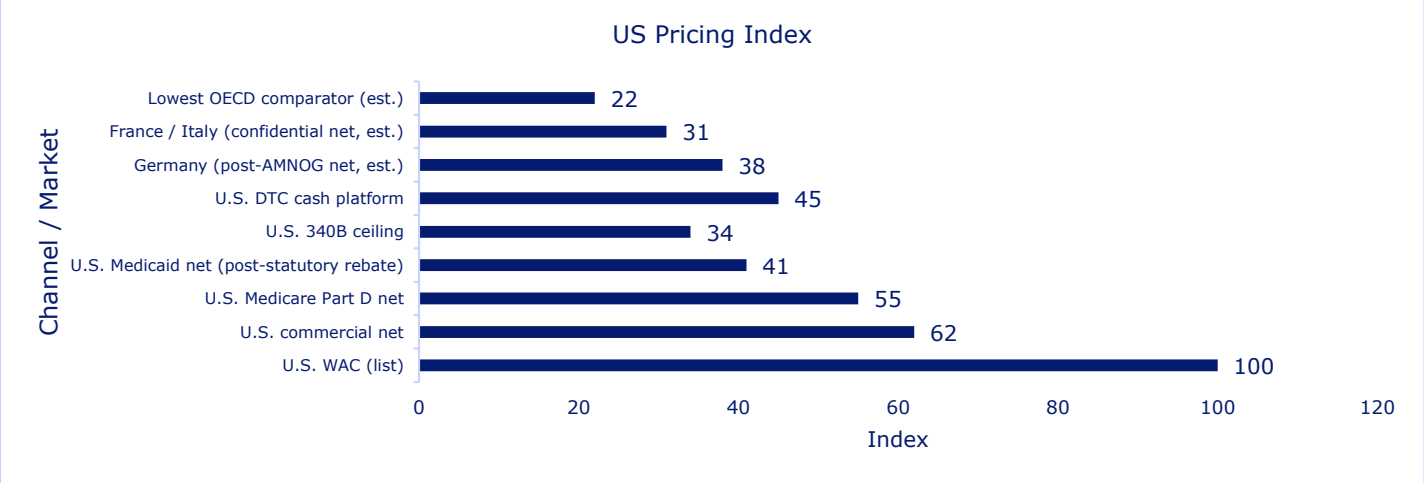
All other high-income countries that use external reference pricing (ERP) do so on a monopsonistic basis: one payer, one counterparty to negotiations, one price. The United States does not have such architecture. It has Medicare Parts B and D, Medicaid (with statutory rebates and best-price rules), the VA and Federal Supply Schedule, the 340B program, commercial insurers, pharmacy benefit managers and cash-paying patients – all transacting the same molecule at materially different points on the same price curve.

Advisory opinion Adding an international benchmark to a fragmented payer system does not make pricing any simpler, it adds another dimension to a problem that is already multi-dimensional." Most commercial organizations were structured to have country level P&L autonomy. MFN turns that architecture into a liability. This chapter's main argument: U.S. MFN is not a price-cutting event, but a structural re-architecture of how a molecule's global price is governed.

The gap MFN wants to bridge

Comparison (branded, ex-manufacturer, 2024 RAND baseline)	U.S. price as multiple of comparator
All drugs, 33 OECD comparison countries	2.78×
Brand-name originator drugs only	4.22×
Brand-name vs. Germany / France / UK cluster	~3.0–3.5×
Unbranded generics (U.S. *cheaper*)	0.67×

US Price Index: One Molecule, Nine Prices



Index values are standardized to the United States Wholesale Acquisition Cost (WAC = 100). The other variables are relative net-price levels; the figures marked are estimates, and the France/Italy values are confidential net-price estimation.

The policy chain: A short history

It is the end-product of three separate waves of policy pressure over a period of six years. The political cost of the next wave went down with each wave.

Wave One — The Failed Rulemaking (2018-2021)

The CMS Innovation Center's mandatory nationwide demonstration to peg Medicare Part B reimbursement to an international benchmark was struck down on procedural ground, esp. inadequate notice and comment and not on the economic merits.At that time industry generally misinterpreted this distinction. The courts did not say the government could do this. They said the government had not done it right. The sector spent four years preparing to turn a procedural loss into a substantive victory.

Wave Two – Domestic Legislative Precedent (2022-2025)

The Inflation Reduction Act created a domestic negotiation process to establish a "Maximum Fair Price" (MFP) for high-value Medicare drugs, with statutory limits set by non-federal average manufacturer price (AMP) and substantiated by clinical and comparative-value evidence.

First cycle: 10 Part D drugs with negotiated prices effective January 1, 2026, and announced reductions of about 38%–79% off 2023 list prices.

Second cycle: 15 additional Part D drugs; Part B drugs in subsequent cycles.

The important result was not the savings. It was a precedent. The IRA provided MFN supporters with what they had always lacked: an accepted, operating principle that the U.S. federal government sets prices administratively rather than accepts them. Once the principle is accepted, the choice of benchmark is a matter of policy taste.

Wave Three – Executive MFN & Trade Linkage (2025-2026)

• May 2025: Executive Order "Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients" re-instituted MFN as explicit policy, instructing that price targets be communicated to manufacturers and signaling escalation levers – rulemaking, importation pathways, FTC/DOJ action, export restrictions.
• H2 2025: Major oncology, immunology and GLP-1 manufacturers have entered into negotiated agreements with MFN-referenced pricing for Medicaid populations and direct-to-consumer channels in several instances in exchange for tariff relief, Section 232 accommodation and commitments to accelerate regulatory review.
April 2026: Executive action on pharmaceutical imports tied pricing explicitly to trade and industrial policy, making investment in U.S. domestic manufacturing a de facto currency of pricing negotiations.
• 2026 YTD: Two CMS model designs in development based on a 19-country reference basket; White House reporting cites 17 manufacturer agreements and $64bn Medicaid savings over ten years.

The least appreciated evolution in global pricing governance is that the U.S. achieved significant de facto MFN compliance without passing legislation, by tying pricing requirements to trade leverage. You can export that mechanism. Any government with a tariff, procurement or market-authorisation instrument now has a proven template.

"Three Waves: The U.S. Path to MFN"

Figure: "With each wave, the political cost of the next wave fell."

The Mechanics: What Is Actually Referred to

Practitioners always underestimate the degree to which the commercial outcome is dictated by definitional detail rather than the headline principle. Four parameters account for almost all of the variance.

The basket of comparators. It is very different benchmarks if the reference set is limited to four to six large European economies or to all OECD economies with a GDP per capita above some threshold. Bigger baskets include lower-priced markets and pull the benchmark down. The CMS model designs contemplate a 19-country basket at the aggressive end of this range. Gross vs. net. U.S. list prices are heavily rebated; European prices often have their own confidential discounts. This is not an apples-to-apples comparison of a foreign list price versus a U.S. net price, and in several heavily rebated categories (insulins, respiratory, some immunology) it can result in a benchmark that is higher than the actual U.S. net price. But, benchmarking a foreign net to a U.S. net is the single most punitive configuration possible.

Population coverage. A Medicaid-limited MFN price is nothing like one across Medicare Parts B, D and cash channels. Scope defines whether MFN is a manageable margin event or a portfolio-level revenue reset. Scope also influences spillover: Medicaid best-price interaction and commercial "me-too" contracting mean that a narrowly targeted policy is seldom narrow in practice.

Conventions for currencies and timing Volatility depends on whether conversion is at spot rates, trailing averages or purchasing-power parity and whether the benchmark is updated quarterly or yearly. A quarterly-refresh, spot-FX design puts foreign-exchange risk squarely into U.S. gross-to-net forecasting, a risk most finance functions today hedge for revenue translation, but not for price setting.

Design parameter	Low-impact configuration	High-impact configuration	Est. change in U.S. net price
Comparator basket	4–6 large economies	Full OECD ≥ GDP/capita threshold (19-country model)	**10–20 pp**
Price basis	Net-to-net, verified	Foreign list vs. U.S. net	**15–35 pp**
Population scope	Medicaid / DTC only	All federal + commercial spillover	**3–5× exposure multiple**
Refresh cadence	Annual, trailing FX	Quarterly, spot FX	High forecast variance (±8–12% intra-year)

Insight for negotiation teams. These four parameters are the entire negotiating surface. Arguing the principle of MFN is a losing position; arguing basket composition, net-to-net verification, scope carve-outs and refresh cadence is a winnable one. Every percentage point conceded on the principle should be traded for a definitional concession, which is where the value actually sits.

Quantified Business Impact

The exposure distribution below is derived from modelling across a representative branded portfolio. These are **directional planning ranges, not point forecasts**, and must be stress-tested against asset-specific gross-to-net structures.

Archetype	Exposure	Est. reduction vs. current U.S. net realisation (full-scope MFN)	Principal complication
Small-molecule specialty, mature EU reference prices	High	25–45%	Established, observable foreign prices; no defence
Physician-administered biologics (buy-and-bill)	Moderate–High	15–30%	Provider margin compression restricts access even if the manufacturer absorbs the cut
U.S.-first launches, no/delayed EU launch	Low (near-term)	0–10%	Exposure crystallises at first ex-U.S. launch
Rare disease / orphan	Unpredictable	0–60%	Thin comparator sets — one small market can set the global floor
Mature brands facing LOE within 36 months	Low economic	n/a	Erosion dominated by generic entry, not MFN

Central portfolio insight. *The most expensive asset is not necessarily the most at-risk asset. Risk is driven by the* ***spread between U.S. net price and the lowest transacted ex-U.S. price*** *— irrespective of absolute price level or revenue.* ***Triage on dispersion, not on revenue.*** *A $400m asset with 6× dispersion is a more urgent problem than a $2bn asset with 1.8× dispersion.*

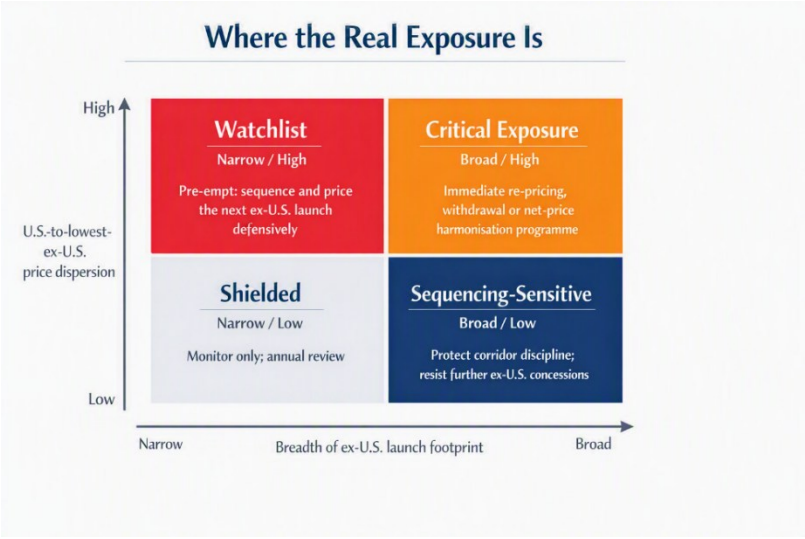


Figure: Exposure categories are based on the relative width of the ex-U.S. launch footprint and U.S.-to-lowest-ex-U.S. price spread. High/Low and Broad/Narrow are directional classification**.**

Launch-sequencing distortion. If the U.S. price is determined by the lowest ex-U.S. price, the rational manufacturer response is to wait out or not enter lower-priced markets. Signs of growing gaps in launches are already apparent in smaller European and Asia-Pacific markets. The U.S. patient gets price relief; the Slovakian, Portuguese, Greek or Malaysian patient loses availability.

This is an access-equity harm of an access-equity policy — and it needs to be stated explicitly in the concluding chapter, not buried in the risk section. It is also the only single strongest advocacy argument available to industry because it is empirically demonstrable rather than rhetorical.

Confidentiality Breach. MFN is effective only when foreign prices are visible. Thus, continued pressure from the U.S. undermines the confidential-discount system that European payers rely on. Such payers have a great incentive to resist. The probable equilibrium is that MFN implementation increasingly depends on estimated, not actual, foreign net prices—a technically weak evidentiary base that invites administrative challenge and that clients should be prepared to contest asset-by-asset.

Proliferation of channels. Direct-to-consumer cash platforms have become an MFN-adjacent release valve that allows manufacturers to offer lower cash prices outside of the traditional rebate architecture. This partly separates list price from patient cost but adds a fourth or fifth price point per molecule, with commensurate complexity in best-price, government-price-reporting and channel-conflict management.

5.4 Pricing by manufacturing. "Linking tariffs makes capital expenditure conditional on the pricing negotiations. "Site selection and pricing in the past were done by separate hierarchies reporting to different people and now have to be governed together. Manufacture commitments have become a tradable pricing asset.

Two effects to add to the standard list

R&D portfolio re-weighting. The expected NPV falls fastest for assets that provide modest incremental benefit in crowded classes where the weakest market sets the global price floor. So expect capital to flow to the high-unmet-need, high-differentiation assets where premium pricing survives referencing, and away from marginal line extensions.

M&A and deal structure effects. Now reference-price contamination is an audit item. More contingent value rights, geography-carved licenses and "ex-U.S. rights excluded" structures aimed at keeping a partner's low-priced market from setting an acquirer's U.S. floor are coming

"The MFN Doom Loop"

Break-points (shown as external levers): net-to-net verification · corridor pricing · differential-pricing safe harbours · confidentiality-preserving data exchange.

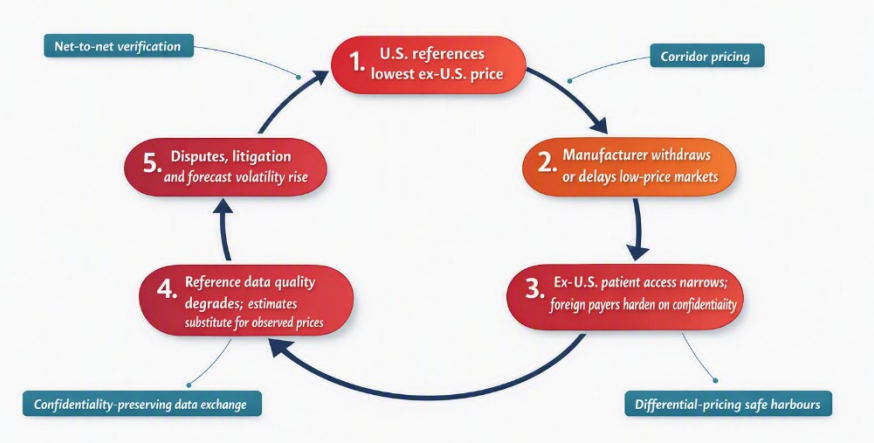


Figure: MFN policies may unintentionally reduce global access and pricing transparency.

Implications for Price, Reimbursement and Market Access

Dimension	Direction of travel	Practical consequence for the U.S. market
List price	Downward pressure on WAC; renewed interest in list-price resets	Lower list reduces 340B and Medicaid rebate liability but destabilises PBM rebate economics and formulary position
Net price	Structural compression, 15–35% depending on configuration	Gross-to-net bubble deflates; finance must re-baseline multi-year revenue models
Rebate architecture	Migration from rebate-driven to net-price-driven contracting	PBM value proposition weakens; direct contracting and DTC channels expand
Reimbursement	Benchmark becomes an input to coverage, not just to payment	Payers increasingly reference MFN price as the ceiling in commercial negotiations, importing federal terms into private contracts

Structural Overview — The Inversion

For three decades the United States functioned as the terminal node of the global pricing system: it read prices, it did not export them. Ex-US regulators referenced each other; the US referenced no one and was referenced by no one. That asymmetry was the load-bearing wall of the global corridor — it allowed the industry to concede in Spain, defend in Italy, and absorb erosion in Japan, because none of those concessions travelled westward.

That wall has fallen. Three simultaneous developments have converted the US from a reader into a source:

1. IRA Maximum Fair Prices (MFPs) — statutorily published, government-negotiated net-equivalent prices for selected molecules.
2. MFN / international-reference rulemaking — proposals that make ex-US prices a direct input into US reimbursement or procurement.
3. Direct-to-patient and cash-price channels — manufacturer-published prices that create a second, visible US number outside the gross-to-net system.

The result is a bidirectional referencing loop. Concessions made abroad now flow into US calculations, and US published figures now flow into ex-US baskets that were historically insulated by the "US is not comparable" argument. Every jurisdiction analysed in the preceding chapters must now be re-modelled with the US as both an upstream and downstream node.

The Four Price Layers of the US Market

Layer	Definition	Visibility	Referencing Risk
WAC / List	Published wholesale acquisition cost	Public	Historically the only exported figure; increasingly dismissed as fictional
Commercial Net	Post-PBM rebate realisation	Confidential (contractual)	Low direct, high inferential via gross-to-net disclosures
Statutory Net	Medicaid AMP/best price, 340B ceiling, FSS/Big Four	Formula-derived, partially public	High — computable by third parties
MFP (IRA)	Negotiated maximum fair price	Published by statute	Critical — an attested, government-endorsed net figure

The MFP is the strategic problem. It is exactly what the industry spent twenty years arguing could not exist: a knowable, official, net price. The "un-attestable" defense used in Italy and France once one exists in the US, weakens by association — and, as shown in the Australia chapter, the Deed of Agreement had already provided the counter-example abroad.

Gross-to-Net as Structural Weakness

The US gross-to-net bubble was a commercial mechanism. It is now an analytical exposure. Characteristics:
• Combined Reporting. Financial reporting discloses company-level gross-to-net percentages, allowing regulators and analysts to infer product-level nets within acceptable error bands.
• Inference at the class level. Where a therapeutic class has a known formulary structure, the rebate corridor is narrow and deducible without any contractual disclosure.
• Asymmetric collapse. One MFP publication in a class calibrates the perceived net of the whole class, including non-selected molecules.

The operative conclusion: US confidentiality is no longer a discrete asset per contract, it is a correlated asset at the class level that fails in the aggregate. Confidentiality-based risk models systematically underestimate exposure per contract.

Transmission Mechanics — How a US Number Travels

Pathway	Mechanism	Affected Jurisdictions	Latency
Direct basket inclusion	US published price added to an ERP basket	Canada, Gulf states, selected LATAM	6–18 months
HTA leverage	Payer cites MFP as evidence of achievable price	UK, Australia, Canada	Immediate at next review
Negotiation anchoring	MFP used rhetorically in confidential talks	France, Italy, Spain, Japan	Next renegotiation cycle
Reverse contagion	Ex-US net used as MFN input into US price	US (self-referencing)	Rulemaking-dependent
Political spillover	Public comparison drives legislative action	All	12–36 months

The fourth pathway is the one most frequently under-modelled. Under a net-attested MFN regime, an Italian confidential rebate — historically the industry's "strongest shield" — becomes a **US price determinant**. The shield does not merely fail; it inverts into a liability.

Scenario Exposure Model

Modelled as index values against a baseline of 100 for global corridor integrity:

Regime	Description	US Impact	Ex-US Corridor Impact	Combined Corridor Index
A. List-referenced MFN	US references published ex-US list prices	Moderate	Low (list defensible)	≈ 85
B. Net-attested MFN	Manufacturers must attest ex-US net	Severe	Severe (shields void)	≈ 45
C. Haircut-imputed	Standardised discount applied to list	Moderate–High	High (arbitrary, uncontestable)	≈ 60
D. Lowest-in-basket	US pays lowest observed comparable price	Severe	Catastrophic for launch sequencing	≈ 35

Regimes B and D are existential to the current architecture. A and C are survivable with disciplined list-price governance. The strategic implication is that it's more valuable to defend the distinction between list and net than to defend any one price point. Regime C is unattractive but is the rational fallback to argue for: it keeps the confidentiality boundary and agrees to a quantified, negotiable penalty.

The Question of Attestation

The industry's position that ex-US net prices are un-attestable because of contractual confidentiality, clawback structures, volume-contingent rebates, and multi-year true-ups is technically defensible in Italy and France, weak in Australia, and irrelevant in Germany and Japan, where published equals net.

The disadvantage is that it is stated as a generality. One counter-example (an Australian Deed, a Japanese NHI listing) is sufficient to characterize the whole position as evasive. The tenacious argument is not one of impossibility but of incomparability:

- Former US prices are results of budget-constrained administrative processes, not market valuations.
- They include non-transferable local volume guaranties, formulary exclusivity and timing of access.
- Threshold-derived price (Australia, UK) compares local willingness-to-pay with a local opportunity cost, not value of the asset.

Recommended posture: Forget the impossibility claim. Embrace the economic-function claim. accept your math, challenge your meaning.

The US Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing
1	**Launch-price architecture.** Set US list with explicit modelling of its role as an exported reference, not solely as a gross-to-net starting point	Global Pricing Committee	**T−24 months**
2	**MFP-adjacency mapping.** Identify which in-line and pipeline assets sit in classes where an MFP publication will calibrate perceived net	Pricing Intelligence	**T−18 months**
3	**Attestation-readiness audit.** Determine, per market, whether net price is contractually determinable; classify markets as attestable / inferable / genuinely opaque	Legal / Global Pricing	**T−12 months**
4	**Advocacy repositioning.** Replace blanket un-attestability messaging with market-architecture-specific non-comparability arguments	Corporate Affairs	**T−12 months**

5	**Launch-sequencing revision.** Re-order ex-US launches so that low-price, high-reference jurisdictions follow rather than precede US and anchor markets	Global Launch Governance	**T−9 months**
6	**Scenario re-baselining.** Re-run portfolio NPV under Regimes A–D; set walk-away thresholds per market	Finance / Strategy	**Annual**
7	**Gross-to-net disclosure discipline.** Review external reporting granularity for inferential leakage at class level	Investor Relations / Finance	**Continuous**

Government Authority Must Follow Disclosure

The historical governance failure is that the US business has US pricing authority but the consequences of US pricing are in the hands of the global portfolio. This is no longer tenable with the inversion.

Shifts needed:

• Expand list price authority. The US WAC decisions have to be ratified by a global body that owns corridor integrity, not the affiliate that owns US revenue.
• Price the external costs. Local access concessions should include an internal transfer charge reflecting modeled corridor damage, so that affiliate incentives are aligned with enterprise value.
• Think of sequencing as a pricing decision. Launch order is now an act of price setting; it must be handled with the same rigor as the price itself.

• Institutionalize the transmission map Keep a model of jurisdiction to jurisdiction referencing alive, updated at every regulatory change, and make its output a mandatory input to any pricing approval.

Conclusion — The Death of Asymmetry

The U.S. was never just the biggest market. It was the structural reason the global pricing system worked. Its opacity absorbed the consequences of past US transparency, so that the industry could trade published concessions abroad for secret realizations at home. The trade is closing.

Three conclusions are plain.

1. First, opacity is a depleting stock. It can be used more or less wisely but not repaired. Every disclosure, statutory, financial or negotiated, is a permanent withdrawal. Governance must apply the same discipline to it as to patent life.

2. Secondly, the nature of the risk has changed. The central exposure is no longer the price level of any one market but the correlation structure across markets. A portfolio that is individually well priced and structurally badly sequenced will underperform one that is individually mediocre and structurally coherent.

3. Third, the defense has to be specific. The blanket un-attestability argument is now a liability: it is falsifiable in at least three jurisdictions and invites the characterization of bad faith. Each pricing mechanism has an economic function. The defensible ground is that administratively derived, budget-constrained, threshold-tested prices are not market valuations, and cannot be transplanted without destroying the conditions that produced them. Guiding Principle for the United States: Protect the list-net distinction as the key asset Govern US list price as a global export not a domestic input Sequence launches as a pricing decision Argue non-comparability, not impossibility

United Kingdom

Executive Summary

The United Kingdom holds a position in the MFN debate wildly out of proportion to its commercial size. This represents some 2-3% of the global pharmaceutical revenue, but is embedded in the reference baskets of an estimated 20+ countries and is a named comparator in the US reference-basket designs under development.

Five conclusions frame the chapter:

1. The UK has no external reference pricing – and that is exactly what makes it dangerous. Spend is controlled thru a revenue clawback (VPAG) and a cost-effectiveness gate (NICE), not price benchmarking. The published list price is relatively benign, the net price is confidential and among the lowest in Western Europe.

2. The UK is the single most consequential "definitional" question in U.S. MFN design. If MFN means UK list, exposure is limited. If it says UK net then the UK is a global price floor. Our modeling shows the difference between these two outcomes is worth 12-25 percentage points of U.S. net price on a mature specialty portfolio.

3. UK payment rates have increased on a structural rather than cyclical basis. The industry rebate has gone from 5.1% (2021) to the low-to-mid 20s% (2023–2026) — a fourfold-plus increase in five years that has turned the UK from a modest-margin market into a negative-contribution market for several asset archetypes.

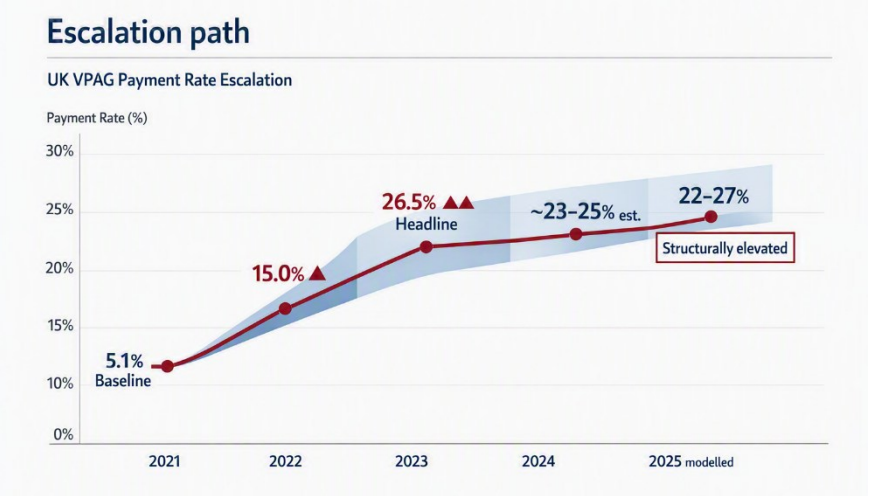
4. The NICE threshold has never been uprated. The range of £20,000–£30,000 per QALY, set in 1999, is worth about £38,000–£57,000 in 2026 money. The UK has shut its access gate by some 45-50% in real terms and has never made a policy decision to do so.

5. For clients, the UK question is no longer 'what price can we get? The question is, "can we afford to be seen here at all? Launch deferral, list price protection, confidentiality preservation and, in an increasing number of cases, commercial withdrawal are now board level decisions with global not local consequences

Why the UK Matters Far More Than Its Market Size

Metric	United Kingdom	Context / Peer Comparison
Share of global branded pharma revenue	~2.2%	U.S. ~47%; EU5 ~20%; Japan ~7%
Population	~67 million	Comparable to France and Italy; ~1/5th of U.S.
Branded medicines spend (NHS, net)	~£17–19bn p.a.	~10% of total NHS budget
Formal ERP / MFN system	None	Unusual among OECD peers
Cost-effectiveness gatekeeper	NICE (and SMC in Scotland, AWTTC in Wales)	Binding funding mandate in England
Spend control mechanism	VPAG (voluntary) / Statutory Scheme (default)	Revenue cap + clawback
Manufacturer payment rate (2025 est.)	~23–25%	Up from 5.1% in 2021
Average list price multiple vs. lowest OECD	~2.8x	U.S. ~4.2x; Germany ~2.1x
Estimated net price multiple vs. lowest OECD	~1.3x	U.S. ~1.8x; Germany ~1.1x
Number of countries referencing UK in ERP baskets	20+	Including Canada, Ireland, Netherlands, Gulf states, parts of CEE and Asia-Pacific

Figure*: UKVPAG Payment Rate Escalation*



Insight: UK is architecturally relevant, not commercially. A UK price can generate more revenue for a manufacturer outside the UK than they will ever generate inside the UK. And the single most important number in this chapter is not the £17-19bn of NHS spend, it is the 20+ downstream reference relationships that pass UK prices into markets worth many multiples of the UK itself.

Dual Control Architecture in the UK

UK does not set prices. It sets two distinct limits – one on the use of a medicine, one on total industry earnings – and gives the manufacturer the choice of a list price between them. The separation of the two is important to correctly model UK exposure.

- NICE – the volume gate
  Threshold: £20,000–£30,000 per QALY for standard technologies; up to £50,000 per QALY for end of life/severity modifier; £100,000–£300,000 per QALY for Highly Specialized Technologies (rare disease).
  Never uprated: The threshold was set in 1999 and has not been indexed. This is equivalent to about £38,000-£57,000 per QALY in 2026 values (inflation adjusted). Effectively it is 45-50% tightening in real terms, passively done.
  Funding mandate: NICE recommendation is positive, within 90 days NHS England must fund (30 days for cancer). This gives NICE a rare power: it is not advisory, it is the on/off switch for the market.
  The commercial consequence: The gate is binary and the threshold is fixed, so the manufacturer has only one lever to pass the gate: discount depth. NICE thus works as a price-setting mechanism in disguise as an assessment mechanism.

VPAG – the cap value

- Mechanism: The increase in NHS spending on branded medicines is capped (around 2% p.a under the 2024-2028 agreement). Sales exceeding the cap are paid back to DHSC as a percentage of revenue clawback.
- Two-tier design: VPAG differentiates between newer active substances and older/off-patent branded medicines, with a substantially higher rate applied to the older tier. This is by design: it is a legacy revenue tax to create headroom for innovation.
  Statutory Scheme parity: companies that decline VPAG are in the Statutory Scheme which is designed to prevent arbitrage. There is no opt-out.
- Insight: VPAG isn't a discount, it's a tax on revenue that is paid after the fact at a rate the manufacturer can't predict at launch. This is the key difference for MFN modeling. The discount can be quarantined, structured and kept confidential. A percentage-of-revenue clawback is portfolio-wide, retrospective and effectively public in the aggregate, making it far harder to defend as "not a net price" in a reference-pricing dispute.

The third, more muted layer: agreements on commercial access

Beyond NICE and VPAG there is an increasing layer of confidential Patient Access Schemes (PAS), Commercial Access Agreements and Managed Access Agreements (including the Cancer Drugs Fund and Innovative Medicines Fund). Routine confidential discounts are common; outcome-based and volume-tiered deals are increasingly common for high-cost specialty and ATMPs.

VPAG is on revenue net of PAS so the layers compound. A 40% PAS plus a 24% VPAG rate gives a net realization of about 46% of list - not 36%. The most common source of UK forecast overstatement that we see in client portfolios here is modeling error

"The UK Net Price Waterfall"

Step	Value (£)	Cumulative
List price (annual cost per patient)	10,000	10,000
Confidential PAS discount (−35%)	−3,500	6,500
VPAG clawback (−24% of post-PAS revenue)	−1,560	4,940
Procurement / homecare / wastage	−300	**4,640**
Net realisation		**~46% of list**

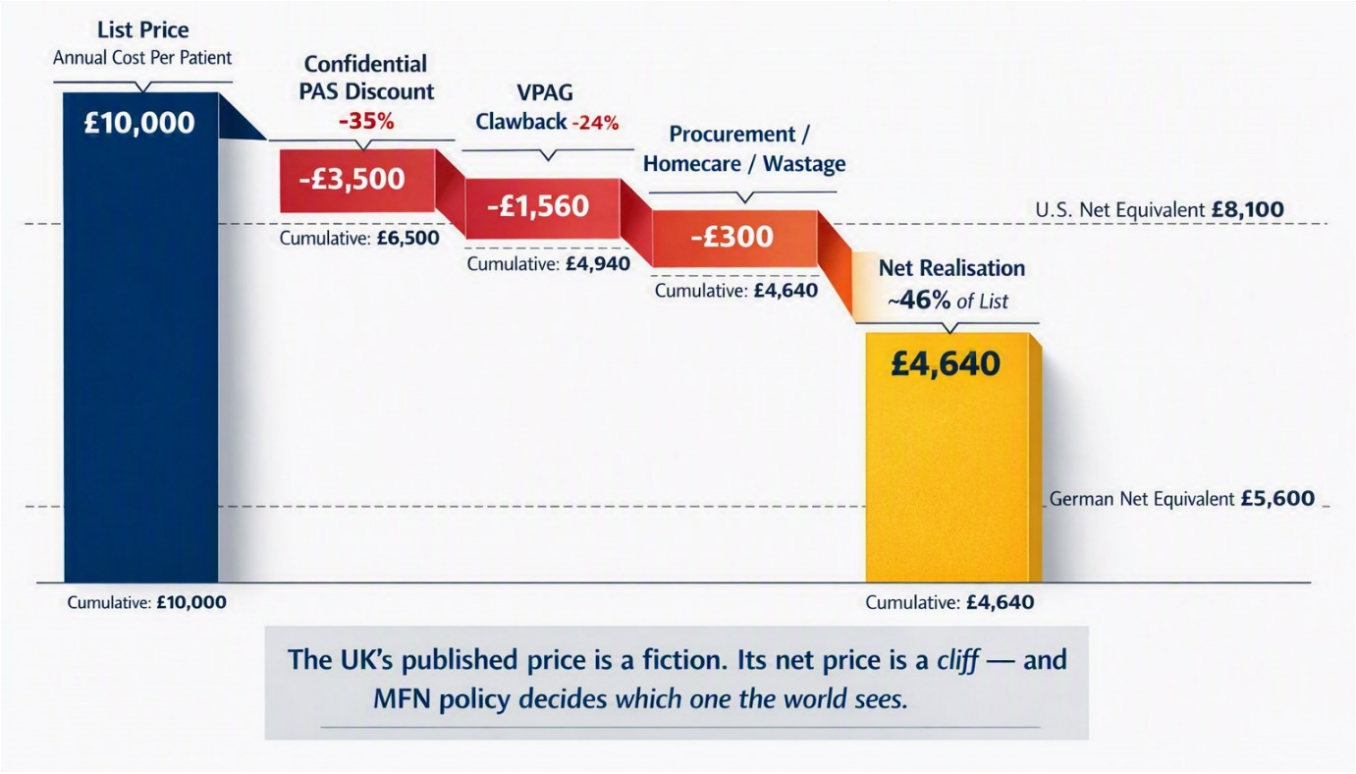


Figure : UK Net Price Waterfall List bar

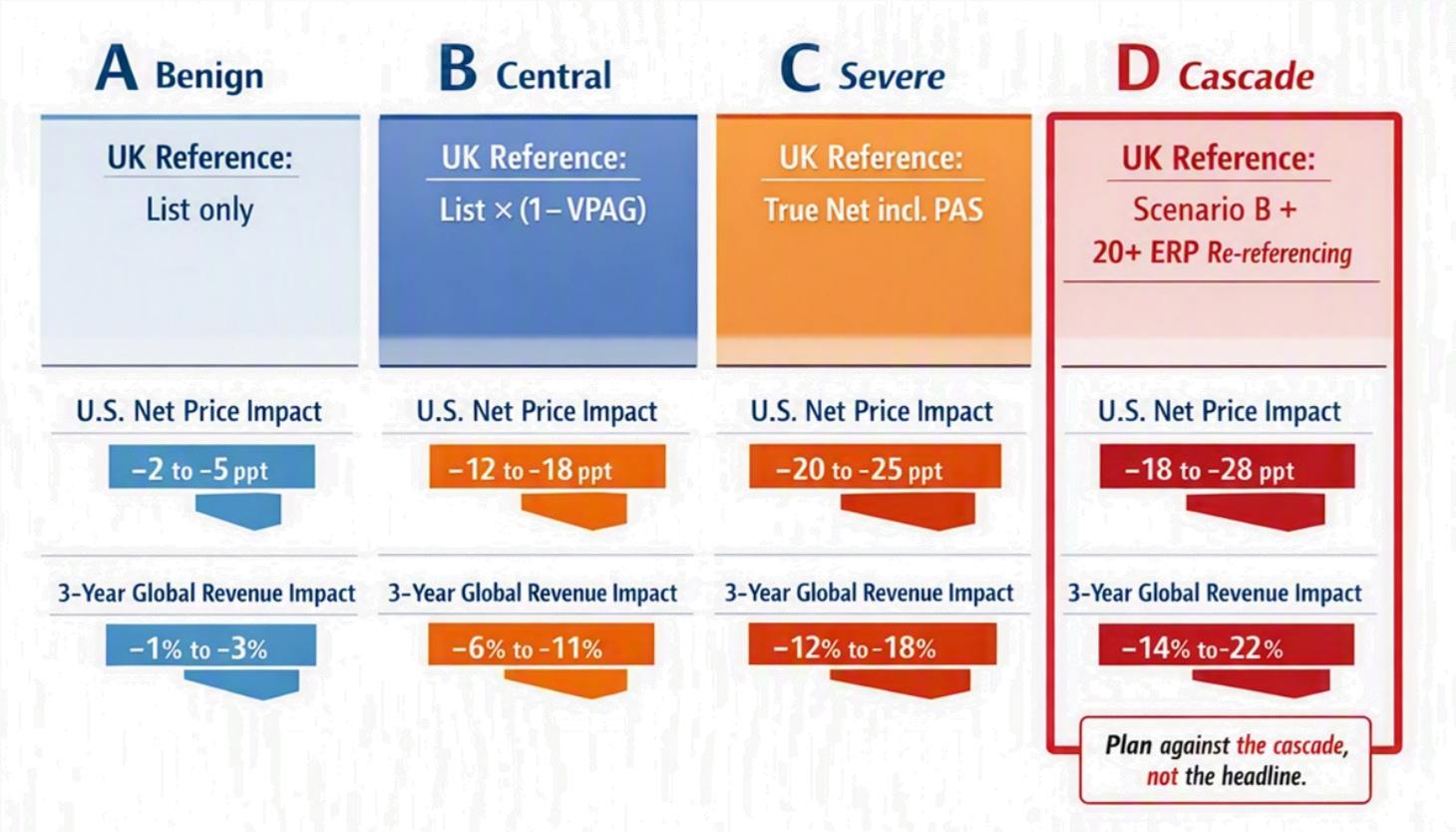
The MFN Conundrum: Which UK Price Travels?

MFN references…	Observability	U.S. price impact	Manufacturer exposure
UK list price	Fully public (dm+d, BNF)	Modest. UK list is mid-pack; not a global floor.	Low–Moderate. UK becomes one comparator among several.
UK list minus VPAG	Derivable from public data	Material. Payment rate is published annually.	High. This is the most likely realistic outcome — it is *calculable without any company disclosure.*
UK true net (incl. PAS)	Confidential today	Severe. Establishes a hard global floor.	Critical. Would require disclosure that breaches existing NHS commercial agreements.

Insight – the key most clients miss: The debate usually boils down to "list vs. net" as if confidentiality were a protection for the manufacturer. It doesn't. Published VPAG payment rates. There is no need for a company to cooperate with a U.S. authority to compute UK list × (1 − published VPAG rate) and call that a net price. The UK is thus the only major market where a defensible net-price proxy can be constructed unilaterally from public data. That's the real MFN risk, not the depth of NHS discounting**.**

Quantified scenarios (mature specialty portfolio):

Scenario	UK reference used	U.S. net price impact	Global revenue impact (3-yr)
A — Benign	List only	−2 to −5 ppt	−1 to −3%
B — Central	List × (1 − VPAG)	−12 to −18 ppt	−6 to −11%
C — Severe	True net incl. PAS	−20 to −25 ppt	−12 to −18%
D — Cascade	Scenario B plus the 20+ downstream ERP baskets re-referencing the reduced UK price	−18 to −28 ppt	−14 to −22%



Scenario D is the one to plan against. MFN does not act in isolation; it interacts with the pre-existing ERP web. A UK price reduction is referenced by Canada, Ireland, the Netherlands, the Gulf and much of CEE — which then feed *their* reduced prices back into other baskets. We model the secondary cascade at 1.4–1.8x the primary effect over 36 months.

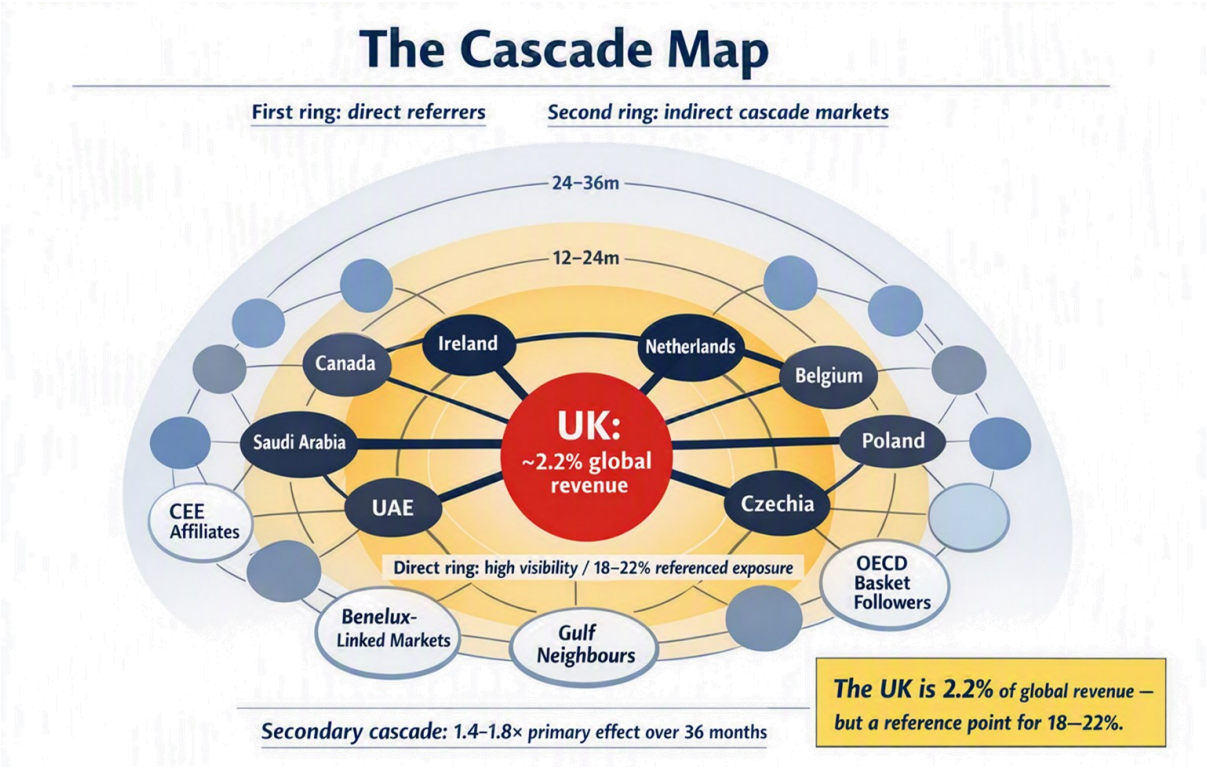


Figure: The Cascade Map

Strategic Implications and Playbook

Launch sequencing and deferral Risk

A first wave UK launch sets a low, publicly-derivable net price before the global baseline is set. Play: Sequence UK after U.S., Germany, Japan high price anchor markets and after ERP sensitive basket pricing. Limit initial indication scope to limit the reference basis where the funding mandate creates pressure to launch early.

Cost: The delay to the UK launch has consequences for reputation, politics and patient access, which are becoming more evident to Parliament, the ABPI and patient groups. Also, it loses the certainty of reimbursement that only the NICE funding mandate delivers. Deferral is a defensible tactic for 6-18 months, not a strategy of indefinite absence.

Decision rule: Defer if the UK is in ≥8 downstream reference baskets and the projected UK net realization is <55% of the global weighted-average net price. Otherwise, launch on time and control exposure with structure, not time.

Privacy Protection

Risk: VPAG rates are published, PAS discounts are not. Confidentiality is built on a single layer, and that layer is the most vulnerable to demands for disclosure under transparency-oriented policy.

Play:

- Value shifted from price to structure Outcome-based agreements, volume-tiered arrangements, indication-based pricing and free-stock/first-cycle arrangements provide equivalent NHS value but resist reduction to a single unit price. A price that can't be expressed as a number can't be called one.
- Explicitly contract for confidentiality. Ensure that NHS commercial agreements have clear non-disclosure provisions that survive change in third country law, and that any obligation to disclose is a renegotiation, not an automatic release.
- Encourage net-to-net comparison. Where disclosure is inevitable, the defensible position is to compare UK net with US net – taking into account 340B, Medicaid rebates, IRA negotiated prices and PBM concessions. Most likely outcome to fight is selective disclosure of foreign net versus domestic list.

Corridor and list-price management

The dilemma is that raising the UK list to offset VPAG erosion increases the MFN and ERP exposure. Reducing the UK list to reduce that exposure is a permanent damage to the reference position and cannot be undone without political cost.

Play – price corridor. Set an upper bounds per asset (the point at which UK list becomes materially damaging to the U.S. and ERP position) and a lower bounds per asset (the point below which downstream referencing markets erode

faster than UK volume compensates). Manage list price in that corridor and take all incremental value thru confidential structures.

Governance Requirement: Escalate UK list-price decisions to global pricing committee for approval. In our experience, local-optimised UK list decisions destroy more value than any other single pricing action in Europe.

Segmentation of the portfolio by archetype

UK exposure is not evenly spread. It is very archetype-dependent, and portfolio-wide averages hide the assets that are actually relevant.

Archetype	UK net realisation	MFN cascade exposure	Recommended posture
Rare disease / HST	High (60–75% of list)	Low — few referrers use HST prices	Launch and defend. UK is a favourable market.
First-in-class specialty, strong QALY case	Moderate (45–60%)	High	Sequence late; corridor-price tightly.
Me-too specialty in crowded class	Low (30–45%)	High	Conditional launch; exit if PAS depth exceeds threshold.
Mature branded / post-LOE	Very low (25–35%)	Moderate	Active exit candidate. Older-tier VPAG rate is punitive.
Vaccines / tendered products	Low	Low — tender prices poorly referenced	Retain; low cascade risk.
Oncology (CDF/IMF route)	Moderate	High	Managed access; resist price-based concessions.

Insight : The biggest unrecognized value leakage is in the mature branded segment. Many clients still import legacy assets into the UK at a negative contribution margin post VPAG because the decision is taken at country level on a gross-revenue basis and is never re-tested against the older-medicines payment rate. A portfolio scrub of post-LOE branded assets typically recovers 3-8% of European contribution within one budget cycle.

Retreat as a means – and its limits

Commercial withdrawal is no longer hypothetical but observed. It's legitimate but it's a one-way door and the consequences go way beyond the UK."

Preconditions prior to withdrawal are considered:

1. Net realization below variable cost to serve sustained for two VPAG cycles.

2. No structural or indication narrowing alternative feasible.

3. Cascade modeling shows that continued UK presence is globally net destructive, not just locally unprofitable.

4. UK patients have clinically viable alternatives, or there is a defined compassionate supply route.

Price considerations in the decision: parliamentary & media exposure, damage to ABPI relationship, loss of UK clinical trial & MHRA regulatory good will, risk of precedent from other clawback markets, reentering challenge (a withdrawn asset reentering the UK generally finds itself in a materially worse NICE & commercial position than at original launch).

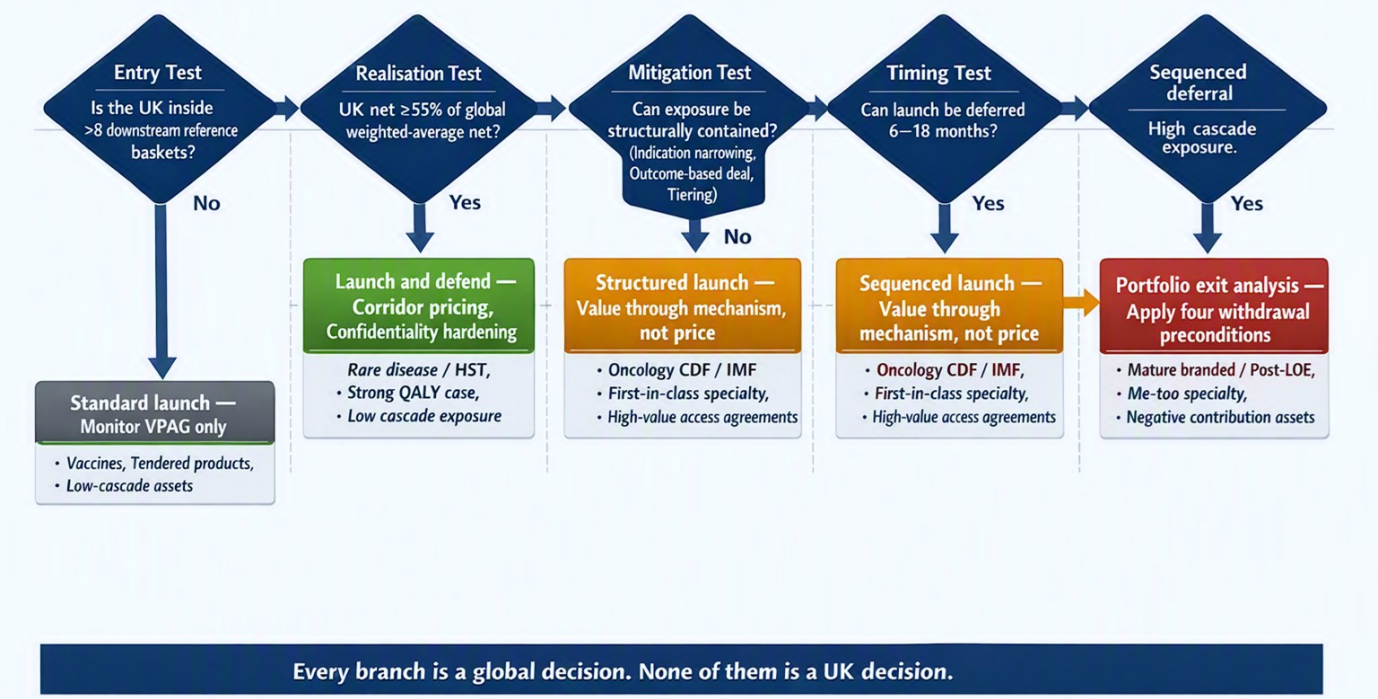
Middle paths, in order of preference: indication narrowing → withdrawal from Statutory Scheme tier only → managed access via CDF/IMF → supply-only without promotion → full withdrawal.

Engagement with policy

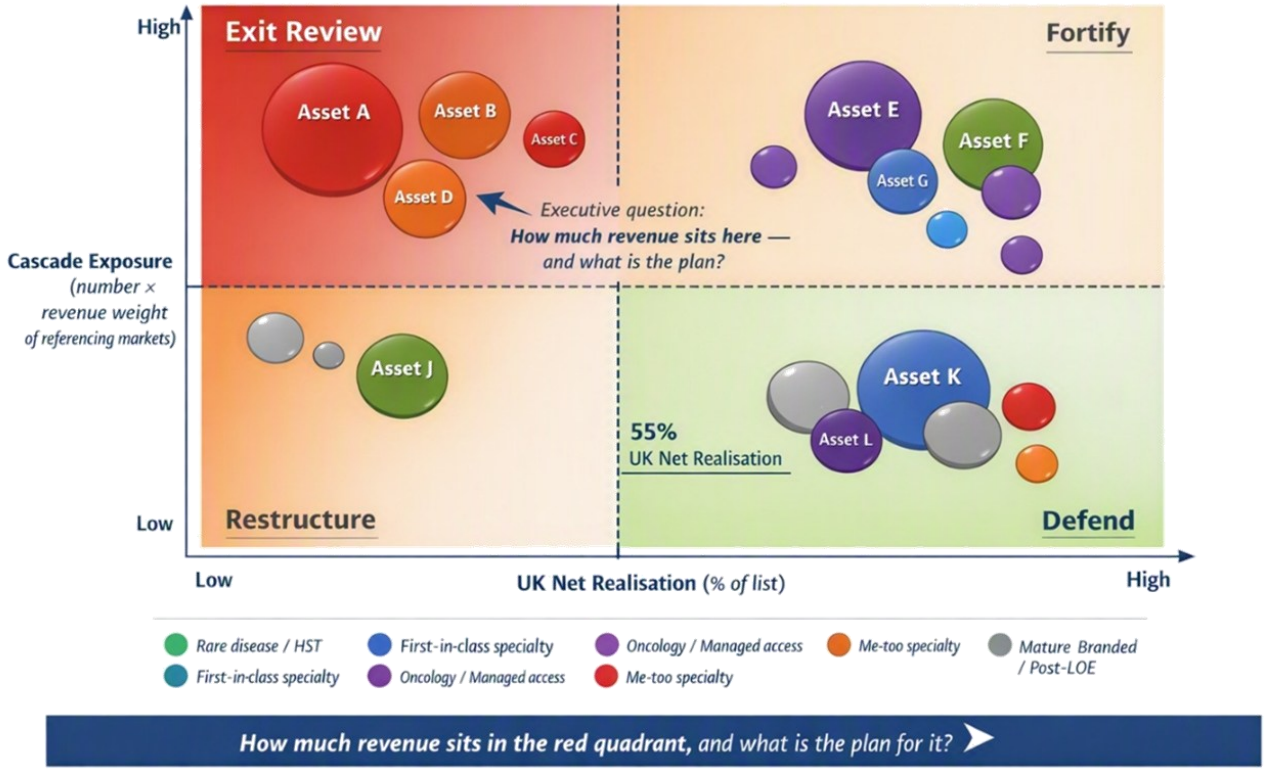
The 2024–2028 VPAG is due for review at a scheduled date and the UK government's parallel ambition to grow life-sciences investment sits in direct tension with a payment rate in the mid-20s. That tension is the advocacy opportunity.

Priorities: (i) uprating or formal indexation of the NICE threshold; (ii) a lower, ring-fenced payment rate for newer active substances; (iii) statutory protection of commercial confidentiality; (iv) explicit government-to-government engagement on the treatment of UK prices in U.S. MFN design. The fourth is the most valuable and the most neglected – this is a trade question being treated as a pricing question.

"UK Market Access Decision Tree"



"Exposure Heat Map



Twelve-Month No-Regret Actions

#	Action	Owner	Horizon
1	Recompute UK net realisation across the portfolio with compounded PAS + VPAG mechanics	Global Pricing	30 days
2	Map every downstream basket referencing UK, weighted by revenue	Market Access	60 days
3	Run Scenario D (cascade) against the top 10 assets by revenue	Strategy / Finance	90 days
4	Audit NHS agreements for confidentiality durability under third-country disclosure	Legal	90 days
5	Scrub post-LOE branded portfolio against older-tier VPAG rate; identify exit candidates	Country + Global	120 days
6	Establish global-committee approval gate for all UK list-price changes	Governance	120 days
7	Define per-asset pricing corridors with explicit upper and lower bounds	Global Pricing	180 days
8	Build the trade-policy advocacy case on UK-in-MFN, jointly with ABPI and U.S. affiliates	Corporate Affairs	12 months

Actions 1 and 2 are prerequisites for everything else and are typically achievable with existing data. Clients who cannot answer *"what is our true compounded UK net, and who references it?"* within 30 days do not yet have a UK strategy — they have a UK budget.

Conclusion

The United Kingdom is the most vivid example of the central thesis of this white paper: in an MFN world, the importance of a market is based on its visibility, not its size.

The UK has built a system with remarkable internal coherence – a cost-effectiveness gate that guaranties uptake once passed, and a revenue cap that guaranties affordability no matter what is passed. It works, on its own terms, for the NHS. It was, however, designed in and for a closed domestic context. And it has one structural vulnerability that its designers never had reason to think about. Its control mechanism is published; its pricing is not. That asymmetry permits any external authority to produce a credible UK net-price proxy without the involvement of UK or manufacturer.

Thus, three propositions follow for manufacturers.

- First, the UK cannot be run as a country P&L. Its pricing decisions are global decisions and must be taken under global governance.
- Second, value must shift from price to structure – what can't be expressed as a unit price can't be exported as one.
- Third, it is no longer a question of choosing between a good UK price and a bad price; it is a question of choosing between a defensible UK presence and an indefensible one – and for a meaningful minority of assets, the honest answer is that the UK is no longer a market worth being visible in.

France

Executive Summary—Five Propositions

1. Germany is the structural antithesis of France. Germany publishes a binding net price and nothing is hidden. France publishes an inflated face price and hides almost everything material. That asymmetry is not a curiosity under MFN - it is the single most important fact about France. It is an asset that most manufacturers are failing to defend at the moment.

2. The French price published is a fiction and that deliberately. The Journal Officiel's prix facial is the result of a political bargain: CEPS offers a defensible headline number in return for confidential remises which yield the real saving. The estimated gross-to-net erosion for specialty assets is now 20-35% and the wedge is widening annually.

3. France's exposure is thus entirely a function of the U.S. imputation methodology. If U.S. rulemaking means observable prices, France is a benign to helpful comparator. If it applies assumed discount haircuts or requires net disclosure, France is a tough comparator — and the industry loses a structural defense it cannot rebuild.

4. France imports German pricing at the same time. The European price guaranty for ASMR I-III products places the French facial price at the floor of Germany, Spain, Italy and the UK. So Germany's published Erstattungsbetrag automatically goes to France. This means that the German negotiation is in part a French negotiation eighteen months beforehand.

5. Time, not price, is the binding constraint in France. Median access timelines of 450-550 days post-EU approval vs. Germany's ~130, mean that France's contribution to global erosion is increasingly thru delayed revenue recognition and forgone exclusivity runway, rather than negotiated price itself.

The French Market: Size, Structure and Locus of Control

France is the second largest pharmaceutical market in Europe and a core EU5 country. It combines universal statutory coverage, a centralized price-setting authority and one of the most aggressive aggregate cost-containment mechanisms in the OECD..

Metric	France	Context / Peer Comparison
Share of global branded pharma revenue	~4.5%	U.S. ~47%; Germany ~9.5%; UK ~2.2%; Japan ~7%
Population	~68 million	Comparable to UK; ~80% of Germany
Reimbursed medicines spend (net)	~€28–32bn p.a.	~14–15% of ONDAM
Formal ERP system	Yes — partial	European price guarantee: DE, ES, IT, UK basket
HTA body	HAS / Commission de la Transparence	SMR and ASMR determinations
Price-setting body	CEPS (Comité économique des produits de santé)	Interministerial; negotiates with manufacturers
Framework governing negotiation	*Accord-cadre* CEPS–LEEM	Multi-year, periodically renegotiated
Published price	Prix facial (*Journal Officiel*)	List price — not net
Confidential rebates	Remises (product-level and aggregate)	Not published; commercially protected
Aggregate clawback	Clause de sauvegarde	Industry-wide; ~€1.6bn+ scale in recent years
Average list price multiple vs. lowest OECD	~2.3x	U.S. ~4.2x; UK ~2.8x; Germany ~2.1x
Estimated net price multiple vs. lowest OECD	~1.4x	U.S. ~1.8x; UK ~1.3x; Germany ~1.1x
Countries referencing France in ERP baskets	20+	Belgium, Portugal, Greece, CEE, Gulf states, Canada (PMPRB)

Insight : France is the only major European market where the published price is materially and systematically growing at a margin above the transaction price. Every other chapter of this paper is concerned with the risk of a low observable price. France fears the opposite risk, that the apparent price is proved false.

The Architecture: How a French Price Is Actually Constructed

French pricing is a four-step process in which clinical assessment, price negotiation, confidential rebating and aggregate clawback each work on a different logic — and only the second stage produces a public number.

Phase One - HAS and the Transparency Committee

The Commission de la Transparence makes two determinations that determine all that follows. They are often confused by non-French teams, and the confusion is costly.

Determination	What it measures	What it controls	Scale
SMR (*Service Médical Rendu*)	Absolute clinical value in context — severity, efficacy, safety, place in strategy, public health impact	Whether the product is reimbursed, and at what rate	Important (65%) / Modéré (30%) / Faible (15%) / Insuffisant (0% — no listing)
ASMR (*Amélioration du SMR*)	Relative improvement over the existing comparator	Price negotiation leverage	I (major) → II (important) → III (moderate) → IV (minor) → V (no improvement)

• SMR insufficient is not a pricing setback, but a commercial extinction event. There is no fallback to low price: the product is simply not listed.
• ASMR IV or V eliminates the price floor. An ASMR means the manufacturer has to demonstrate cost savings versus the comparator – in effect a price at or below current therapy. ASMR IV will only permit a price where economic savings are demonstrated.
• ASMR I-III is the entry to the European price guaranty (Section 4) and to accelerated dépôt de prix self-declaration procedures.
• The choice of the comparator is critical and is not up to the manufacturer. The Commission selects the comparateur clinically relevant, which it will select from the most used in French practice and not the one that is most favorable to the dossier.

Insight: Over the last two decades ASMR ratings have experienced a structural downward drift with ASMR I–II now comprising a low single digit percentage of assessments and ASMR V being the modal outcome. On base rates, global teams that model France on a hypothetical ASMR III are modeling the wrong country. It is not the dossier strategy arguing for a high ASMR that matters. It is the dossier strategy engineering the comparator set so that a high ASMR is arguable at all. That work is done at protocol design, not submission.

Stage Two: CEPS and the Creation of the Prix Facial

CEPS is an interministerial committee and not a payer. It strikes an accord-cadre with the industry association LEEM, and optimizes for a specific, and unusual, objective: delivering budgetary savings while protecting the published price.

The published price (prix fabricant hors taxes, published in the Journal Officiel) is a matter of public record, and every ERP system in the world scrapes it.
• CEPS is explicitly aware of this. If a defensible face price can be maintained, it is a bargaining chip available at a low domestic cost, since the domestic saving is made up elsewhere.

• That chip is consideration for secret rebating. This is the essence of the French system.

Phase Three – Remises – Where the Money Really Flows

Remises are contractual, confidential and invisible to outside observers. They come in all sorts and are often stacked on one product:

Rebate type	Trigger	Typical structure
Remises de volume (price–volume conventions)	Sales exceed agreed thresholds	Tiered clawback, steepening at higher bands
Remises de première année	Early-access reconciliation	Repayment of the gap between free-set early-access price and the eventual negotiated price
Remises conditionnelles / performance	Outcomes shortfall, indication drift	Payment-by-result, coverage-with-evidence
Remises "produits"	Negotiated at listing	Flat percentage off facial, undisclosed
Remises de fin d'année	Aggregate reconciliation	Portfolio-level settlement

Estimated aggregate gross-to-net erosion:

Period	Est. remises as % of reimbursed sales
2015	~6–8%
2019	~10–13%
2022	~15–20%
2025 (est.)	~20–25% blended; 30–35%+ for high-volume specialty

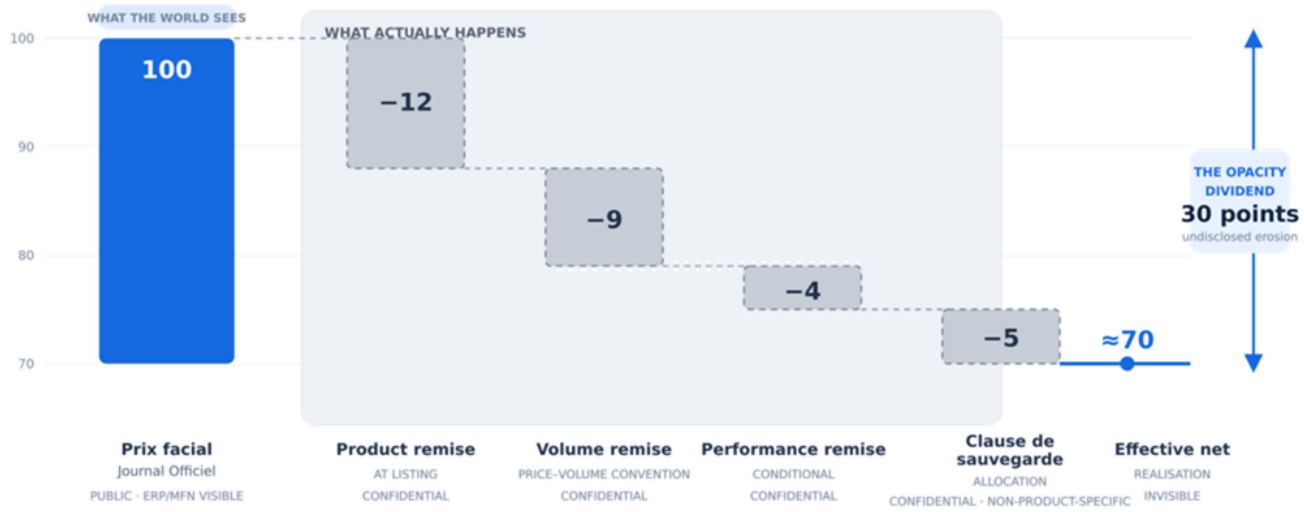
Stage Four – Safeguard Clause: The Layer of Uncontrollability

At the product level, rebating is topped by an industry-wide clawback. If the total reimbursed turnover exceeds the threshold (montant M) set each year in the LFSS, the industry as a whole reimburses the surplus, pro rata by market share.

• Not product-specific and not manageable by the individual producer. A company can maintain its own volumes flat and still get paid, because a competitor grew.
• It has grown steeply from a residual mechanism to a multi-billion euro annual charge.
• It’s invisible in every price database on earth. It never reaches the facial price and is rarely even picked up in internal gross-to-net reporting at product level.

Insight: France is a one layer discount market for most global pricing models. It is a four layer market and the two biggest layers, remises and sauvegarde, are the two that never appear in any observable price. The result is that the internal French net-price reporting is often inflated even within the manufacturer, which in turn corrupts the global corridor the company believes it is defending.

"The French Gross-to-Net Wedge"



"The price published for France is a reasonable proxy for its net price. It is not a net price estimate."

MFN Conundrum: The Opacity Dividend and Its Loss

France most clearly demonstrates the paper's main methodological point: under MFN, visibility matters more than a low price.

U.S. imputation approach	Effect on France's role	U.S. net price impact	Manufacturer exposure
A — Observable prices only (facial price as published)	France appears mid-to-high in the basket; may raise the reference average	Neutral to +2 ppt (protective)	Low. France offsets Germany and Japan.
B — Assumed haircut (flat statistical discount applied to all ERP markets)	France penalised on an assumption, not evidence; haircut may under- or over-shoot	−5 to −12 ppt	Moderate. Accuracy is arbitrary; the manufacturer cannot correct it without disclosure.
C — Net disclosure mandate (attested transaction prices required)	The wedge collapses; France converges toward Germany	−12 to −22 ppt	Severe, and irreversible.
D — Lowest-in-basket referencing with net disclosure	France joins the floor-setting cohort alongside Germany	−18 to −30 ppt	Critical.

The asymmetry that defines French strategy

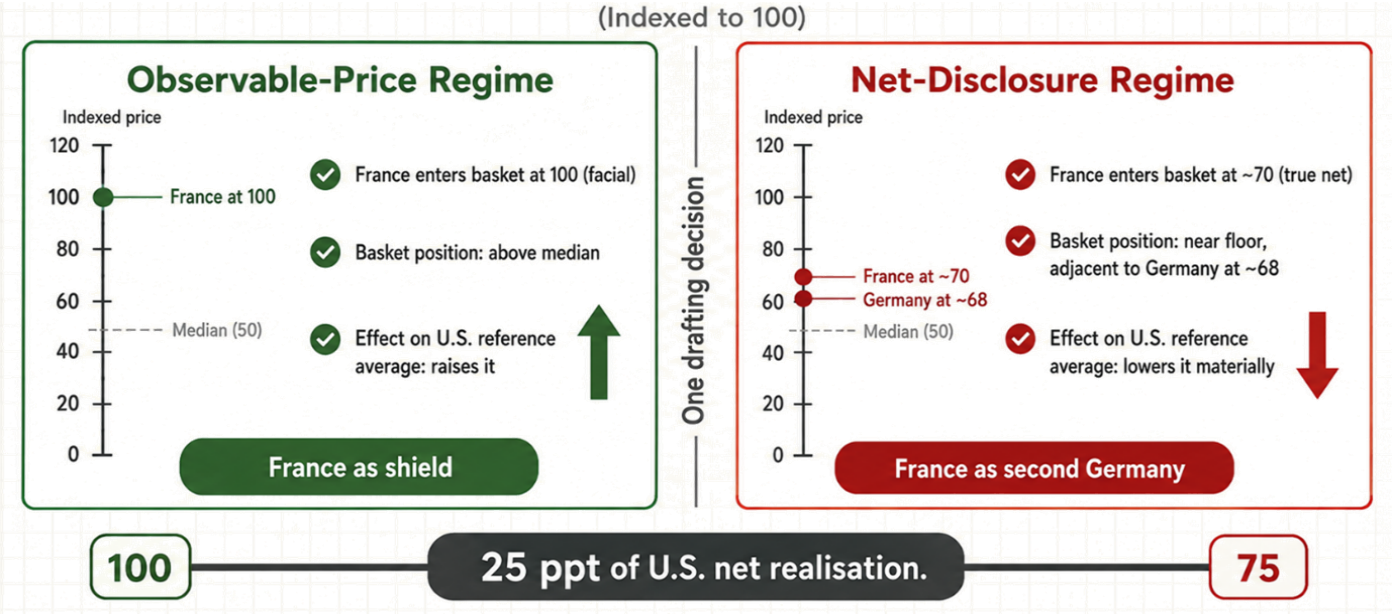
- France is one of the very few markets in the global basket where the protection of the U.S. price can be found under Regime A. That protection disappears under Regime C. France is a second Germany. The difference between the best and worst case for France is therefore roughly **25 percentage points of U.S. net price realisation — a wider range than for any other single market in the basket, and one determined entirely by a technical drafting decision in Washington rather than by anything CEPS, HAS or the manufacturer will do in Paris.
- This produces an uncomfortable but unavoidable conclusion: the highest-value French advocacy is not conducted in France. Time spent defending the facial price with CEPS is worth a fraction of time spent

ensuring that U.S. rulemaking references observable prices without imputed haircuts. The French negotiation protects an asset; the U.S. methodology determines whether that asset has any value at all.

- The disclosure trap. Another danger is peculiar to France. Manufacturers under pressure to demonstrate that their French net price is not as high as the facial price — for example, to argue against a punitive assumed haircut under Regime B — face an obvious temptation to disclose actual remise levels. Doing so would:
    - Breach the confidentiality provisions of CEPS conventions, with direct contractual consequences;
    - Destroy the opacity dividend permanently, since disclosure cannot be reversed;
    - Reset CEPS's own incentives, since the committee protects the facial price only because it is unobservable in substance. Once the wedge is public, CEPS has no reason to grant a high facial price and every reason to negotiate the published number down instead.

Insight: The rational response to an unfavourable assumed haircut is not disclosure. It is advocacy for aggregated, third-party-verified, or attested-range methodologies that permit correction without itemised transparency — and, failing that, acceptance of an imperfect haircut as the lesser outcome. A haircut can be renegotiated at the next rulemaking. Disclosure cannot be undone.

"France's exposure is not determined in France."



The European Price Guarantee — France as an Importer of German Prices

France operates a partial, one-directional external reference mechanism that runs in the opposite direction from Japan's.

Component	Description
Eligibility	Products rated ASMR I, II or III (and, under some accord-cadre provisions, ASMR IV with demonstrated savings)
Reference basket	Germany, Spain, Italy, United Kingdom
Mechanism	The French facial price is guaranteed not to fall below the lowest price obtained in the basket, for a defined period (typically five years) from listing
Direction	Import only. France draws prices in; it does not export a mechanism outward
Practical effect	The German *Erstattungsbetrag* and the UK's published list function as inputs to the French guaranteed floor

Why this matters more than it appears

The guarantee is presented — and generally understood internally — as a protection. It is better read as a transmission channel. Its practical consequences:

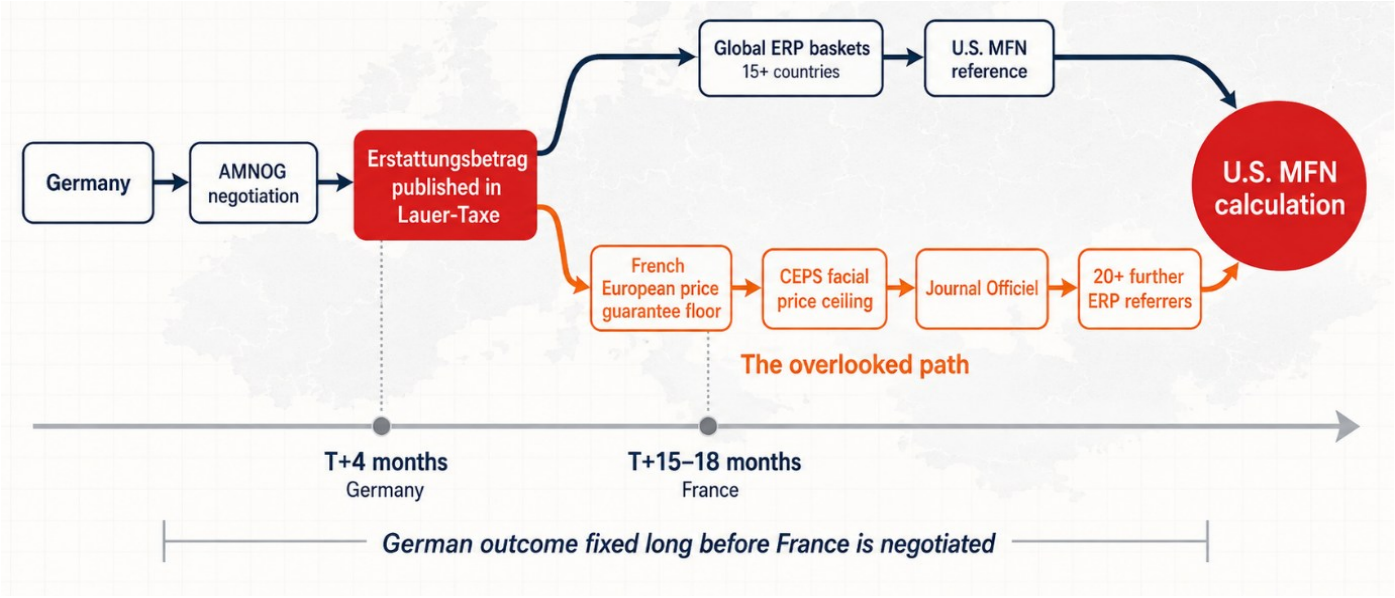
1. Germany's negotiation outcome becomes a French input. A weak Erstattungsbetrag does not merely set a global floor via Lauer-Taxe publication; it lowers the number France is guaranteed against, typically twelve to eighteen months before the French negotiation concludes.

2. The guarantee floors the facial price, not the net price. Remises sit entirely below it. A manufacturer can therefore secure the full benefit of the guarantee and still experience 30% net erosion — and frequently does. The guaranty is for the number that the world watches. That is the number that counts under Regime A, and does not count under Regime C.

3. It converts sequencing errors into compounding errors. Launching in Germany before the German dossier is optimised now damages France mechanically, in addition to damaging the U.S. via MFN and the wider ERP cascade via Lauer-Taxe.

Insight: Chapter 3 argued that the AMNOG negotiation is a global pricing event. France is the proof. The German Erstattungsbetrag is not one comparator among many for France — it is a codified statutory input to the French floor. Companies that run Germany and France as sequential country negotiations rather than as a single linked decision are, in effect, negotiating against themselves.

"The European Transmission Chain"



"Germany does not merely compete with France in the basket. Germany sets France's floor."

The Access-Delay Problem — Where French Value Is Actually Lost

For an increasing share of the portfolio, the dominant source of French value destruction is not the negotiated price. It is elapsed time.

Metric	France	Germany	Comment
Median days, EU approval → reimbursed access	~450–550	~130	Among the slowest in Western Europe
Share of EMA-approved products available	~55–65%	~85–90%	Gap widest in oncology and rare disease
Effective loss of on-patent runway	~15 months	~4 months	Non-recoverable

The pain of the early-access mitigation. France operates one of Europe's more generous pre-reimbursement schemes (accès précoce, with accès direct alongside it), permitting a manufacturer-set indemnity price before the CEPS negotiation concludes. this is really good: revenue starts early, at a self-declared price, and patient access is real.

But the scheme is reconsidered in the past. After the final price is negotiated, the manufacturer reimburses the difference between the price paid for the indemnity and the negotiated price, subject to capped-clawback provisions. The commercial consequences are underestimated in many ways:

- Revenue from early-access is provisional revenue. Material overstatement of French performance in the interim period where it is recognized without a corresponding repayment provision. The correction usually comes in a later reporting period under a different country manager.
- A high indemnity price increases the eventual clawback, and can irritate CEPS in the negotiation it precedes.
- The indemnity price can still be scraped and used as a reference French price in the applicable window despite MFN – a truly perverse result in which a temporary fully-repayable price contaminates the global corridor.

Insight: The correct question for France is no longer "what price can we secure?" but "what is the net present value of fifteen months of delay against the price differential we are negotiating for?" For most specialty assets under realistic discount rates and remaining-exclusivity assumptions, the delay costs more than the price gap. Teams trying to get the last three percentage points of facial value while the dossier is still incomplete are working hard to destroy value

Quantified Exposure — France Under Alternative Regimes

Mature specialty portfolio, three-year horizon:

Scenario	France's role	U.S. net price impact	Global revenue impact (3-yr)
A — Observable prices only	Basket-raising comparator	+1 to +3 ppt (protective)	+1 to +2%
B — Central: assumed haircut (15–20%)	Mid-basket, imputed	−5 to −12 ppt	−3 to −7%
C — Net disclosure mandated	Converges with Germany	−12 to −22 ppt	−7 to −14%
D — Net disclosure + lowest-in-basket	Joint floor-setter	−18 to −30 ppt	−12 to −20%

Separate, not additive, effects to model: compounding
• German transmission via the price guaranty: further 2-5 ppt where the German outcome is weak, with a 12-18 month lag.
• Delay in access: 3-6% of asset lifetime revenue lost regardless of price achieved, and non-recoverable.

• Downstream ERP cascade: France is referenced by 20+ markets; a French facial reduction cascades at ~0.4–0.7x into the cohort.

Insight: France is the only market in this paper that has a positive case. That should be seen as a finite, defensible asset with an identifiable failure mode, not a permanent feature of the landscape. These assets are often lost not thru a policy defeat, but thru an inadvertent disclosure, an inconsistent internal reporting, or even a well-intentioned commitment to transparency made elsewhere..

The France Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing (rel. to EU approval)	Success measure
1	Comparator engineering. Design the pivotal comparator around French clinical practice as the Commission de la Transparence will define it — not the global standard of care	Clinical Development + Global HEOR	T−48 to T−36 months	Proposed comparator accepted without substitution at CT review
2	ASMR base-rate discipline. Forecast France on observed ASMR distributions by therapy area, not on the rating the asset team believes it deserves; carry an explicit ASMR IV/V downside	Global Pricing Intelligence	T−30 months	Base-rate-anchored forecast presented; downside case visible at board level
3	Germany–France as one decision. Approve the target Erstattungsbetrag only after modelling its effect on the French guaranteed floor and the downstream cascade	Global Pricing Committee	T−24 months	Single linked approval recorded; sequential country sign-offs eliminated
4	Price-guarantee eligibility call. Determine early whether ASMR I–III is realistically attainable; if not, build the unprotected-path plan rather than discovering it at negotiation	Global HEOR + France Market Access	T−18 months	Eligibility position and fallback both documented and funded
5	Confidentiality protocol. Codify who may reference French net data, in what aggregation, in which jurisdiction — with mandatory escalation to General Counsel for any exception	Legal + Global Pricing	T−18 months, then standing	Zero unauthorised disclosures; protocol audited annually against investor and regulatory filings
6	Early-access economics. Model indemnity revenue net of expected clawback and book the repayment provision at recognition, not at reconciliation	Global Finance + France Market Access	T−12 months	No material restatement of French performance in later periods
7	U.S. methodology advocacy. Concentrate effort on how prices are read — observable-only, attested ranges, no imputed haircut — rather than on whether France appears in the basket	Corporate Affairs + U.S. Market Access	Continuous	Position filed in every relevant consultation; no net-disclosure or attestation mandate adopted
8	Delay compression. Prepare the HAS dossier in parallel with the EMA submission and pre-agree the accès précoce route before approval, rather than after	France Market Access + Regulatory	T−6 months	Time to reimbursed access reduced ≥10% against company baseline
9	Product-level gross-to-net. Model remises, clause de sauvegarde exposure and early-access clawback as separate, visible layers — never as a blended country discount	Global Pricing Intelligence	T−12 months	Complete French waterfall visible to the Global Pricing Committee at asset level
10	Walk-away threshold. Fix the French net realisation below which listing is declined, together with the global-erosion trigger that overrides local revenue arguments	Global Pricing Committee	T−12 months	Threshold agreed before negotiation begins, not during it

Insight: Items 3, 5 and 7 are load-bearing; the rest are optimization. If a company makes one disclosure or one bad drafting decision, it can execute the other seven perfectly and still lose the French position entirely. Sequence the effort accordingly – most organizations invest in inverse proportion to impact here because the high impact items have no local owner and no local metric.

Governance – Transparency as a liability?

France needs a governance inversion that local teams will instinctively resist as it makes them stop maximizing the one number they are measured on.

Element	Legacy model	Required model
Price approval authority	France country leadership within regional bands	Global Pricing Committee; France MA and Global HEOR advise
Objective function	Maximise prix facial; minimise time to listing	Minimise global net erosion, treating opacity as the defended asset
Exposure metric	First-cycle facial price vs. target	Multi-cycle impact across all four U.S. regimes, including guarantee transmission and cascade
Germany relationship	Independent, sequential negotiations	One linked decision; German target tested against French floor consequence
Confidentiality	Local contractual obligation	Board-level global asset with a named custodian and audit trail
Early-access revenue	Recognised as earned	Recognised net of provision; treated as provisional throughout
Walk-away authority	Undefined in practice	Pre-authorised, quantified, globally held
Performance measurement	Facial price achieved; French P&L	Contribution to global realisation; speed to reimbursed access

The repeat failure is not a bad negotiation. A good local decision with an invisible global cost. A favorable price on the face of it purchased with deeper remises; a transparency commitment made in an unrelated forum; an aggregated disclosure which turns out to be de-anonymisable at product level. In each instance the position of the French is worsened and the responsible individual never appears anywhere in the causal chain. Governance therefore has to be preventive, not diagnostic — by the time you can measure the effect, the asset is lost.

Watch List — Signals That Change the French Calculus

Signal	Interpretation	Response
U.S. rulemaking proposes net-price disclosure or manufacturer attestation	Regime C or D becomes the base case	Highest-priority advocacy; immediate portfolio-wide re-sequencing review
U.S. adopts an imputed haircut above ~20%	France's protective value is neutralised without any disclosure occurring	Push for attested-range correction; do not answer with disclosure
Accord-cadre renegotiation increases remise visibility	The opacity dividend is eroding structurally, from the French side	Escalate to General Counsel; model the post-opacity French position immediately
Germany lands an unusually low Erstattungsbetrag in-class	French guaranteed floor depressed, effective 12–18 months forward	Re-run French and cascade corridors; reassess French launch economics
Clause de sauvegarde threshold lowered or restructured	Contingent clawback becomes larger and less forecastable	Increase provisioning; escalate to industry-level advocacy on predictability
Indemnity prices confirmed as referenceable abroad	A temporary, fully repayable price begins contaminating the global corridor	Reconsider indemnity level; seek explicit carve-out in U.S. methodology
HAS guidance shifts toward lower ASMR ratings	Guarantee eligibility narrows across the portfolio	Reweight to the unprotected path; intensify comparator engineering upstream
CEPS starts negotiating the facial price rather than the remise	The wedge is closing; France's basket role is changing	Treat as leading indicator of regime change; reassess France's strategic function entirely

Conclusion – The French Chapter

France operates on inverted logic. Germany publishes a low net price and exports that price. Japan issues a dropping price and re-imports the effects with its own reference mechanism. The United Kingdom hides a high list behind a low net. France, which charges a high price for its face and exports its secrecy – and it is not the price but the secrecy which is the asset.

This chapter should leave you with three propositions.

1. The first principle is the gross to net wedge strategy. The 20–35% differential between the Journal Officiel price and true net realization is what allows France to enter an MFN basket as a basket-raising comparator and not a floor-setter. Depending on one drafting decision in Washington, that wedge is worth anywhere from +3 to −30 percentage points of U.S. net attainment. One disclosure, in any forum, by any employe, can destroy it forever. Disclosure is final, an unflattering haircut is negotiable at the next rulemaking. Every pressure decision should be driven by that imbalance.
2. Second, France is importing German prices under the radar. The Erstattungsbetrag is a legal input into the French floor, set twelve to eighteen months before CEPS meets by the European price guaranty. A company that runs Germany and France as a sequential National Negotiation (i.e. a company that negotiates against itself) will not see the loss in either country's P&L.
3. Thirdly, time is the loss which dominates in France. The lost exclusivity runway at 450–550 days to reimbursed access is greater than the value of the price differential under negotiation for most specialty assets' forgone revenue. Teams, meticulously, deliberately, and with full conviction, destroying value by extracting the last three points of facial price while the dossier remains incomplete.

The governance conclusion is a direct consequence. That number is not set in Paris, nor by the manufacturer. So you cannot manage France as a country P&L optimizing a published number. Whether or not the industry has a hand in shaping it is decided in Washington, in language that will be drafted.

The governing principle in France: Your French price is not determined by the number CEPS approves, but by the number the United States chooses to read. Protect the first, win the argument for the second, never trade one for the other.

Germany 

If the United Kingdom is the market for which the net price can be inferred, Germany is the market for which the net price is printed.

Germany is Europe's biggest pharmaceutical market, its fastest launch market and – uniquely among major economies – the only one to negotiate a confidential-style rebate and then publish the resultant price in a commercial database that any authority, anywhere, can subscribe to. The Erstattungsbetrag is not a list price, not an estimate, and not a leak. It is a negotiated, legally binding net price approved by the government and published in the Lauer-Taxe and reproduced throughout the world in days.

The five conclusions of this chapter are:

1. Germany is the only important comparator in any U.S. MFN design — not because its prices are the lowest, but because they are the lowest verifiable prices. The MFN policy needs an administrable reference. Germany supplies one free of charge to the referencing authority.

2. AMNOG offers speed in exchange for permanence. The first six months (previously twelve, now shortened) of free pricing buys rapid patient uptake. The subsequent Erstattungsbetrag becomes an almost irreversible anchor, subject only to renegotiation in the event of new evidence, indication expansion or the arrival of a comparator.

3. The whole story is the observability gap. UK net prices are subject to VPAG confidentiality and require modeling. German net prices is a field in the database. In an MFN world that favors defensibility and auditability, the auditable number wins, even if it's the lowest.

4. Germany's exposure compounds via the ERP cascade. More than fifteen jurisdictions directly refer to Germany; a further tranche refer to those referrers. Thus, a single Erstattungsbetrag concession passes thru two rings of price formation before it ever gets imported into a U.S. MFN basket.

5. The strategic center of gravity has moved upstream. Value is won or lost in the selection of comparators and the design of the dossier – twenty-four to thirty-six months prior to the negotiation – not across the negotiating table with the GKV-SV.

Central estimate: Under a central-case MFN construction referencing published European net prices, Germany alone accounts for 10–20 percentage points of U.S. net price erosion for mature specialty portfolios, and 40–55% of total European MFN attribution in our reference model. _____

The Reform Overlay 2024-2026: What's different?

Since 2022, the AMNOG framework in Section 2 has been considerably tightened. Companies are systematically underestimating their German exposure if they are using pre-2022 assumptions.

Reform element	Instrument	Effect on net price	Effective from
Free-pricing window shortened	GKV-FinStG	*Erstattungsbetrag* applies from month 7 rather than month 13	2023
Guardrails (*Leitplanken*)	GKV-FinStG	Statutory price ceilings tied to added-benefit rating; caps negotiation upside	2023
Combination therapy surcharge	GKV-FinStG	20% mandatory discount on combinations without demonstrated combined benefit	2023
Manufacturer rebate increase	GKV-FinStG	Statutory rebate raised from 7% to 12%	2023–2024
Price moratorium extension	Rolling legislation	List prices frozen at 2009 levels for pre-existing products	Extended to 2026
Orphan revenue threshold reduced	GKV-FinStG	Automatic benefit status lost above €30m annual revenue (from €50m)	2023
Confidential price option	Medical Research Act (MFG)	Optional confidentiality of the *Erstattungsbetrag*, at a cost	2024–2025

The *Leitplanken* — Statutory Ceilings on Negotiation

The guardrails are the most under-appreciated reform. They convert what was a negotiation into a formula-bounded exercise:

G-BA added-benefit rating	Guardrail effect	Practical net price outcome
Major / considerable (*erheblich / beträchtlich*)	Premium permitted above comparator	80–90% of list retained
Minor (*gering*)	Price must sit below the comparator cost	60–75% of list
Non-quantifiable	Comparator-linked ceiling	60–75% of list
No added benefit	Price must be below comparator; no premium available	<60% of list; frequently below viability threshold

Commercial consequence. The downside tail has been legislated. A "no added benefit" result had previously left room for compromise thru negotiation. It now generates a mechanical low, published, globally visible price. A German "no added benefit" result on an MFN-exposed asset no longer a local disappointment. It's a global pricing event.

The Confidentiality Option – A Costly, Partial Escape

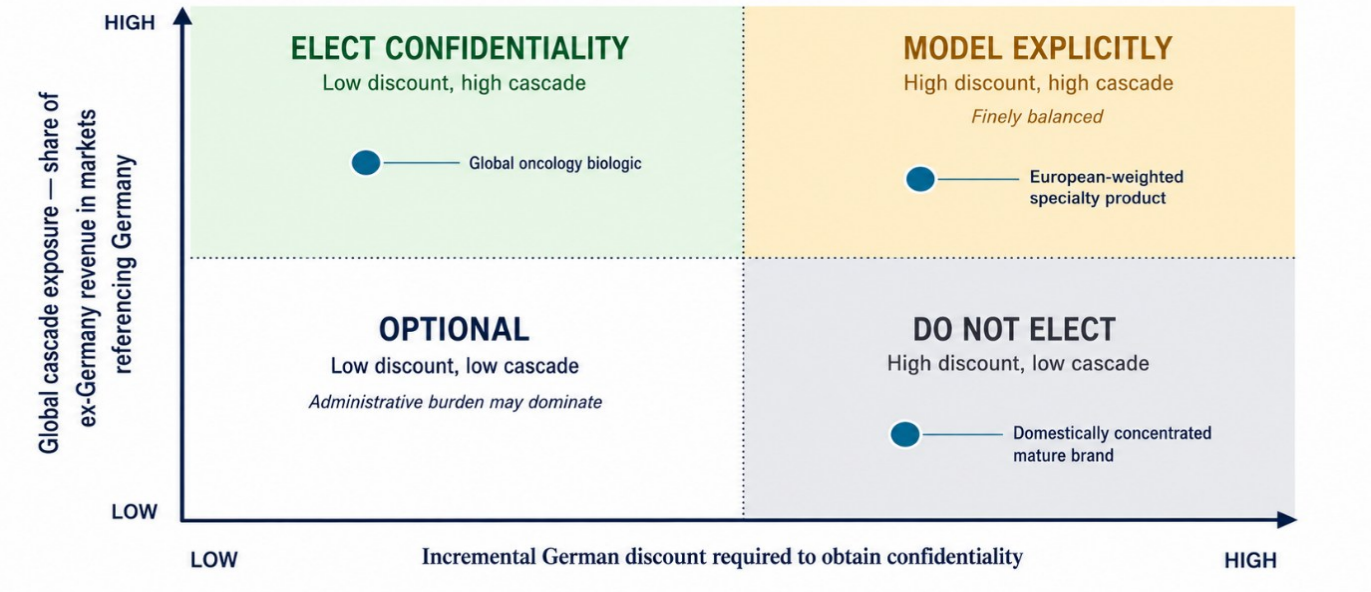
The Medical Research Act opened up for the first time the option to keep the Erstattungsbetrag confidential. It's not a solution and can't be considered as a solution.

Dimension	Assessment
Availability	Optional, manufacturer-elected, per product
Price of the option	Additional mandatory discount (materially reducing the German net price itself)

Operational burden	Pharmacies and wholesalers transact at list; complex reconciliation and clawback machinery
Leakage risk	High. Reimbursement flows, tender data and supply-chain reconciliation create multiple inference points
Durability	Politically contested; subject to review and possible repeal
MFN protection	Partial at best. Obscures the headline figure; does not eliminate inference

Insight : In Germany, confidentiality means you'll get less observability for a lower net price. This trade-off only makes sense if the global cascade value of opacity is greater than the incremental German discount – which is normally the case for high revenue, heavily referenced assets in broad indications and rarely the case for low volume or narrowly referenced products. This calculation has to be run asset by asset with the global P&L as unit of analysis, not the German one.

"The Confidentiality Trade-Off"



"Confidentiality is bought with net price. Only buy it where the cascade is worth more than the discount."

Quantifying the Cascade: Germany's Second-Order Effect

Direct MFN referencing understates German exposure. The full effect requires modelling the ERP network.

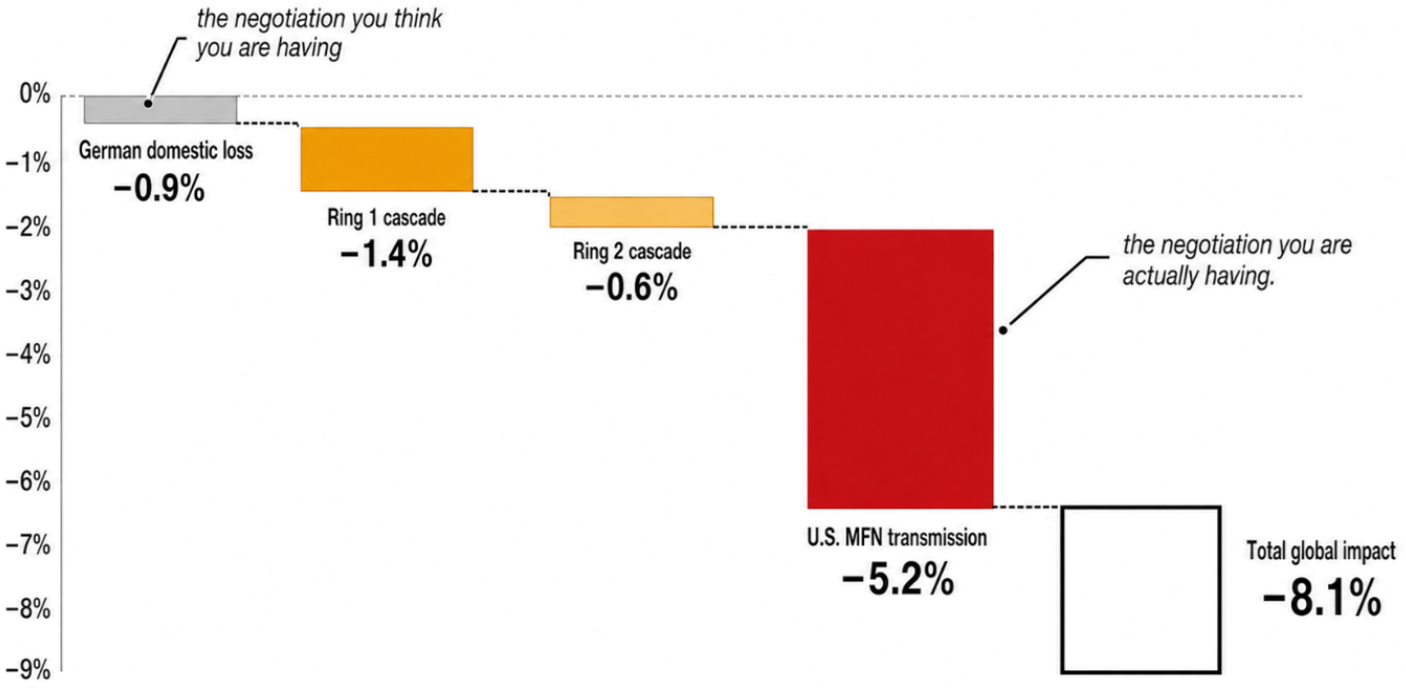
Cascade ring	Composition	Share of global branded revenue	Transmission lag
Ring 0	Germany	~9.5%	Immediate
Ring 1	Direct referrers: Austria, Switzerland, Netherlands, Belgium, Nordics, Czechia, Poland, Hungary, Slovakia, Slovenia, Croatia, Greece, Portugal, Gulf states, selected Asian markets	~11–14%	6–18 months
Ring 2	Markets referencing Ring 1	~6–9%	18–36 months
Combined addressable	Rings 0–2	~27–32%	—

Modelled three-year revenue impact of a 10% reduction in the German *Erstattungsbetrag* (Mature specialty asset with typical geographic mix)

Effect	Mechanism	Estimated global revenue impact
Direct German revenue loss	Volume × price reduction	−0.8 to −1.0%
Ring 1 ERP transmission	Basket recalculation at next review	−1.1 to −1.6%
Ring 2 secondary transmission	Delayed, partially attenuated	−0.4 to −0.8%
U.S. MFN transmission	German net price enters reference basket	−3.5 to −7.0%
Total		**−5.8 to −10.4%**

Insight : The German deal is trading at approximately 6–10x its domestic value on a revenue multiple. A German concession of €20m a year is a €120-200m a year global decision de facto. Organizations that delegate German pricing authority to a country general manager – however competent – have mis-allocated the decision right.

"The German Multiplier"



Germany Versus the UK: The Comparative Frame

The two chapters resolve into a single strategic contrast that should govern European sequencing decisions.

Dimension	United Kingdom	Germany
Control instrument	VPAG revenue cap + NICE cost-effectiveness	AMNOG benefit assessment + binding negotiation
Net price formation	Aggregate rebate across portfolio	Product-specific negotiated price
Observability	Confidential — must be inferred	Published in Lauer-Taxe
Speed to patient	Slow (NICE appraisal cycle)	Fast (immediate reimbursement at launch)
Net price level	Low (~1.3x lowest-OECD multiple)	Lowest in Western Europe (~1.1x)
Direct ERP referrers	Few	15+
MFN exposure mechanism	Inference and disclosure risk	Direct citation
Primary defensive lever	Launch deferral; confidentiality preservation	Comparator strategy; benefit dossier; confidentiality election
Reversibility	Moderate — scheme renegotiated periodically	Low — anchor persists across lifecycle

Insight : UK is a disclosure risk; Germany is a structural anchor. UK exposure can be mitigated thru information governance. You can only provide German exposure with proof – created years in advance. These require completely different organizational capabilities, budgets and lead times and should not be combined in one work stream for "European pricing risk".10. The Germany Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing (relative to EU approval)	Success measure
1	Comparator war-gaming. Model every plausible G-BA comparator (*zweckmäßige Vergleichstherapie*) and its price consequence under the guardrails	Global HEOR + Germany Market Access	T−36 to T−30 months	Comparator scenarios priced; trial design adjusted where feasible
2	Evidence alignment. Ensure pivotal trial comparator, endpoints and subgroups satisfy G-BA evidentiary standards, not only regulatory ones	Clinical Development + HEOR	T−36 to T−24 months	G-BA-compliant endpoint set locked before protocol finalisation
3	Early G-BA consultation (*Beratungsgespräch*)	Germany Market Access	T−24 months	Documented comparator guidance obtained
4	Global corridor definition. Set the minimum acceptable *Erstattungsbetrag* derived from global MFN and ERP tolerances — not from German affordability	Global Pricing Committee	T−18 months	Board-approved floor price, in writing
5	Confidentiality election analysis. Run the trade-off with global P&L as the unit of account	Global Pricing + Finance	T−12 months	Documented elect / do-not-elect decision with quantified rationale
6	Dossier construction and stress-testing	Germany Market Access + HEOR	T−12 to T−3 months	Independent mock-IQWiG review completed

7	Launch-sequencing decision. Confirm Germany's position in the global launch order against the corridor	Global Commercial Leadership	T−6 months	Sequence ratified; deferral case prepared if corridor breached
8	Negotiation mandate. Issue a global mandate with an explicit walk-away price	Global Pricing Committee	T+1 month	Walk-away authority pre-delegated, not improvised
9	Combination-therapy defence. Pre-empt the 20% combination discount with dedicated combined-benefit evidence	Clinical + HEOR	Continuous	Surcharge avoided or mitigated
10	Cascade monitoring. Track Ring 1 and Ring 2 basket recalculations triggered by the published price	Global Pricing Intelligence	T+6 months onward	Downstream repricing anticipated, not discovered
11	Renegotiation readiness. Prepare for indication expansion and new-comparator triggers, each of which reopens the price	Germany Market Access	Lifecycle	No unplanned *Erstattungsbetrag* reduction
12	Policy advocacy. Engage through vfa and EFPIA on guardrail proportionality and confidentiality durability	Corporate Affairs	Continuous	Position represented in consultation responses

Insight : Look at the position of the owners. Eight of the twelve actions are completed outside Germany, and four are with global committees. This is the practical implication of the consideration of Germany as a global pricing anchor: The country organization implements, but does not decide..

Governance — Reallocating the Decision Right

Most organisations retain a governance model designed for a world in which German pricing affected German revenue. That model is now a source of value leakage.

Governance element	Legacy model	Recommended model
Price approval authority	Country GM, within regional band	Global Pricing Committee, with country input
Objective function	German revenue and access speed	Global net realisation across the cascade
Escalation trigger	Deviation from regional band	Any breach of the global corridor floor
Walk-away authority	Rarely defined	Pre-authorised, quantified, documented
Evidence budget owner	Country / regional	Global HEOR, ring-fenced for AMNOG
Performance measurement	German market share, launch speed	Corridor compliance; cascade-adjusted realisation

The single highest-yield governance change is the last one. As long as German leadership is measured on access speed and local uptake, the organisation will systematically over-concede on price — rationally, from the country's perspective, and destructively from the group's.

Watch List — Indicators That Change the German Calculus

Signal	What it would indicate	Strategic response
Repeal or restriction of the confidentiality option	The escape route closes	Re-baseline all European exposure models upward
Extension of guardrails to additional benefit categories	Further compression of negotiation range	Accelerate evidence investment; revisit launch sequencing
Expansion of the price moratorium beyond 2026	Continued erosion of legacy portfolio economics	Reassess mature-brand viability in Germany
Formal U.S. MFN rule specifying published European net prices	Germany's role becomes explicit and codified	Trigger portfolio-wide corridor review
EU HTA Regulation joint clinical assessments maturing	Partial displacement of national dossiers; new leverage points	Rebuild dossier strategy around joint assessment outputs
Increase in confidential-price elections across the industry	Reduced observability of the German benchmark	MFN attention likely migrates to the next most observable market

Insight : The last row is worth paying special attention to. If a widespread confidentiality election occurs, Germany’s status as the global observable floor erodes and MFN attention will shift to the next most transparent market. In this situation, the exposure doesn’t disappear, it moves. Manufacturers should model where it moves to before assuming German opacity fixes the problem.

Conclusion — The German Chapter

Germany has become the world’s most powerful pharmaceutical price-setter without ever wanting to be one. It does not have an external reference pricing system, does not claim extraterritorial reach and only negotiates on behalf of German patients and German payers. Its influence is a result of one design decision: publication.

That choice turns a domestic debate into a global one. This means that the Erstattungsbetrag negotiated in Berlin is a term of the manufacturer’s contract in the United States, imported without negotiation, without consent, and without compensation, in economic substance. The 2023-2025 reforms have amplified this effect by replacing negotiable outcomes with formula-bound ones and legislating the downside tail. The confidentiality option gives some relief but at the cost of the very net realization it seeks to protect.

The strategic conclusion is therefore immediate. German market access cannot be optimized locally. It needs to be globally governed, funded years in advance, and evaluated against a cascade-adjusted target, not a domestic one. Companies that make the shift will view comparator strategy as a global capital allocation decision. Those who don't will eventually find out, years later, that their global price floor was set in a negotiation they never escalated.

The rule which rules in Germany: the price you publish is not the price you get, it’s the price you take.

Italy

Executive Summary — Judgments of Key Importance

1. The manufacturer himself does not know the net price at the point of sale only in the case of Italy in this paper. The last realization is decided at Company level, retrospectively, thru an expenditure clawback nationally, distributed over the industry months or years after the revenue is booked. This is opacity by construction, not opacity by negotiation.

2. Italy's published ex-factory price is a fiction of extraordinary depth. The Gazzetta Ufficiale price is on top of a statutory hospital discount layer, on top of a managed entry agreement layer, on top of a mandatory confidential discount layer, and on top of an ex-post payback. The gross-to-net wedge is 25-45% cumulatively and is wider than France and materially wider than Germany.

3. This makes Italy the industry's most powerful methodological argument in U.S. rulemaking — and its most fragile. No net price at product level is available for Italy. Any U.S. attestation requirement for Italy would therefore, by statutory design, require manufacturers to certify an unknowable figure at the time of certification.

4. Italy transmits to France. Italy is in the French European price guaranty basket with Germany, Spain and the UK. The French guarantyd floor is lowered with a 12–18 month lag by an Italian ex-factory price cut -- the same transmission channel identified for Germany in Chapter 5, but on a second track.

5. The key Italian risk is not the AIFA negotiation. It is the regions and the pay-back. Payback liability is unhedgeable, mostly unforecastable and assigned by market share, not product. Regional formulary delay – another 100-200 days after national listing. These alone are more influential on Italian economics than any negotiated price is.

The Italian Market: Composition, Size, Price Regime

Italy is the fourth largest pharmaceutical market in Europe and one of the most institutionally complex, with a combination of centralized national price negotiation and substantially devolved regional purchasing.

Metric	Italy	Context / peer comparison
Share of global branded pharma revenue	~3.5–4%	U.S. ~47%; Germany ~9.5%; UK ~2.2%
Population	~59 million	Comparable to UK, France
Public pharmaceutical spend	~€25–27bn p.a.	~17–18% of total SSN expenditure
National authority	AIFA (Agenzia Italiana del Farmaco)	Post-2023 reform: single CSE commission replaces CTS/CPR
Formal ERP system	None statutory	Informal comparison used as negotiating input
Published price	Ex-factory, in *Gazzetta Ufficiale*	Fully observable; substantially unrepresentative
Confidential discount	Mandatory for hospital products	Not disclosed; contractually protected
Ex-post clawback	*Ripiano* / payback	Company-level, retrospective, share-allocated
Direct-purchase expenditure ceiling	~8.5–8.65% of national health funding	Persistently breached
Annual industry payback exposure	~€1.0–1.4bn	50% of direct-purchase overspend
Average list price multiple vs. lowest OECD	~1.9x	U.S. ~4.2x; UK ~2.8x; Germany ~2.1x
Estimated net price multiple vs. lowest OECD	~1.05–1.15x	Among the lowest in Western Europe
Countries referencing Italy in ERP baskets	20+	Including France's statutory guarantee basket

Insight : Italy shares the structural position of France – high observed price, low unobserved net – but with two aggravating featuresFrance does not have: an ex-post clawback which no product-level model can predict with confidence, and twenty-one regional buyers who negotiate below the national price. Negotiating the wedge of France. Banked is Italy's wedge.

Four Levels of Price Formation

The Italian net realization is the residue after four sequential deductions, of which only the first can be meaningfully controlled by the manufacturer.

2.1 Level One The AIFA Deal

- Once the marketing authorization is obtained, the price and reimbursement is negotiated with AIFA's CSE . Since the 2023 governance reform, the former scientific (CTS) and pricing (CPR) functions have been merged into a single commission.
  Inputs: therapeutic added value, budget impact, comparator cost, prices obtained in other European markets and forecast volumes.
  Output: published ex-factory price, a class of reimbursement (A — reimbursed; H — hospital; C — non reimbursed), and a negotiated contract usually 24 months.

Commercial reality: The advertized price is deliberately high, as it is understood by both parties to be nominal. AIFA extracts value below the headline line, where nothing is visible.

Layer Two - Confidential Discounts

AIFA requires a confidential discount from the published ex-factory price for hospital-administered and most specialty products. It is contractually protected and not reported to other jurisdictions, to the regions in full detail or publicly.
• Magnitude: 20-40% for hospital specialty; deeper in competitive classes.

Function: enables Italy to publish a headline price that is European-credible, which matters to Italy because 20+ markets reference the price Italy publishes, whilst paying substantially less.

Layer Three – Managed-Entry Agreements and the AIFA Registries Italy has the most advanced managed-entry infrastructure in Europe, carried out thru the AIFA monitoring registries (registri di monitoraggio).

MEA type	Mechanism	Practical effect
Payment by result	Full reimbursement of non-responders	Highest manufacturer risk; common in oncology
Risk sharing	Partial reimbursement for non-responders	Shared downside
Cost sharing	Discount on initial treatment cycles for all patients	Predictable, volume-linked
Success fee	Payment only on demonstrated response	Deferred and contingent revenue
Capping / budget ceilings	Free product above agreed volume or expenditure	Converts upside volume into zero-revenue supply

Registry-based reconciliation is administratively heavy and frequently slow, meaning MEA repayments land in reporting periods well after the associated revenue.

Countertop — The refund

In Italy, the public expenditure for pharmaceuticals is limited to a fixed percentage of the national health fund, thru two channels: retail/territorial and direct purchase (hospital and specialty). Where the channel for direct purchase is above the ceiling, the pharmaceutical industry repays 50% of the overspend, and apportions it between the companies in proportion to their share of the relevant market.

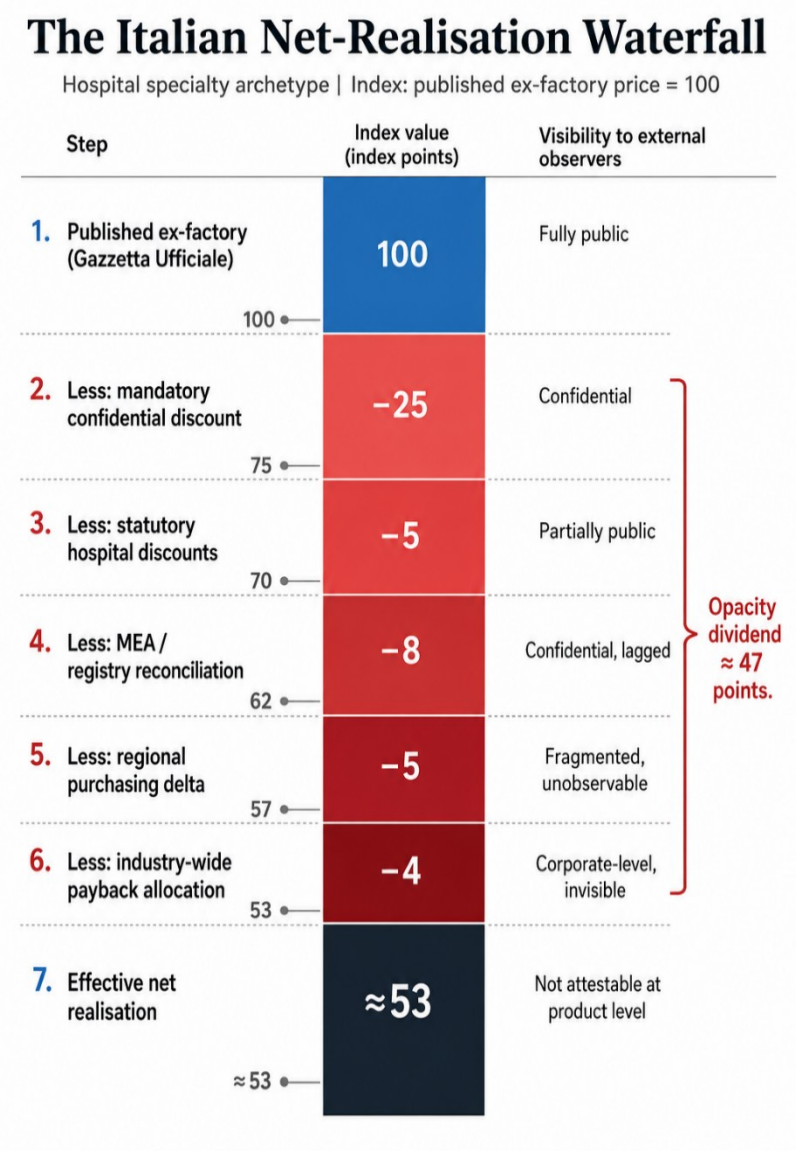
This is the key feature of Italian economics for four reasons:
• It is a collective, not a causative. Liability is allocated by market share, not by whether a particular product contributed to the breach. A company may keep its price flat, its volume flat, and have a higher debt because its denominator changed.
• Retrospective. Determinations are often made post hoc, subject to recalculation and litigation, and often land two or more reporting periods after the revenue was recognized.
• Stability of structure. The ceiling was calibrated to a therapeutic landscape that is no longer there. Oncology, rare disease and cell and gene entrants regularly push aggregate direct-purchase spend above the threshold, making the breach an annual certainty rather than a periodic event.

• It is invisible at product level. Payback is not included in any product specific pricing, contract or invoice. It is a corporate level charge that never impacts the commercial architecture it silently taxes.

Insight: The payback should be modeled as a corporate tax on Italian market share, rather than as a pricing variable. It scales with the company's success relative to the rest of the industry, it does not scale with a product's price. Teams that treat it as a discount will mis-specify it every time. The perverse outcome is that beating the market in Italy automatically raises your share of a fixed national debt.

"The Italian Net-Realisation Waterfall"

"Italy's list price is observable. Italy's net price is not merely confidential — it does not exist as a single number at the point of sale."



The Regional Layer — Twenty-One Second Negotiations

AIFA sets the national price. It does not deliver market access. The 21 regions and autonomous provinces control hospital budgets, formularies (*prontuari terapeutici regionali*) and tendering, and each operates its own gatekeeping.

Regional friction	Mechanism	Commercial consequence
Formulary lag	Regional therapeutic committees must add the product after national listing	100–200 additional days before first meaningful sales
Tender-level erosion	Regions and area-wide purchasing bodies run their own tenders on nationally listed products	A "net-of-net" price below the national confidential level

Budget siloing	Regional deficits create direct incentives to restrict or delay high-cost adoption	Uneven national uptake; slower peak-share attainment
Prescribing controls	Regional treatment plans, specialist-only restrictions, centre designation	Effective volume caps not reflected in the national agreement
Access inequity	Adoption varies materially between northern and southern regions	National forecasts systematically overstate addressable volume

Insight : The biggest mistake in Italian modeling is to use national listing as the market entry event. It is the prerequisite for twenty-one more entry events. Any launch model that does not include a regional friction coefficient (100-200 day delay and a differentiated regional uptake curve) will overstate the first two years of Italian revenue by a wide margin, and will overstate the peak year contribution against which global pricing trade-offs are judged.

Italy: Under the U.S. MFN System

Italy's exposure profile is the most regime-dependent of any of the markets studied in this paper. It's the industry's best protection and its worst liability, subject to a methodological decision made in Washington.

U.S. regime	What is referenced	Italian exposure	Assessment
A — Observable prices only	Published ex-factory	Protective. Italian list sits mid-basket at ~1.9x lowest-OECD	Best case. Italy anchors the basket materially above its own net reality
B — Observable, with standardised haircut	Published price less a uniform gross-to-net adjustment	Neutral to mildly adverse. A generic haircut under-corrects for Italy's ~47-point wedge	Manageable; argue for country-differentiated haircuts
C — Net-price disclosure / attestation mandate	Certified net realisation	Severe. Attestation is not merely commercially undesirable — it is technically impossible at the point of certification	Primary risk. The compliance impossibility is the strongest available argument
D — Lowest-in-basket, net basis	Lowest observed net across basket	Catastrophic. Italy's ~53 index lands at or near the floor	Italy becomes the single price-setting market for the U.S. portfolio

Quantified exposure (mature specialty portfolio, steady state):

Scenario	Italian contribution to U.S. net erosion	Global revenue impact (3-yr)
A — Observable only	−1 to −3 ppt	−1 to −2%
B — Standardised haircut	−4 to −8 ppt	−2 to −5%
C — Net attestation	−15 to −25 ppt	−9 to −16%
D — Lowest-in-basket, net	−22 to −32 ppt	−14 to −22%

The argument from impossibility. This is worth stating explicitly because it is the most defensible methodological position the industry has in any market covered by this paper:

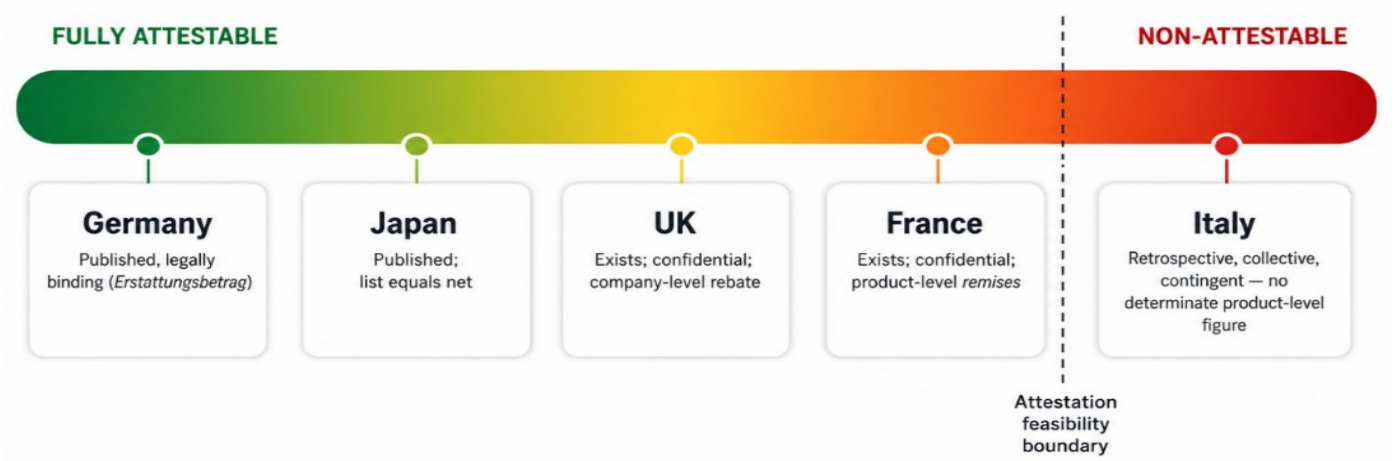
1. The payback amount is determined at the end of the reporting period.
2. It is allocated by company, not product, market share.
3. It is routinely recalculated and litigated, sometimes for years.
4. Regional tender deltas and registry reconciliations are resolved separately, on lagged schedules.

Therefore, at the time of a U.S. attestation there is no Italian product-level net price. To ask a manufacturer to certify one would be certifying an estimate of a collective, contingent, retrospective liability—under penalty. This is

not a commercial preference argument. It's an argument about the definitional impossibility of compliance and it should be filed as such in every relevant consultation.

Insight: The Erstattungsbetrag exists and is published in Germany, and a net price exists but is confidential in the UK, but in Italy the net price does not exist as a determinate figure at product level. The entire Italian advocacy position is the difference between confidential and non-existent. It must be argued with technical precision, not as a plea for confidentiality or it will be dismissed as special pleading.

"Confidential vs. Non-Existent: The Attestability Spectrum"



"Everything to the right of this line cannot be certified — only estimated. Rulemaking that ignores this distinction converts an accounting impossibility into a legal exposure."

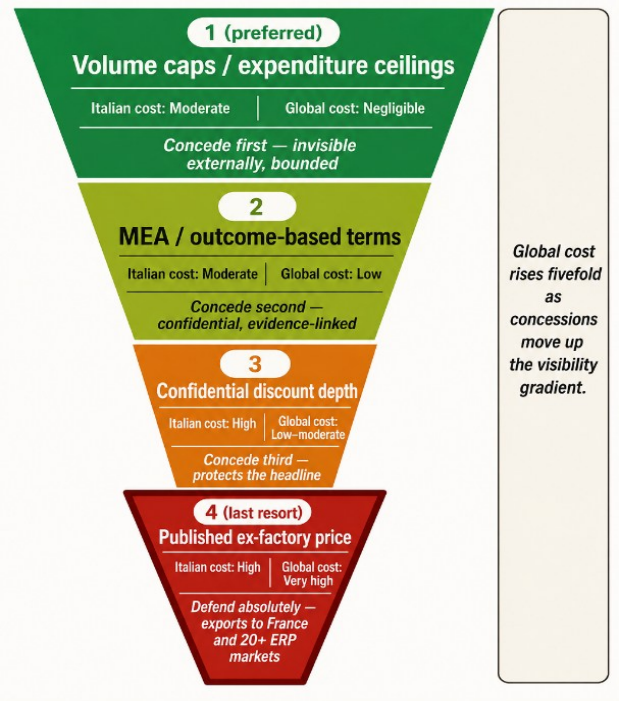
Second Transmission Channel: Italy to France

It is shown that the European price guaranty based on favorable ASMR ratings creates a de facto floor for the French prix facial, based on the German Erstattungsbetrag. Italy is in the same basket of guaranties.

- Mechanism: The French guaranty is linked to the published prices of major European comparators – Germany, Italy, Spain and the UK. That calculation takes Italy's Gazzetta Ufficiale price at face value.
- Effect: The Italian published ex-factory price falls and this drags down the French guarantyd floor with a lag of 12–18 months, whatever the actual fate of the Italian net realization.
- The asymmetry: For Italy, as value is extracted below the published line, AIFA has little need to cut the headline. This is good but not guarantyd – contract renewal renegotiations, generic or biosimilar entry in class and periodic AIFA repricing exercises all exert downward pressure on the published figure.
- Consequence: Each published-price concession in Italy must be valued in excess of the Italian revenue impact. It has an embedded French cost and downstream cost throughout the wider ERP cascade via France.

Insight: Opacity in Italy doesn't last – ultimately. It lives only as long as confidential discount terms, registry reconciliation data and regional tender results are not published. Every disclosure, be it a voluntary transparency initiative, litigation discovery, regional freedom-of-information releases or U.S. reporting mandate, is irreversible. There is no process for making an Italian net price confidential again, once published. Italian confidentiality, therefore, must be considered a strategic asset, not subject to renewal and disclosure decisions at local level must be referred to the global pricing committee, regardless of how routine or locally justified they may seem

"Where to Concede: The Italian Negotiation Hierarchy"



The cheapest concession in Italy is always the one nobody else can see.

Portfolio Segmentation — Differentiated Italian Exposure

Italian exposure is not uniform. It is driven by channel, class intensity and registry burden rather than by therapeutic novelty alone.

Archetype	Gross-to-net wedge	Payback exposure	MFN cascade risk	Recommended posture
Hospital specialty / oncology	40–50%	Highest — direct-purchase channel	Severe under Regimes C/D	Maximum headline defence; heavy MEA use; full registry modelling
Rare disease / orphan	35–45%	High	Severe — small volumes, extreme prices attract scrutiny	Value-based MEA; argue non-comparability in U.S. filings
Cell and gene / ATMP	30–50%, highly variable	High	Severe — outcome-linked payment defies attestation	Instalment and outcome structures; treat as attestation test case
Retail specialty (Class A)	20–30%	Moderate — separate territorial ceiling	Moderate	Standard corridor management
Mature brands, pre-LOE	25–35%	Moderate, share-driven	Low	Manage for cash; accept erosion; avoid headline cuts
Post-LOE / biosimilar-exposed	50%+ via tender	Low	Low	Regional tender strategy; consider portfolio exit

Insight : The archetype most often mispriced is cell and gene therapy. Italian instalment and outcome-linked payment structures create a net realization that is not only unknown, but genuinely indeterminate over the lifetime of the outcome window – often five years or more. Companies launching ATMPs in Italy should be aware that they are creating the most clear factual record of attestation impossibility and should document it contemporaneously for use in U.S. rulemaking.

The Italy Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing (relative to EU approval)	Success measure
1	Headline-price floor mandate. Establish a globally binding minimum published ex-factory price below which no Italian agreement may be signed	Global Pricing Committee	T−18 months	Floor documented and communicated to Italy MA before negotiation opens
2	Concession hierarchy briefing. Train the Italian negotiating team on the Tier 1–4 hierarchy; require centre approval for any Tier 4 movement	Global Pricing + Italy MA	T−15 months	Zero unapproved headline concessions
3	Registry and MEA modelling. Model registry reconciliation as a baseline deduction with explicit lag assumptions, not as a contingency	HEOR + Finance	T−12 months	MEA deduction and timing variance appear in the base-case forecast
4	Payback provisioning. Accrue payback at corporate level on projected portfolio market share, not current-year product sales	Finance	Standing	Provision variance within ±15% of final determination
5	Regional access mapping. Map formulary and tender timelines for the top 8–10 regions by addressable volume, in parallel with AIFA negotiation	Italy Market Access	T−9 months	Regional friction coefficient embedded; first-year forecast revised
6	French transmission modelling. Quantify the effect of the Italian headline on the French guaranteed floor and downstream ERP cascade	Global Pricing Intelligence	T−12 months	Italian headline valued at full global cost, not Italian revenue cost
7	Attestation-impossibility dossier. Compile the technical evidence — statutory basis, allocation methodology, litigation history, settlement lags	Corporate Affairs + Legal	T−6 months, then continuous	Dossier filed in all relevant U.S. consultations
8	Confidentiality governance. Classify Italian discount, registry and tender data as non-renewable strategic assets; escalate all disclosure decisions	Legal + Global Pricing	Standing	No unescalated disclosure events
9	Gross-to-net waterfall build. Construct a product-level Italian waterfall capturing all four layers, with explicit uncertainty bands	Global Pricing Intelligence	T−12 months	Full waterfall visible to the global committee, uncertainty quantified
10	Walk-away threshold. Define the Italian net realisation, inclusive of payback and regional delta, below which listing is declined	Global Pricing Committee	T−12 months	Threshold set before negotiation pressure arrives

Insight : Actions 1 and 2 are disproportionately valuable for their costs. Almost all the disastrous Italian results can be attributed to a local team sacrificing headline price for speed or volume – a rational decision against a local scorecard and a value-destroying one against a global scorecard. The intervention is not an exercise in analytical sophistication. It's a written constraint, it's early, and it's got escalation authority attached to it."

Governance — Managing a Market Whose Net Price Cannot Be Known

Element	Legacy model	Required model
Price approval authority	Italy country leadership within regional bands	Global Pricing Committee, with Italy MA and HEOR as advisers
Objective function	Maximise Italian revenue; secure listing quickly	Defend the published headline; concede only below the visibility line
Payback treatment	Below-the-line finance adjustment, reviewed annually	Standing corporate provision, modelled on portfolio share, owned by Finance
Access assumption	National listing equals market access	National listing plus 100–200 days of regional friction, region-weighted
Exposure metric	Italian net realisation, product level	Contribution to global realisation, including French guarantee transmission
Confidentiality	Handled locally, transactionally	Non-renewable strategic asset; all disclosure escalated centrally
Walk-away authority	Undefined in practice	Pre-authorised and quantified globally, inclusive of payback
Performance measurement	Italian P&L	Global corridor integrity; headline defence; access speed

Italy's governance failure to guard against is more subtle than France's. In France it's a local team paying over the odds for the facial price they negotiate. In Italy the danger is that a local team trades the facial price – because in Italy it is the least painful concession available – and treats it as such. The published ex-factory price is the only Italian variable with almost no domestic consequence and very large international consequence. This asymmetry is not apparent from Milan, only from the Center and that is precisely why the constraint must come from the Center.

Watch List — Indicators That Change the Italian Calculus

Signal	Interpretation	Response
U.S. rulemaking proposes net attestation	Regime C becomes base case; Italy shifts from shield to primary liability	File attestation-impossibility dossier immediately; re-run all corridor models
Direct-purchase ceiling raised or payback restructured	Italian net realisation improves; forecastability increases	Revise provisions; reassess portfolio-level Italian investment
Payback allocation moves from share-based to product-based	Liability becomes attributable — and therefore attestable	Material adverse change. The core advocacy argument weakens substantially
AIFA moves toward publishing net or discounted prices	Opacity dividend collapses irreversibly	Highest-priority advocacy; reassess Italian launch sequencing globally
Regional purchasing centralised into national tendering	Regional delta disappears; net price becomes more determinate	Reassess both exposure and the attestability argument
French guarantee basket reweighted toward Italy	Italian headline transmission to France intensifies	Raise the Italian headline floor; escalate defence priority
Major payback litigation resolved against industry	Liability crystallises; provisioning assumptions must rise	Increase provisions; reassess Italian portfolio economics
Sustained AIFA repricing exercise across a therapeutic class	Published prices fall; French floor and ERP cascade follow with lag	Model downstream cost before conceding; consider class-level defence

Conclusion – The Italian Chapter

Italy is the limit case of the five previous markets this paper has argued for. Germany publishes a net price and exports that. Japan prints a price that's both list and net, and re-imports whatever the rest of the world does to it. There is a net price to the UK, but it's hidden. France has a net price which is at product level but contractually protected. Italy has no net price at the product level at all, only a published fiction, four layers of deduction landing

on four independent timetables, and a collective national debt apportioned by market share long after the revenue has been booked and reported.

That is not a technicality. It is the whole Italian strategic position, and it cuts both ways with remarkable force.

This chapter will leave three points intact.

1. Italy's protection is definitional not contractual, and that must be the argument. Finally, the position of the industry in every other European market is reduced to a request: respect our confidentiality. Only Italy has a greater claim: the figure you are asking us to certify does not, at the moment of certification, exist and cannot be made to exist, because it is a function of an ex-post, collective, litigated liability determined by the behavior of the whole industry. It's not an argument about the desirability of disclosure but the viability of compliance. It's materially more sustainable in a rulemaking process. But it will only work if it is drafted with technical precision – statutory citations, allocation methodology, settlement lags, litigation history – and never as a general appeal for commercial confidentiality. Well argued, it can set the methodological boundary for the entire basket. And badly argued, it's dismissed as special pleading, and takes the credible markets with it.
2. Second, the published price is the only Italian variable that counts internationally. And it is the only Italian variable with almost no domestic consequence. AIFA is calculated below the visibility line, thru confidential discounts, registries and volume ceilings. It has little institutional need for a lower headline. For its part, the manufacturer has every interest in defending it, since that headline enters the French guarantyd floor and twenty or so reference baskets, at a global cost estimated at three to five times the equivalent concession made confidentially. But it is exactly what a locally incentivized team will offer first because it is the cheapest in Italy. This is the most severe clash between local rationality and global value identified anywhere in this paper, and it cannot be remedied by analysis alone. It needs a written floor, issued before negotiations open, with escalation authority attached.
3. Third, complexity is an asset, and it's losing value. Italy's shield is institutional friction: 21 regional buyers, retrospective clawbacks, registry reconciliation lags, contractual confidentiality. Each of these is a possible target for reform, and every reform that increases determinacy – product-based payback allocation, national tender centralization, net-price publication – turns Italy from the industry's strongest methodological shield into the market that sets the global floor. There is no going back. An disclosed Italian net price cannot be re-concealed and a payback made attributable cannot be made collective again. The Italian opacity should therefore be treated as a wasting asset: monitored at all times, defended at all costs, and never traded away for local advantage on the assumption that it will be there next cycle.

What Italy broadens is the larger lesson that in an MFN world, it is not the size of the market that counts, but the observability of the market. Italy accounts for less than four per cent of world branded revenue. It could set the reference floor for a portfolio that earns nearly half its revenue in the United States under a net-disclosure regime. This result is irrelevant to the Italian market, the patients' need or the value of the medicines. It is simply a matter of what numbers happen to be visible and the methodological choices of a regulator on another continent who will never negotiate with AIFA, never see a regional tender and never receive a payback determination."

The rule for Italy: your Italian net price is not a figure you bargain about, it is a residue you find out about, months later, from the behavior of a whole industry. Save the only number anyone else can see. Put the impossibility of the rest on record.

Spain 

Executive Summary

For pricing purposes Spain is not one market but two. The retail channel is one of the more transparent pricing environments in Western Europe, with ex-factory prices published monthly and a gross-to-net wedge of only some ten points. The hospital channel is also among the most opaque, with product-level realization determined by 17 regional tender systems that are not fully observed by any central authority. MFN exposure is therefore not a country characteristic in Spain but a channel characteristic.

Spain breaks the defensive pattern set by France and Italy. A high published price protects a low net price in those markets. The industry's interest is in keeping observability of the headline. For Spain's retail channel, the published price is close to the net price and is structurally low. Spain is the only big European market where a U.S. regime of "observable prices only" -- the regime the industry is lobbying for everyplace else -- increases exposure instead of reducing it.

The price of Spain is small domestically and disproportionate in transmission. Spain is a commercial minor, representing about 2% of global branded revenue. But it is in reference baskets all across Portugal, Greece, Central and Eastern Europe, the Gulf and – crucially – Latin America, including Brazil's CMED basket. A Spanish concession is not left in Spain, it moves along the Iberoamerican corridor in one or two cycles of revision.

Time is the binding constraint in Spain, not price. When the regional formulary listing is included, the median time from the EU marketing authorization to effective patient access is over 550-650 days and a significant share of EMA-approved medicines never achieve national financing. For specialty assets, the value lost by delay will routinely be greater than the value lost by negotiated price.

Strategic stance: segment that by channel, defend absolutely the Nomenclátor price, concede only within the hospital tender stratum, where dispersion among seventeen buyers makes any one price unattainable, and where Spain's structure begins to resemble Italy's.

Market structure and basic measures

In Spain medicines are financed thru the Sistema Nacional de Salud (SNS) . Pricing is centrally determined and access regionally. The Comisión Interministerial de Precios de los Medicamentos (CIPM) determines the maximum ex-factory price (precio industrial máximo) of any medicine to be publicly financed. Once it has been set, that price is published in the Nomenclátor Oficial, updated monthly and can be freely downloaded.

Metric	Spain	Context / peer comparison
Share of global branded pharma revenue	~2.0%	U.S. ~47%; Germany ~9.5%; UK ~2.2%; Italy ~3.8%
Population	~48.8 million	Similar to Italy; ~58% of Germany
Governance model	Central pricing, regional financing and access	17 autonomous communities + 2 autonomous cities
Central price body	CIPM (Ministry of Health, with Economy and Finance)	Sets maximum ex-factory price
HTA / positioning	IPT process under the reformed evaluation network	Increasingly economic, not solely clinical
Retail price observability	Full — published in Nomenclátor	Contrast: UK net confidential; Italy net indeterminate
Hospital price observability	Minimal — regional tender, confidential	Comparable to Italy at regional level
Mandatory statutory deduction	7.5% on SNS sales (reduced rate for orphan medicines; higher rate for older products without generic competition)	Applied automatically, not negotiated

Insight : The most dangerous feature of Spain is the combination of a low published retail price and a wide downstream referencing. Germany has a low net price, but it receives 9.5% of the world's revenue, so the trade is at least commercially rational." Spain prints a similarly observable price for one-fifth of the revenue. Spain is the worst value in the European portfolio on a pure exposure per euro earned.

The Two Spains: Channel as the Factor Determining Exposure

All of the strategic conclusions of this chapter follow from one structural fact: the Spanish retail and hospital channels have opposite observability profiles and hence opposite MFN risk profiles.

The Retail Channel - No Pay for Transparency

In the case of medicines dispensed thru community pharmacy price formation is centralized and highly visible:

• CIPM sets a maximum ex-factory price, considering budget impact, therapeutic positioning, comparator prices and, informally but consistently, prices already established in other EU markets.
• The price is published monthly in the Nomenclátor, at product and presentation level, in machine-readable format. There is no veil of secrecy to penetrate.

• Sales of SNS are subject to a statutory deduction of 7.5% (lower for orphan medicines, higher for older products without generic competition). This is a statutory levy, not a negotiated rebate. It is uniform and predictable, and so can easily be modeled by any external observer.
• Internal reference pricing (sistema de precios de referencia) results in price collapse into homogenous groupings after generic or biosimilar entry, leading to some of the steepest post-LOE price cliffs in Europe.

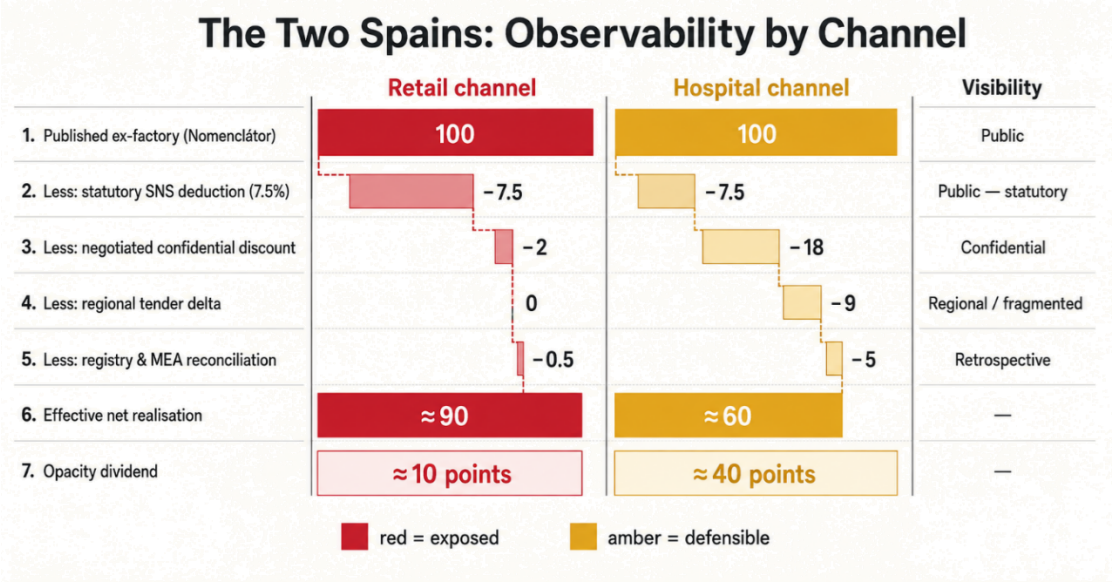
Bottom line: A defensible Spanish net price for a retail product can be built by an external regulator from public data with an error band of a few percentage points. No other major European market has this.

The Hospital Channel—Opacity in the Absence of Control

For hospital-administered and specialty medicines – the part of the innovative portfolio that dominates – the central price becomes a ceiling, not a price.

• The maximum is the CIPM price; actual acquisition price depends on regional and hospital level tenders (concursos, acuerdos marco and increasingly centralized regional purchasing platforms).
• Seventeen autonomous communities carry out independent procurement, formulary and budget processes. There are quite a few other sub-regional or hospital-consortium tenders below that.
• Managed entry and outcomes-based agreements are run thru the national outcomes registries, with retrospective adjustments that settle months after dispensing.
• Confidential discounts, volume-price agreements and expenditure caps are additional to those negotiated bilaterally and protected contractually.

What you get is dispersion not a price. The same molecule may be worth materially different net values in Andalucía, Cataluña and the Basque Country in the same quarter. This structural feature starts to reproduce the Italian attestation problem, although for different reasons and with weaker legal foundations.



Two channels, one country, opposite MFN risk. Any strategy that treats Spain as a single exposure is wrong in both directions.

Regional Decentralisation: Access Friction as the Dominant Value Loss

Spain's central price decision is a *permission to begin*, not an entry to market. Following CIPM pricing and national financing approval, the manufacturer faces a second, longer, and far less structured process.

Layer	Body	Typical incremental delay	Determines
National financing decision	Ministry of Health / CIPM	300–400 days from MA	Whether the product is reimbursed at all, and at what maximum price
Therapeutic positioning	IPT process	Concurrent / overlapping	Positioning, restrictions, comparator framing

Regional formulary inclusion	Autonomous community commissions	90–180 days	Whether the product may be prescribed regionally
Hospital formulary (*Comisión de Farmacia y Terapéutica*)	Individual hospital	60–150 days	Whether the product may be used in that institution
Tender / framework agreement	Regional platform or hospital	30–120 days	Actual acquisition price

Synergistic effects

• Non-financing is not a tail risk, it is a real outcome. In Spain, a large share of EMA-approved medicines are not financed by the SNS and, when they are, restricted positioning often significantly reduces the eligible population below the label.
• Access inequality is a predictive problem and a policy issue. For the same medicine, regional uptake differences can exceed twofold, making national volumes forecasts systematically unreliable for the first eight quarters.
• Exclusivity runway is quietly consumed. With an asset protected effectively for 10 years, 600 days of delay represents 16% of the commercial life, a greater loss of value than any conceivable price concession.

Insight: Model Spain with an explicit regional friction coefficient of 150-250 days on top of national listing and an eligible-population haircut of 20-40% versus label. Forecasts based on national approval dates and label populations overstate Spanish NPV by a factor that in a typical case exceeds the whole negotiated discount.

Spain Under US. MFN: Where the European Defence Fails

The industry's argument in Washington that it can only refer to observable, verifiable prices because net prices cannot be attested has been built on France, Italy and the UK, its methodological backbone. Spain is the market in which that argument boomerangs on its authors.

MFN regime	What is referenced	Spanish outcome	Assessment
A — Observable prices only	Published Nomenclátor ex-factory	Spain enters the basket near its true retail net; hospital wedge protected	Adverse for retail; benign for hospital
B — Observable, minus standard gross-to-net haircut	Published price less a uniform assumed discount	Spain over-discounted relative to reality; retail exposure worsens	Most adverse regime for Spain
C — Net-price disclosure mandate	Attested product-level net	Retail: trivially compliant. Hospital: dispersed across 17 purchasers, weak attestation	Severe for retail; contestable for hospital
D — Lowest price in basket	Minimum observed	Spain competes with Italy and Greece for basket floor	Catastrophic

Quantified exposure (Mature specialty portfolio, Spain considered in isolation):

Scenario	Spanish reference used	U.S. net price impact	Notes
A — Benign	Nomenclátor list only	−4 to −8 ppt	Higher than the equivalent French figure, because the Spanish wedge is thin

B — Central	List less standardised haircut	−8 to −14 ppt	Haircut methodology penalises transparent markets
C — Severe	Attested net, retail methodology extended to hospital	−14 to −22 ppt	Assumes hospital attestation is conceded
D — Extreme	Lowest-in-basket, Spain at or near floor	−20 to −30 ppt	Spain becomes the binding constraint for the entire portfolio

The internalization asymmetry to internalize: Spain's revenues are around 2% of global branded revenue and can set the reference floor in Regimes C and D for a portfolio that earns close to half its revenue in the United States. The exposure-to-earnings ratio is around ten to one – the least advantageous of all in the European set. France and Italy, at least, buy their transmitted risk with opacity. Spain transmits similar risk and offers almost no defensive cover at all in the retail channel.

The methodological pitfall Regime B is of particular interest because it is the regime most likely to emerge from a well intentioned rulemaking process. A uniform gross-to-net haircut applied across the basket – say 25%, calibrated to the European average – is administratively elegant and directionally right for France, Italy and the UK. When applied to Spanish retail prices, where the real wedge is eight to twelve points, it creates a non-existent discount. Thus, the industry's own advocacy for haircut methodology contains a hole in the shape of Spain. Any submission proposing a flat haircut without channel level differentiation is arguing against itself.

Insight: French advocacy can't be run on the Spanish template. The French argument is look not behind the published price. The Spanish argument is that the published price is near net in one channel and meaningless in the other and no single national figure can be constructed. These are different filings and you can make it worse by filing the wrong one in the wrong market than filing nothing.

The Iberoamerican Corridor: Spain's secret weapon

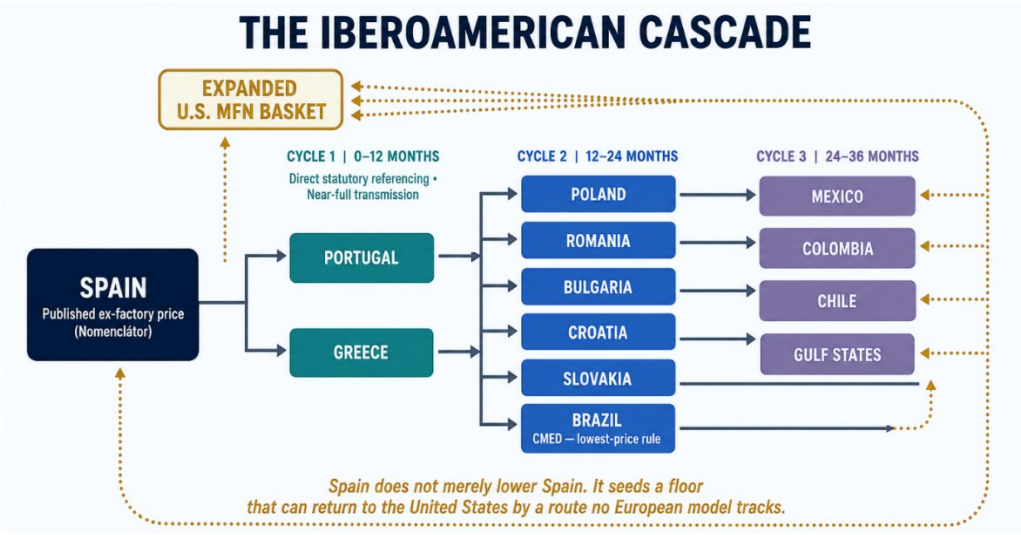
Spain's direct MFN exposure understates its true systemic weight, as it sits at the head of a referencing chain that no other European market occupies.

Downstream Market/bloc	Mechanism	Lag	Transmission strength
Portugal	Statutory ERP basket including Spain	6–12 months	Very high — Spain is a core comparator
Greece	Lowest-of-three EU basket	6–12 months	Very high
CEE (Poland, Romania, Bulgaria, Croatia, Slovakia)	ERP baskets with high Spanish inclusion	12–18 months	High
Brazil (CMED)	Statutory basket including Spain, at the *lowest* observed price	12–24 months	Very high — lowest-price rule
Mexico, Colombia, Chile, Argentina	Formal or informal Spanish anchoring, reinforced by linguistic and regulatory alignment	12–36 months	Moderate–high
Gulf states (Saudi Arabia, UAE)	Multi-country baskets including Spain	12–18 months	Moderate

The single Spanish price concession cascades thru Portugal and Greece in one revision cycle, thru CEE and Brazil in two, and thru the broader Latin American set in three. The compounding effect Brazil's CMED mechanism looks at the lowest price in its basket as a reference, so a fall in the Spanish price does not just drag down the Brazilian average, it can directly pull down the Brazilian ceiling. That ceiling then feeds into the regional Latin American referencing. And, under a U.S. regime that goes beyond OECD comparators, may come back in to the U.S. calculation from a completely different direction.

Estimated cascade multiplier: factoring in the transmission of ERP downstream, a 10% reduction in the Spanish published price leads to an estimated 1.8× to 2.4× multiple of the direct Spanish revenue impact at steady state over three revision cycles. The multiplier is even higher for assets with meaningful Latin American exposure.

Insight: The Spanish negotiation is actually a Portuguese, Greek, Brazilian and Latin-American negotiation at the same time. A Spanish price authority, delegated to a team measured on Spanish revenue, is, by structure, authority to trade a small P&L gain for a multiple of the loss elsewhere.



2% of global revenue. 20+ downstream baskets. A 2.0× cascade multiplier. Spain is the cheapest place in Europe to lose the most money.

LOE Cliff & Internal Reference Pricing

Spain's sistema de precios de referencia warrants separate discussion because it controls the last phase of the asset's life cycle, and therefore determines the published price at which the world will judge the product for the rest of its life.

Mechanism The molecule is grouped into a homogeneous group on entry of a generic or biosimilar. The reference price is set at the cheapest presentations in a group. All products in the group must be offered at or below that price to be eligible for public financing. There is no bargaining and no transition period of practical significance.

Implications:

• Instant and near complete price collapse. Reductions of 40% to 70% at grouping formation are routine and there is further erosion as the grouping is revised.
• The price collapse is still published . Whereas a confidential rebate expires with a contract, the post-LOE Nomenclátor price is a permanent public artifact that is always available to every downstream referencing authority.
• Contamination of cross-presentation Grouping logic can capture presentations and formulations which are still protected and drag their published prices down with the genericised form.
• Spillover to portfolio. A collapsed Spanish price for one molecule sets the expectations of payers for the next asset in the same therapeutic area, in Spain and across the cascade.

Insight : The loss of exclusivity in Spain is not only a revenue event, but a global reference event. Lifecycle teams should model the downstream ERP effects of forming Spanish groupings with the same rigor as the launch price, and should consider presentation-level withdrawal or delisting where the published-price damage exceeds the residual Spanish margin.

The Spain Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing (relative to EU approval)	Success measure
1	Channel classification. Formally designate every asset as retail-exposed, hospital-protected, or mixed, and assign a distinct MFN exposure profile to each	Global Pricing Intelligence	T−30 months	Every Spanish asset carries a channel-specific exposure rating
2	Nomenclátor floor. Set a written minimum published ex-factory price, approved globally, before CIPM engagement begins	Global Pricing Committee	T−24 months	Floor issued in writing; no local authority to breach it
3	Cascade modelling. Quantify the full downstream ERP consequence of each candidate Spanish price across Portugal, Greece, CEE, Brazil and Latin America	Global Pricing Intelligence	T−18 months	Cascade multiplier quantified per asset; embedded in the negotiation mandate
4	Below-the-line concession architecture. Pre-design confidential discount, volume-cap and MEA structures that deliver AIFA-equivalent value to CIPM without touching the published price	Spain Market Access + Global Pricing	T−18 months	Concession menu approved; published-price protection ranked first
5	Hospital dispersion evidence file. Document tender-level price variation across autonomous communities to support an attestation-impossibility argument for the hospital channel	Spain Market Access + Legal	T−12 months	Evidence file assembled; dispersion statistically characterised
6	Differentiated U.S. advocacy. File a Spain-specific methodological position opposing flat gross-to-net haircuts and asserting channel-level heterogeneity	Corporate Affairs + U.S. Market Access	Continuous	Spanish position filed separately from the France/Italy submission
7	Regional access sequencing. Prioritise the autonomous communities representing the largest eligible populations and shortest formulary cycles; run them in parallel, not in series	Spain Market Access	T−6 months onward	Time to 60% population coverage reduced by 20%+
8	Friction-adjusted forecasting. Rebuild Spanish forecasts with a 150–250 day regional coefficient and a 20–40% eligible-population haircut	Global Finance + Commercial	T−12 months	Forecast variance in first eight quarters within ±15%
9	Non-financing contingency. Define, in advance, the conditions under which Spanish listing is declined and the asset is managed through named-patient or private channels	Global Pricing Committee	T−12 months	Walk-away threshold quantified before negotiation begins
10	LOE reference-event planning. Model grouping formation, cross-presentation contamination and downstream cascade impact; evaluate selective delisting	Lifecycle + Global Pricing	LOE −24 months	Post-LOE published-price trajectory managed, not merely observed

Governance — The Market Where Local Success Is the Failure Mode

Element	Legacy model	Required model
Price approval authority	Spain country leadership within regional bands	Global Pricing Committee, with a written Nomenclátor floor issued pre-negotiation
Objective function	Secure financing; maximise access speed and volume	Minimise global cascade erosion; treat the published price as a global asset held in Spanish custody
Exposure metric	Spanish net revenue	Spanish revenue less cascade-transmitted loss across 20+ downstream markets
Concession hierarchy	Whatever CIPM will accept	Published price protected absolutely; all value conceded below the line
Channel treatment	Single national exposure	Retail and hospital modelled, negotiated and defended separately
Advocacy focus	CIPM and regional payers	U.S. rulemaking on haircut methodology and channel differentiation
Walk-away authority	Undefined; non-financing treated as failure	Pre-authorised and quantified; non-financing accepted where cascade cost exceeds Spanish value
Performance measurement	Spanish listing achieved, time to access	Contribution to global realisation, net of cascade transmission

The governance problem of Spain has a specific form, and a particularly acute one. A local team in France, optimizing for facial price, inadvertently causes global harm. First, the published price will be offered in Spain, which is the concession that CIPM finds easiest to accept, the one with the least evident domestic cost, and where a local team will do exactly what it is asked to do – secure financing in a market with one of the lowest financing rates in Western Europe. There is an active opposition to local competence and global value. Nothing in analytical briefing can remedy this. Only a written floor with escalation authority can overcome the local incentive to treat the Nomenclátor price as a negotiable commodity. The floor has to be issued before the first CIPM meeting, has to be quantified on a per presentation basis not on a per molecule basis and has to have an explicit statement that breaching it requires Global Pricing Committee sign-off in writing. Anything softer will be rightly interpreted as a target, not a limit.

Insight: If the Spanish committee has authority on paper is not the real test of governance. Is the bonus of the country manager in Spain linked to a Portuguese or Brazilian price outcome? The governance architecture only works until the incentive architecture crosses borders.

Watch List — Signals That Change the Spanish Calculus

Signal	Interpretation	Response
U.S. rulemaking proposes a flat gross-to-net haircut across the reference basket	Regime B becomes base case; Spanish retail exposure is systematically overstated	Escalate the Spain-specific submission immediately; separate it from the France/Italy filing to avoid contradiction
CIPM tightens the financing rate or extends *no financiado* decisions to new specialty classes	Access risk rises; pressure to concede published price intensifies	Reconfirm the Nomenclátor floor in writing; activate the non-financing contingency pathway
Autonomous communities move toward joint or centralised procurement	Hospital dispersion narrows; the attestation-impossibility argument weakens	Reassess hospital-channel opacity value; migrate concession structures toward MEAs and volume caps
Brazil (CMED) revises its basket or lowest-price rule	The return path to the U.S. either widens or closes	Re-run cascade multipliers; adjust the Spanish floor to reflect changed downstream weight

Portugal or Greece formalise Spain as a mandatory comparator	Cycle-1 transmission approaches full pass-through	Increase the cascade multiplier in the negotiation mandate; raise the floor accordingly
Reference-price grouping rules extended to additional presentations or devices	Cross-presentation contamination risk rises materially at LOE	Bring LOE reference-event planning forward; evaluate selective delisting earlier
Spanish published prices begin appearing in U.S. comparative datasets	Spain has entered the observable set regardless of formal basket inclusion	Treat every Spanish published price as a U.S.-visible price from that point onward
A competitor concedes a headline Nomenclátor price in a shared class	Payer expectations reset across the class and the cascade	Prepare defensive evidence on class heterogeneity; resist read-across at CIPM and in downstream markets

Conclusion

Spain is the market that is most likely to be underestimated and least able to absorb that underestimation. It is small enough to delegate, transparent enough to reference, and central enough to an Iberoamerican referencing chain that a concession to solve a domestic financing problem can travel thru twenty downstream baskets, and by way of Brazil's lowest-price rule, return to the United States from a direction that no European exposure model tracks.

The structural asymmetry to internalize Spain earns some 2% of global branded revenue and can set the reference floor for a portfolio that earns almost half its revenue in the United States under Regimes C and D. The exposure-to-earnings ratio is around ten to one – the least advantageous of all in the European set. France and Italy, at least, buy their transmitted risk with opacity. Spain carries similar risk but in retail almost no defensive cover whatsoever.

The Spanish strategy should be defined in three final propositions.

1. **First,** the channel dichotomy is the defining constraint. Spain's retail and hospital markets are effectively distinct regulatory environments. The retail channel is transparent, statutory and fully observable – a leaky environment that creates downstream MFN risk with no defensive cover. The hospital channel is opaque, regionalized and fragmented, providing a structural opportunity for confidential, unattestable concessions. Any strategy which does not split the portfolio, the negotiation and the advocacy between these two channels is a fundamental mismatch with the reality of Spanish exposure.
2. **Second**, the cascade effect is the main performance measure. What matters for Spain's systemic importance is not its 2% revenue share but that Spain is at the top of a referencing cascade passing thru Portugal, Greece, CEE and Latin America with a potential return path thru the U.S. via Brazil's lowest-price rule. A Spanish price concession is an option for the global pricing of the portfolio. Therefore, Spanish performance should be judged on the basis of the overall global effect of the Spanish price including the 1.8×-2.4× cascade multiplier. Indeed, a team that wins fast Spanish listing at the expense of the published retail price has, in all likelihood, destroyed more value in the Iberoamerican corridor than it created in Spain.
3. **Third**, the industry's lobbying should be made market-specific. The dominant US lobbying position that net price cannot be certified is a strong defense for Italy and the UK. If applied blindly to Spain, it leads to a fatal contradiction: it invites regulators to standardize haircut methodologies that disadvantage transparent markets. Spanish retail prices are already near net so a flat 25% haircut generates a discount of around fifteen points that doesn't exist, actively worsening exposure. Spain needs a separate submission that disentangles observable retail prices from hospital tender dynamics that cannot be tested, and explicitly makes the case against aggregation at the national level.

The governance conclusion is straightforward. It is the only one in the European set where local competence is the failure mode. This is not a training challenge or an analytics challenge. It is an authority problem and is solved only by taking the published-price authority away from the country and vesting it in writing in the global committee.

The rule of thumb for Spain: Don't let a 2% market price a 50% portfolio.

Australia

Australia is a standard outlier in global pricing governance: 1.5-2% of global branded revenue, single national payer, predictable process, country team that rarely escalates. This treatment is a category error of the same order as the Spanish one, but for a completely different structural reason.

Australia matters because it is the purest cost-effectiveness market in the developed world and it publishes the result. The Pharmaceutical Benefits Advisory Committee (PBAC) does not initially negotiate a price based on a comparator basket, an ex-factory anchor or a budget impact ceiling. It sets a price using an incremental cost-effectiveness ratio, applies a threshold that has never been formally published but is well understood by every participant, and then demands that the sponsor price at or below the resulting figure. What comes out is not a negotiated settlement between a manufacturer's ask and a payer's budget. It is an analytically derived willingness-to-pay figure, published in a downloadable schedule updated monthly.

That mix – low by international standards, fully machine-readable, analytically derived – makes Australia the most citable low-price in the OECD.

Australian exposure has three structural features:

1. First, full list observability with a large sensitive wedge. The Approved Ex-Manufacturer Price (AEMP) is published for each item listed in the PBS Schedule. Below that there are Special Pricing Arrangements (SPAs) which provide confidential rebates that on high-cost specialty assets often reach 30-60% of the list price. Australia thus has a France-like opacity dividend with a Spain-like publication discipline, with the wedge being larger than France's but the published figure more accessible than any European equivalent.
2. Second automatic downward adjustment by statute. Price disclosure, the F2 generic-entry reduction and the anniversary reductions under the 2022 Strategic Agreement, are set, not negotiated. Australia, like Japan, erodes by rule, not negotiation.
3. Third and most underrated: flow-on cost-minimisation. If the PBAC accepts a cost-minimisation analysis against an existing comparator then the new entrant is priced to that comparator. But the reverse is also true – a low price set anywhere in a therapeutic reference group diffuses to all members of that group. Australia is the only market in this white paper where a competitor's pricing decision can mechanically lower your published price without any action, submission or negotiation on your part.

Insight: France exports secrecy Italy exports untestability. Spain exports a waterfall. And Australia exports a methodology – that you can analytically derive and publish a defensible price. The Australian number is low not only in relation to an MFN regime, but there is a rationale attached to it. The rationale is the most dangerous export of the bunch, because it is quotable in a way that a negotiated German Erstattungsbetrag is not.

Price Formation — How the Australian Number Is Constructed

The two pathways

Pathway	When applied	Price consequence	Strategic weight
Cost-effectiveness analysis (CEA)	No appropriate comparator, or claim of superior comparative effectiveness accepted	Price derived from ICER against the threshold; the sponsor must demonstrate acceptable cost per QALY	The only route to a differentiated price. Requires accepted superiority.
Cost-minimisation analysis (CMA)	Comparative effectiveness accepted as non-inferior	Price set at the level of the comparator, adjusted for equi-effective dose	Caps the asset at the comparator's price permanently. No premium available.

The decision on the pathway is the single most important decision in the Australian process and it is made by PBAC, not the sponsor. When a sponsor lodges on a CEA basis and is redirected to CMA he has not just lost a premium, but has accepted a price ceiling based on an asset that may have been priced years ago under different evidentiary standards and that price becomes the published Australian figure for the life of the product.

The boundary

The PBAC has never established a formal cost-effectiveness threshold. The market-wide understanding of the range of operating is around AUD $45,000–$75,000 per QALY, with a higher implicit tolerance for severe, rare and end-of-life conditions, and for products addressing high unmet need. Converted at prevailing exchange rates, the upper bound is materially below the thresholds applied, formally or informally, in the United Kingdom and far below observed U.S. willingness-to-pay.

MFN modeling material point: it is not a discount off an international price. It's a new construction. Australia doesn't ask what the product costs elsewhere and discount it, it asks what the product is worth against a threshold and then prices to that answer. The figure that emerges has no memory of the U.S. or German or Japanese price, and thus no defensible relationship to them. When that figure is put into an MFN basket, there is no argument of the form "the Australian price reflects a local discount off a global anchor." Because it doesn't. It is an Australian threshold against an Australian comparator.

The problem of the comparator

In either pathway, the outcome depends on the choice of comparator. PBAC's preference is for the therapy most likely to be displaced in practice which in Australia is often:

- A generic or biosimilar, if available anywhere in the algorithm;
- An old agent that still features in the guidelines although its current use is limited;
- The lowest-cost member in an existing therapeutic class that is the most clinically similar agent.

This preference is significantly more aggressive than the German G-BA's appropriate comparator therapy selection or the French comparator logic, both of which give more weight to clinical proximity. In practice this means that Australian comparator selection tends to anchor low and CMA pricing to a genericised comparator results in a published AEMP that has no relationship to the innovative asset's global price corridor.

Insight: Australia's comparator engineering needs to start at protocol design, not submission. The PBAC comparator is informed by the Australian clinical practice as reflected in Australian treatment guidelines and PBS utilization data. In effect, a trial program is pre-selecting a CMA outcome against the cheapest available option, without producing head-to-head or robustly indirect evidence against the agent actually used by Australian clinicians.

Australia's Opacity Layer – The Special Pricing Arrangement

Mechanism

An SPA allows the published AEMP to be maintained at a level acceptable to the sponsor, while providing an effective price to the Commonwealth thru a confidential rebate. The arrangement is recorded in a Deed of Agreement between the sponsor and the Department of Health, and the rebate quantum is neither published, nor disclosed to state health authorities in a usable form, nor derivable from public data.

Typical structure and magnitude:

Asset category	Published AEMP relative to global corridor	Typical confidential rebate	Effective price as % of AEMP
High-cost oncology / specialty	At or near international list levels	30–60%	40–70%
Rare disease / LSDP-adjacent	Often near-parity with international list	40–70%	30–60%
Broad-population primary care	Modest premium over comparator	5–20%	80–95%
Post-price-disclosure generics	Collapsed	Not applicable	Published ≈ effective

The SPA: The Strategic Center of Australian Pricing

This is why Regime A is survivable in Australia and Regime C SP A is catastrophic. It creates a wedge, often larger than the French one, attached to a published price that can be defended at a level far above the analytically derived effective price.

The critical asymmetry: recommendation of PBAC is in effective-price terms. The published AEMP is negotiable upward within limits, as long as the effective price meets the recommendation. A sponsor who bargains solely on the effective price and takes a low published AEMP has surrendered, for no consideration, the one defensive asset Australia offers.

Insight: In Australian negotiations the published price is often regarded as an administrative residual – the number that falls out once the rebate is agreed. It's the most common mistake and the most expensive mistake in the market. The AEMP should be negotiated as a separate term with its own mandate and its own floor precisely because it is the number the world will read and the effective price is the number only Canberra will see.

The question of durability

The secrecy of the SPA has been well kept. It is protected by contract, the commercial-in-confidence provisions of the freedom-of-information framework and a well-established administrative practice. But it is not without qualification. It has been the subject of inquiries by parliamentary committees, reviews by the Australian National Audit Office and periodic transparency advocacy. The relevant risk is not sudden abolition, but gradual erosion thru aggregate disclosure – publication of category-level averages of rebates, or of total rebate receipts, from which product-level inference is possible for concentrated categories..

Statutory Erosion — The Australian Ratchet

Australia, like Japan, reduces prices by rule. Four mechanisms operate:

Mechanism	Trigger	Magnitude	Reversible?
Statutory price reduction on generic entry (F2)	First generic/biosimilar listing for the molecule	25% immediate, applied to the originator's AEMP	No
Price disclosure	Ongoing, for F2 molecules	Weighted-average disclosed price replaces AEMP; cumulative reductions routinely exceed 80% over successive cycles	No
Anniversary reductions	Scheduled, per the Strategic Agreement	5% at defined anniversaries for eligible items	No
Therapeutic group premium policy	Formation or revision of a therapeutic group	Price aligned to the lowest-priced member; the difference becomes a patient-borne premium	Effectively no

Effect of compounding. The path from AEMP launch to steady state disclosed price is a decline of 80-95% over five to seven years for a molecule that enters generic. This collapsed figure is published on the PBS Schedule indefinitely, and is fully available to every referencing authority and every U.S. comparative dataset.

It matters that it is different from Japan. Japanese erosion is broad, gradual and portfolio-wide. Australian erosion is binary and molecule-specific: the price holds reasonably well until generic entry then collapses almost completely. This means that in terms of MFN modeling, Australian exposure is not a smooth curve but a step function and the step is much larger than anything in the European set.

Flow-on contagion – the mechanism with no European counterpart

This is the aspect of the Australian system that global teams get most consistently wrong.

The mechanics. Where PBAC determines a cost-minimisation relationship between products, or products are within a therapeutic group, a price reduction for one member will apply to the others. The transmission is two-way:
• Downward from comparator to entrant – the usual CMA outcome, capping the new asset.
• Downward from entrant to incumbent – where a new entrant prices lower or where an incumbent faces a statutory reduction, other group members are lowered to the new lowest level.
• Across the group at generic entry – this is the severe case. The collapsed price can be used to reset the reference point for other still protected members of the same group with the loss of exclusivity for any one molecule in the therapeutic group and subsequent disclosure of the price.

Result. A patent protected asset of a manufacturer, with no generic competition and an unchanged clinical position, can see its published Australian price fall substantially because an unrelated molecule of a competitor went off patent. No submission is made. No deal is reached. The published number just moves along the Schedule and from there it is the number an MFN calculation reads.

Scenario	Trigger	Typical published-price impact on protected asset
Competitor lists at lower price in same CMA relationship	New PBAC recommendation	5–20%
Group member undergoes F2 reduction	Generic entry elsewhere in group	15–25%
Group member completes multiple disclosure cycles	Cumulative disclosure	25–60%
Therapeutic group reformed to include lower-cost class	PBAC review	Highly variable; can exceed 50%

Insight : Australian exposure cannot be modeled at asset level. This has to be modeled at therapeutic group level, and the model has to include the LOE calendar of each competitor molecule in the group – including molecules the company does not market. This is the sole market in the set where a competitor's patent cliff is a direct input into your own MFN exposure. Global pricing intelligence functions that only track the company's own portfolio are structurally blind to the majority of Australian risk.

MFN Exposure Under Alternative U.S. Regimes

Regime	Description	Australian contribution to U.S. reference	Assessment
A — Observable list only	Published AEMP referenced as-is	Moderate. AEMP defensible where negotiated deliberately; SPA wedge fully protective	Manageable — the SPA shield holds
B — Standardised gross-to-net haircut	Uniform haircut applied across basket	Variable. A 25% haircut *understates* the true 30–60% specialty wedge, so Australia is treated more favourably than reality	Favourable — the only market in the set where a flat haircut helps
C — Net disclosure mandate	Attested effective prices required	Severe. The Australian effective price exists, is contractually determinate, and is attestable	Critical — Australia becomes a bottom-of-basket contributor
D — Lowest-in-basket	Lowest observed price sets U.S. reference	Severe. Post-disclosure and post-F2 prices are among the lowest published figures in the OECD	Critical — Australia is frequently the basket floor

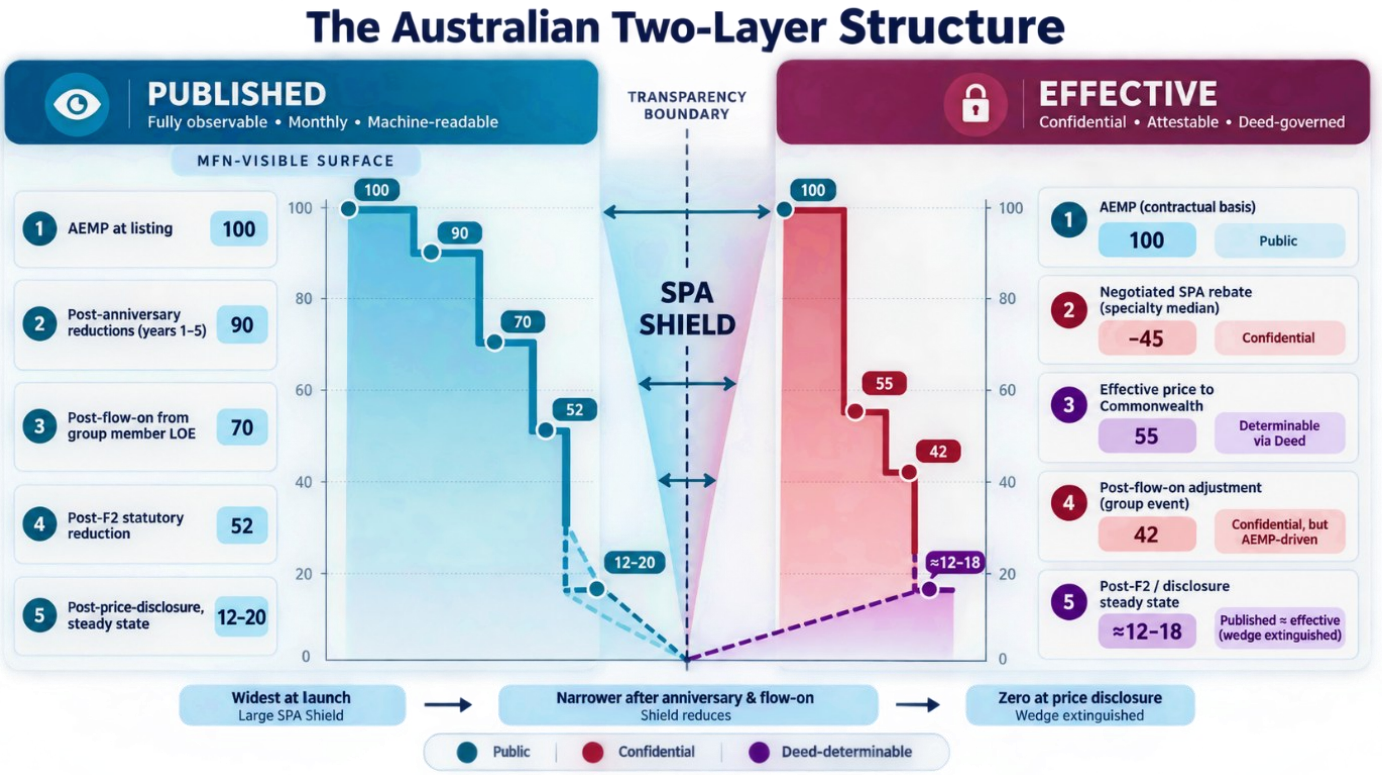
Estimated contribution to U.S. net erosion from Australian inclusion:

Regime	Incremental U.S. net erosion attributable to Australia
A	2–5 percentage points
B	1–4 percentage points
C	12–22 percentage points
D	15–30 percentage points (higher where the asset's group has experienced generic entry)

The distinction in attestation is decisive and adverse. Australia does not apply the Italian defense of no determinate net price of product at point of sale. A Deed sets out the SPA effective price, to the cent, calculated, invoiced and reconciled. An Australian effective price can be produced on demand under a mandate disclosure. Australia is thus

the weak link in the industry's argument of attestation-impossibility, and any global submission that argues blanket inability to attest net prices is vulnerable to being contradicted by Australian practice.

Insight: The global advocacy for the industry has been based on Italy and the UK. Australia makes it false. All a regulator needs to do to show net-price attestation is administratively feasible is to point to one example, and Australia is the cleanest one available. Australian advocacy must therefore be argued on entirely different grounds – not that the price cannot be attested, but that the Australian effective price reflects a threshold-based willingness-to-pay judgment calibrated to a single-payer system with a fixed national budget, and is definitionally non-transferable to a multi-payer market with different opportunity costs.



The Australia Playbook — Actions, Owners, Timelines

#	Action	Owner	Timing (relative to PBAC submission)	Success measure
1	Comparator engineering from protocol design. Build head-to-head or robust indirect evidence against the agent Australian clinicians actually use, evidenced by PBS utilisation data and Australian guidelines	Clinical Development + Global HEOR	T−36 months	Documented comparator hypothesis with PBS utilisation support; CMA-avoidance case built
2	CEA-versus-CMA pathway determination. Establish early whether the asset can sustain a cost-effectiveness pathway; if not, model the CMA-derived ceiling as the base case	Australia Market Access + HEOR	T−24 months	Pathway determination documented; AEMP ceiling modelled under both routes
3	Global AEMP floor mandate. Set a published-price floor independent of, and negotiated separately from, the SPA rebate	Global Pricing Committee	T−18 months	Written mandate issued; local team has no authority to breach
4	Therapeutic group LOE audit. Map every molecule in the current and prospective therapeutic group, including non-portfolio assets, with patent-expiry and biosimilar-entry calendars	Global Pricing Intelligence	T−12 months	Group-level exposure model built; flow-on triggers dated
5	SPA architecture design. Structure the rebate to satisfy the PBAC threshold at effective-price level while defending the AEMP as a distinct commercial term	Australia Market Access + Legal	T−12 to T−6 months	Deed executed with AEMP at or above global floor
6	Attestation-differentiation advocacy. Prepare Australia-specific U.S. submissions arguing threshold non-transferability rather than attestation impossibility	Corporate Affairs + U.S. Market Access	Continuous	Australia carved out of the global attestation argument; no self-contradiction in filings

7	Flow-on early-warning system. Standing monitoring of PBAC agendas, therapeutic group reviews and competitor disclosure cycles	Pricing Intelligence	Continuous, post-listing	Group events identified ≥2 cycles before AEMP impact
8	Pre-disclosure corridor planning. Model the step-function collapse at F2 and pre-position global corridors before the Australian price becomes the basket floor	Global Pricing Committee	T+36 months onward	Post-F2 Australian price excluded or de-weighted in global corridor logic
9	Walk-away definition. Quantify the AEMP below which listing destroys more global value than Australian revenue creates	Global Pricing Committee	T−12 months	Threshold defined and pre-authorised before negotiation pressure
10	Confidentiality integrity review. Audit internal handling of Deed terms; restrict effective-price knowledge to a named list	Legal + Compliance	At execution, annually thereafter	Zero disclosure incidents; aggregate-inference risk assessed

Insight: The only two actions that are not delegatable are actions 3 and 9. The rest of this playbook can be done locally, but with global visibility. The AEMP floor and walk-away threshold has to be set centrally, in writing, before the Australian team enters the room – otherwise the local incentive structure will trade published price for listing speed and that trade is invisible on the Australian P&L and catastrophic on the global one.

Governance—The myth of "low impact"

Australia accounts for about 1-2% of global pharma revenues for most portfolios. This statistic is the most dangerous input into governance design, because it rationalizes delegating a decision with global consequences to a team measured on outcomes that are local.

The failure mode is "local capitulation". An Australian country team is judged by a PBS listing, the time taken to achieve it and the Australian net revenue. If the team gives up the published AEMP and defends the effective price, each one of those metrics gets better. None of them deteriorates when the AEMP conceded is then read into twenty referencing baskets, and into the U.S. calculation, under Regimes C or D. The local optimum and the global optimum are not only different, but are actively opposed.

Governance element	Legacy model	Required model
AEMP approval authority	Australia country lead, within regional band	Global Pricing Committee; local team holds no authority to breach the published-price floor
Effective-price authority	Australia country lead	Australia Market Access, within a globally set threshold envelope
Unit of risk	Individual asset	Therapeutic group, including competitor molecules not marketed by the company
Objective function	Secure PBS listing at acceptable Australian net revenue	Minimise global erosion transmitted via published AEMP; treat Australian revenue as secondary
Exposure horizon	Launch price and first review	Full lifecycle to F2 and steady-state disclosure, with the step-function modelled explicitly
Advocacy posture	Included in global attestation-impossibility submission	Separately argued on threshold non-transferability; deliberately excluded from the attestation argument
Performance measurement	Australian listing speed and net realisation	Global realisation net of cascade impact, with AEMP integrity as a named KPI
Walk-away authority	Undefined	Pre-authorised, quantified, and enforced centrally

Imperatives of governance

Centralize the AEMP floor. The published price is regarded as a global asset on the Australian balance sheet, not an Australian commercial variable. No regional or local teams should be allowed to agree an AEMP below the mandated floor. The only way to vary this should be to escalate to the Global Pricing Committee.

Shift Australia from market risk to methodology risk. The advocacy function needs to stop treating Australia as a minor market and treat it as the primary counter-example to the industry's own defense. Net-price attestation is administratively trivial as can be seen from a single Deed of Agreement in a U.S. rulemaking docket. The industry cannot afford to be blindsided by its own evidence.

Consider non-listing an acceptable outcome. If the PBAC price analytically derived, on publication, would reset global corridors below the walk-away threshold, non-listing must be available as a decision. This means the threshold must be written down before the negotiation starts, because it will never be defensible once a launch date has been communicated internally.

Watch List — Indicators That Change the Australian Calculus

Signal	Interpretation	Strategic response
ANAO or parliamentary inquiry into SPA rebate value	Aggregate-disclosure risk rising; the shield is being tested	Escalate confidentiality advocacy; model Regime C exposure as base case for Australian assets
Publication of category-level rebate averages	Product-level inference becomes possible in concentrated categories	Immediate reassessment of AEMP defensibility; treat effective price as semi-public
PBAC review reforming a therapeutic group to include a lower-cost class	Flow-on contagion event imminent	Re-run group-level model; pre-position global corridors ahead of Schedule change
Competitor biosimilar entry within the group	F2 reduction and disclosure cascade will transmit to protected assets	Activate pre-disclosure corridor planning; brief U.S. and EU teams on published-price change
Strategic Agreement renegotiation with Medicines Australia	Anniversary reduction schedule and disclosure mechanics may change	Re-baseline the erosion ratchet; re-time lifecycle assumptions
U.S. rulemaking cites Australian Deed practice as evidence of attestability	The attestation defence has been falsified publicly	Pivot immediately to threshold non-transferability; disaggregate the global submission by market
Move toward publishing effective prices in the PBS Schedule	The SPA shield is abolished	Fundamental re-assessment of Australian listing economics; walk-away review across the portfolio
PBAC signalling greater willingness to accept clinically proximate comparators	CMA-to-genericised-comparator risk declines	Re-open AEMP ambition; revisit assets previously deprioritised on ceiling grounds

Insight : The Australian watch list is peculiar in that most of its items are events occurring to other companies' products. Your published Australian price is forced by a competitor's biosimilar, a competitor's PBAC review, an unrelated therapeutic group reform. No intelligence functions scoped to the company's own portfolio will detect any.

Conclusion

Australia is the most sophisticated trap in the global pricing environment, systematically underestimated because of the small amount of revenue at stake. It brings together, within a single jurisdiction, the observability of Spain, the rule-based erosion of Japan, the analytical rigidity of a threshold-based HTA system, and one mechanism that has no analog in Europe at all — a flow-on architecture that allows the expiry of a competitor's patent to reduce your listed price without a submission, negotiation or meeting.

Three conclusions should emerge from this section.

1. **First**, the AEMP published is the whole MFN surface and it can be negotiated upwards. PBAC recommends in terms of effective price. The published price can be defended within bounds, at a level well above the analytically derived effective price, as a separate term, but only if it is negotiated as a distinct commercial variable with its own mandate and its own floor. It is an administrative residue which follows when the rebate is agreed and surrendered for no consideration whatever. It's the most common mistake in the Australian

market, and the most expensive, and it's made by teams who think they've negotiated well because the effective price landed where they wanted it to.

2. **Second**, the unit of risk is the therapeutic group, not the asset. Australia is the one market in this set where you have a direct input to your MFN exposure from a rival's patent cliff. An asset that is patent protected, with no change in its clinical position and no generic competition, can lose 25-60% of its published price because an unrelated molecule in the same group has completed its disclosure cycles. Any exposure model built at asset level – that's almost every model in use today – is structurally blind to most of Australian risk. The correction is not analytic sophistication; it is scope. In particular, the model should incorporate the loss-of-exclusivity calendar of molecules the company does not market and has never studied.

3. **Third**, and most important, Australia misrepresents the defense industry itself. The attestation-impossibility argument, based upon Italy's collective retrospective clawback, and the UK's aggregate rebate mechanics, is a strong position in those markets. Here in Australia it is inexcusable. The effective price is in a Deed of Agreement, calculable to the cent, invoiced and reconciled and able to be produced on demand. The administrative feasibility of net-price attestation requires just one clean example for a regulator, and Australia is the cleanest available among OECD countries. The industry's own contracting practice contradicts any global submission that asserts a blanket incapacity to attest net prices and, once embedded in a rulemaking record, the contradiction is not recoverable.

The advocacy consequence is right away. The case has to be put on quite different grounds in Australia. Not that the price cannot be known, but that the price means something different: the Australian effective price is a threshold-based willingness-to-pay judgment, calibrated to a single-payer system operating under a fixed national budget with explicitly defined opportunity costs. It is an answer to the question what is this worth to the Commonwealth in terms of what the Commonwealth must give up to fund it. It is not, nor has it ever purported to be, an estimation of the market value of the product. To translate that number into a multi-payer market with different budget constraints, different opportunity costs and different institutional purposes is not reference pricing; it is a category error. That argument is available, it is intellectually honest, and it is the only argument that survives contact with an Australian Deed.

The shift in governance required is the usual inversion from France and Italy, but more sharply. Australia has a low revenue share which makes delegation look rational and delegation is exactly what destroys the value. The local team is judged on achieved listings and Australian net revenue; both metrics improve when the published price is conceded and neither registers the twenty referencing baskets that read the result. The Global Pricing Committee must set the AEMP floor and the walk-away threshold in writing prior to the negotiation since neither will be defensible once an internal launch date is communicated.

Finally, in terms of the time dimension, Australia is unique in this set of markets. The dividends of opacity in France and Italy are eroded in a slow and unpredictable way. The Australian shield has a known expiration date, first generic or biosimilar entry, which is known to be the date of first generic or biosimilar entry. The F2 reduction and subsequent cycles of disclosure collapse the published price by 80–95% and permanently melds it with the effective price. The collapsed figure then remains on the PBS Schedule indefinitely, machine-readable in its entirety, accessible to all referencing authorities and all US comparative datasets, for as long as that molecule is marketed. Australian MFN exposure, therefore, is not a curve to be managed but a step function to be anticipated, and the anticipation must begin years before the step occurs.

Australia's governing principle

1. Defend the published AEMP as a standalone, globally mandated commercial term
2. Achieve the threshold outcome only thru the confidential SPA
3. Model the therapeutic group and not the asset as the unit of risk
4. Never have Australia appear in the same submission as Italy – because the argument that saves one kills the other.

Japan

Executive Summary

The United Kingdom hides its net price. It is published in Germany. Japan does something that neither market does: it references the United States, then publishes the result.

Japan is the only major economy with a formal, statutory external reference pricing system that includes the U.S. in its reference basket. Japanese prices are benchmarked against the United States, the United Kingdom, Germany and France under the Foreign Average Price (FAP) adjustment. If the U.S. adopted MFN referencing that includes Japan, the two systems would become mutually referencing each other's reductions, forever, with no equilibrium other than the floor.

Japan's pricing framework is defined by five key conclusions:

1. Japan is the only market in this white paper that generates a recursive risk. All other comparators transmit price pressure in only one direction. transmits in both Japan. This is a different class of exposure in terms of structure and should be modelled separately.

2. Prices in Japan are completely transparent and fall in a fixed and predictable pattern. NHI price list (yakka) is the government published price without the rebate layer. List is net. There is no confidentiality option, no VPAG style aggregate clawback and nothing to infer - the observability problem that makes Germany dangerous is, in Japan, complete.

3. Annual revisions have turned a slow erosion into a compounding one. Off-year revisions are now built-in. For a typical branded product, 40-60% of the launch price will be lost in ten years, thru mechanisms that are automatic, non-negotiated and irrespective of the global pricing corridor of the product.

4. Currency has pushed Japan into the cheapest developed market in USD terms. Japanese prices in current exchange rate dollar terms are significantly lower than their policy intent in yen terms. An MFN rule comparing converted prices imports an FX outcome never decided by any Japanese authority.

5. Japan's own policy stance now runs counter to the logic of MFN. The reforms for 2024-2026 are aimed at increasing effective returns on innovation to reverse "drug loss" (doraggu rosu). MFN referencing of Japan would undo those reforms and re-create exactly the disincentive Japanese policymakers are trying to remove.

Central estimate

In a central-case MFN construction including Japan at spot FX, Japan adds 6–14 percentage points to U.S. net price erosion in mature specialty portfolios — and crucially an additional 2–5 ppt per revision cycle thereafter via recursive transmission.

The Japanese Market: Size, Structure, and Price Formation

Japan is the world's third-largest pharma market with universal coverage, near-automatic reimbursement upon approval and government price administration in place.

Metric	Japan	Context / Peer Comparison
Share of global branded pharma revenue	**~5–7%**	U.S. ~47%; EU5 ~20%; Germany ~9.5%
Population	~123 million and declining	Ageing at the fastest rate in the OECD
Population aged 65+	**~29%**	Germany ~22%; U.S. ~17%
Total drug expenditure (NHI)	**~¥11–12 trillion p.a.**	~20% of national health expenditure
Price-setting authority	MHLW, advised by **Chuikyo** (Central Social Insurance Medical Council)	Administered pricing, not negotiation
Formal ERP system	**Yes — Foreign Average Price adjustment**	**Only major market referencing the U.S. directly**
Reference basket	**U.S., UK, Germany, France**	Simple average, with outlier rules
Price observability	**Total — published NHI price list**	List = net; no rebate layer
Rebate / clawback layer	**None**	Contrast: UK VPAG ~25%; U.S. GTN 40–55%

Revision frequency	**Annual** (from biennial)	Off-year revisions since 2021
Average list multiple vs. lowest OECD	~1.6x	U.S. ~4.2x; UK ~2.8x; Germany ~2.1x
Estimated net multiple vs. lowest OECD	**~1.15x**	U.S. ~1.8x; UK ~1.3x; Germany ~1.1x
Generic volume share	~80%+	Policy target achieved; focus shifted to long-listed brands

Insight : Japan is characterized not by the level of its prices but by the fact that list and net are the same. In the U.S. published price exceeds realization by 40-55%. In Japan, the wholesale margin alone is exaggerated. Thus, any calculation of MFN prices based on published prices across markets is comparing a gross number in the U.S. with a net number in Japan, a methodological asymmetry which, if left uncorrected, dramatically exaggerates the apparent U.S. premium.

The formation of prices

Japanese pricing follows a set of rules that are applied sequentially at listing and then reapplied downward throughout the lifecycle.

Initial Listing

New products are priced by one of two methods:

Method	When applied	Basis
Similar Efficacy Comparison	A comparable product exists	Daily-dose price of the designated comparator, adjusted by premiums
Cost Calculation	No comparator exists	Build-up of manufacturing cost, distribution, R&D allocation and a regulated operating margin

The comparator choice is decisive and, as in Germany, is the single highest-leverage point in the entire process. Unlike Germany, however, there is **no negotiation** — Chuikyo applies rules, and the manufacturer's recourse is limited to a single formal objection and, ultimately, withdrawal of the listing application.

Premium Structure

Premiums are the only upward force in the Japanese system.

Price Maintenance Premium (PMP) | Safeguards the product from ordinary revision reductions from launch until generic entry | Innovation criteria; broadly accessible to products meeting innovativeness, orphan, sakigake or unmet-need designations. Withdrawn -- with cumulative repayment -- when generics enter or indication scope lapses | Premiums are cumulative in principle, but limited in practice. A product with an innovativeness premium at the upper end with marketability and pediatric premiums may command a high multiple of its comparator's daily dose price – but such outcomes are infrequent and Chuikyo has been steadily reducing the range of products that qualify for the top tier.

Premium	Typical range	Eligibility
Innovativeness	+70–120%	Novel mechanism, high clinical utility, demonstrable superiority
Usefulness I	+35–60%	Two of three utility criteria met
Usefulness II	+5–30%	One utility criterion met
Marketability I / II	+10–20% / +5%	Orphan or small-population indications
Paediatric	+5–20%	Paediatric indication at launch
***Sakigake* (pioneering)**	+10–20%	Japan-first development designation
Price Maintenance Premium (PMP)	Protects price between revisions	Innovation criteria; **broad

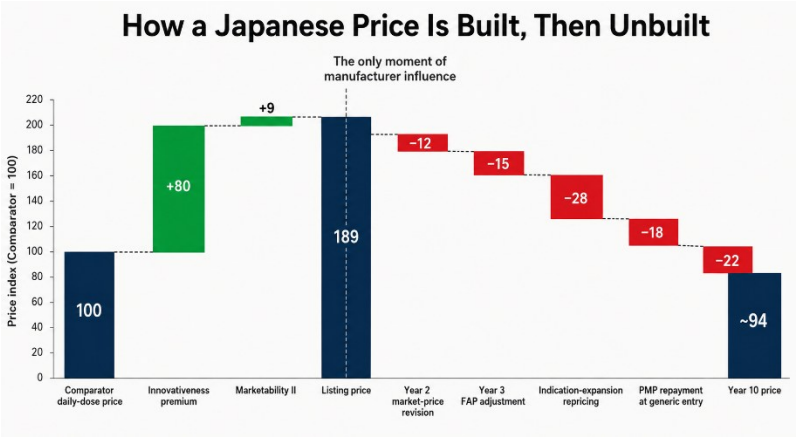
Insight: the only way a manufacturer can influence its Japanese price is thru the premium structure, and this is done entirely before listing. When the price is fixed there is nothing to go up in the system. The evidence generation planned to support premium claims must be complete at the time of the Chuikyo submission, not just planned. Viewed locally, Japanese P&L does not justify the expenditure so companies routinely under-invest here. In an MFN world, seen globally, it almost always does.

Price Revisions – The Downward Pressure of Compounding

The main cause of long-term erosion is the revision system in Japan. Historically, off-year adjustments introduced in 2021 made biennial revisions effectively annual.

Revision type	Frequency	Mechanism
Market-price-based revision	Annual	The NHI price is reset toward the actual weighted-average transaction price between wholesalers and providers, plus a small allowable zone (~2%)
Off-year revision	Annual, since 2021	Captures products whose transaction price has drifted beyond a defined threshold relative to the class average
Foreign Average Price adjustment	At revision and at listing	Adjusts the Japanese price toward the average of the U.S., UK, Germany and France
Repricing for market expansion	Triggered	Applies where sales materially exceed forecast, or where an indication expansion enlarges the eligible population
PMP repayment	At generic entry	Cumulative premium value is clawed back through a step reduction

It differs from every other market in this white paper in three ways:



- The reductions are automatic. There is no negotiation, no counterparty and no discretion to preserve a global corridor.
- They are applied at the product level. That's different from the UK's aggregate VPAG clawback, which leaves the product-level price alone, Japanese price cuts change the published price itself — and thus change what the rest of the world sees.
- They reproduce. Each change is applied to the already reduced basis.

Insight: The UK protects the visible price, then captures the money via a rebate. Japan takes the money by dropping the price you can see. They were economically similar in the pre-MFN world. In an MFN world they are a whole lot different: the UK's mechanism is contained, Japan's is exported.

"Everything to the right of the dashed line is administered, scheduled and public."

The FAP Adjustment and Recursive Risk

The Foreign Average Price adjustment is Japan's statutory external reference mechanism — and the origin of the only genuinely circular exposure in the global pricing system.

Component	Specification
Reference basket	**United States, United Kingdom, Germany, France**
Comparison basis	Published prices in each market, converted to JPY at a defined reference rate
Trigger	Japanese price materially exceeds the basket average
Outlier handling	Where one market's price is an extreme outlier relative to the others, it may be excluded or capped before averaging — a rule originally designed to contain U.S. list prices
Floor protection	Adjustment is bounded; the Japanese price is not driven below a defined proportion of the basket
Direction	**Downward only** — the FAP has historically operated as a reduction mechanism, with upward adjustment available only in narrow circumstances

The Loop

1. The U.S. takes MFN referencing that includes Japan. U.S. net prices are falling toward the international benchmark.

2. The lower U.S. price is included in Japan's FAP basket at the next revision.

3. The basket average declines. Japan's published price is cut.

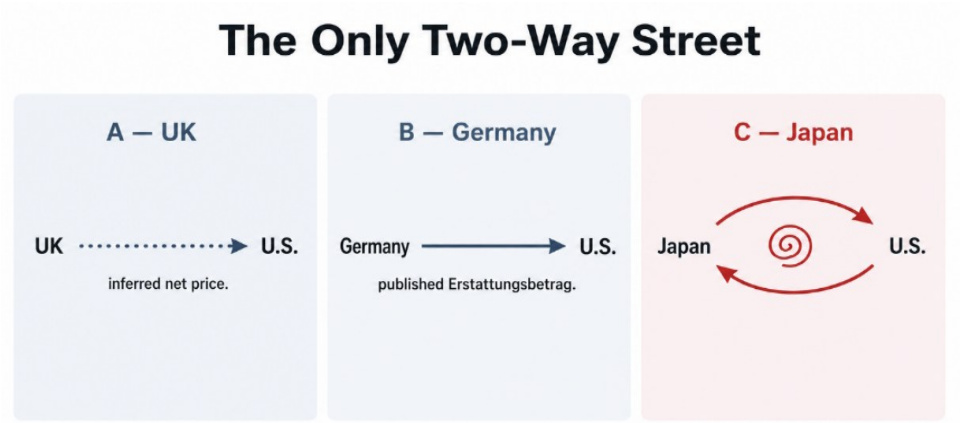
4. The new lower published price in Japan becomes a downward reference point in the next US MFN calculation.

5. Repeat step 2.

Cycle	U.S. net index	Japan index	Comment
Baseline	100	42	Pre-MFN steady state
Cycle 1	82	42	U.S. imports Japan
Cycle 2	82	38	Japan imports lower U.S. price via FAP
Cycle 3	78	38	U.S. re-references reduced Japan
Cycle 4	78	36	Compounding continues
Steady state	**~73–76**	**~34–36**	Convergence toward basket floor

Each iteration is smaller than the last, but the sequence does not converge on a negotiated equilibrium; it converges on the floor of the basket. And Japan's outlier rules, designed to exclude a high U.S. price, offer no symmetric protection against a low one. The mechanism lacks a brake for the scenario it is most likely to face now.

Insight: This isn't modeling curiosity. It is the predictable product of two rule systems working against each other. The implication is important: static MFN impact assessments understate exposure. The central case of 6–14 ppt, a single-shot estimate of Japan's contribution to US erosion, only covers the first cycle. Boards need to see the multi-cycle path, because that's the path the business is actually going to travel on.



Japan is the only comparator that receives what it sends.

Currency: The Uninvited Policy Maker

Japanese prices are set in yen. MFN comparisons are made in dollars. The gap between those two facts has become one of the largest single variables in Japan's global pricing impact.

Scenario	Effect on Japanese price in USD	Effect on U.S. MFN pressure
Yen depreciation	Japanese price appears materially cheaper	**Amplifies** downward pressure on U.S. prices
Yen appreciation	Japanese price appears more expensive	**Attenuates** pressure; may create a temporary optimisation window
Volatility without trend	Reference point becomes unstable	Introduces timing risk — the measurement date determines the outcome

Two consequences follow

1. First, the date of measurement is just as important as price. An MFN rule that samples converted prices at one date imports the spot rate that is there. A trailing average rule imports something quite different. This is a technical drafting question with a nine figure answer for large portfolios and this is exactly the sort of detail that industry comment periods exist to influence.
2. Second, FX propagates in both directions thru the loop. A weaker yen lowers the Japanese contribution to the US benchmark, but raises the JPY-converted value of US, UK, German and French prices in Japan's own FAP basket, relieving downward pressure on the Japanese price. The two effects partially offset - but do not cancel, and the residual is seldom modeled.

Insight : Japan is the only market where a treasury decision is also a decision on market access. Pricing and Finance have to model this together. In practice they almost never do . FX is a translation risk issue for Treasury , Pricing treats the yen price as fixed In an MFN world that separation cannot be maintained**.**

The 2024–2026 Reforms: Counter-Trend Under External Threats

MHLW has openly admitted that ongoing erosion has resulted in "drug loss" — Japanese patients losing access to medicines that are approved and available elsewhere, because launch in Japan is no longer commercially rational**.**

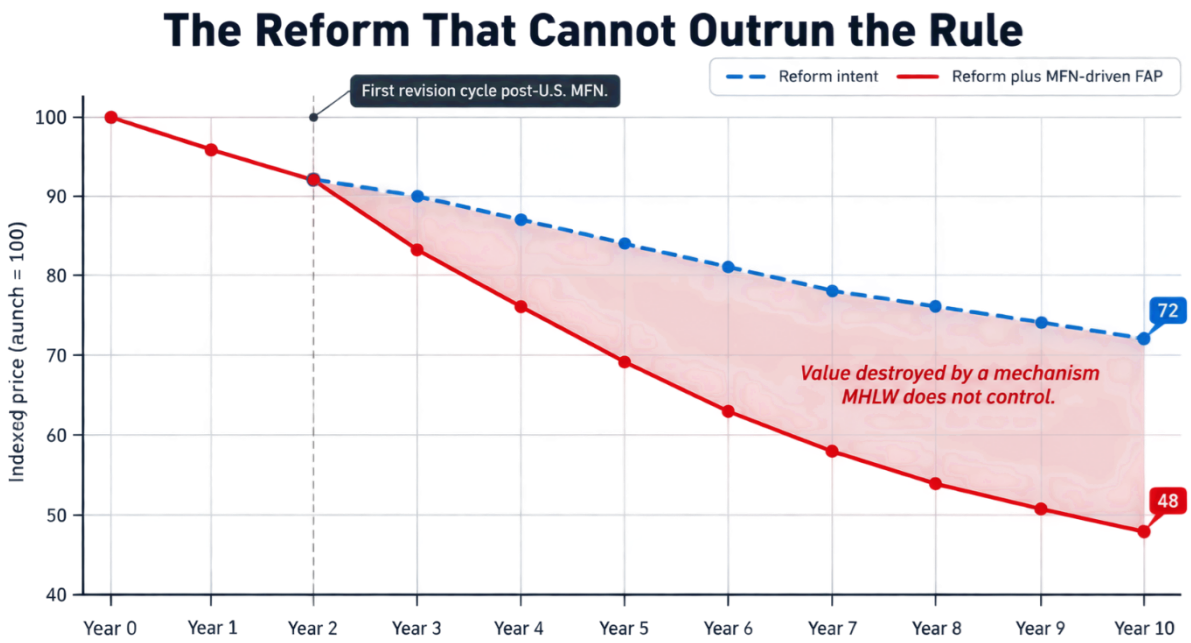
Reform element	Intent
Broadened PMP eligibility	Restore price stability for genuinely innovative products
Enhanced premiums for unmet need and paediatric indications	Address specific access gaps
Improved treatment of orphan and small-population products	Make low-volume launches commercially viable
Recognition of Japan-inclusive global development	Reward simultaneous rather than deferred Japanese entry
Moderation of repricing for indication expansion	Stop penalising the broadening of clinical value
Reduced revision burden on genuinely innovative categories	Slow the compounding erosion curve

The direction of travel is clear, Japan has judged that it priced innovation too aggressively and is attempting a partial correction.

This is a matter of arithmetic, not of intent. All the reforms above are on the listing and revising side of the system. None of them touch the FAP. Further, if U.S. MFN policy lowers the basket average, the FAP will automatically pass that decrease thru to Japanese prices, no matter how generous the premium structure is. Japan can raise the ceiling as much as it want, the FAP lowers the whole building.

Force	Direction	Magnitude	Controllable by MHLW?
Expanded premiums and PMP	Upward	Moderate	Yes
Annual and off-year revisions	Downward	High	Yes
Market-expansion repricing	Downward	Moderate	Yes
FAP adjustment under U.S. MFN	**Downward**	**High and open-ended**	**No**
FX translation	Variable	High	No

Insight: There is a real policy irony here, one worth articulating to boards and to policymakers alike. U.S. MFN referencing of Japan would undermine a Japanese reform program, intended to increase returns to innovation, by employing a device Japan has devised and for a reason that no longer exists. It is a rare case where the commercial argument of the industry and the stated policy objective of a sovereign government perfectly align. That alignment is an advocacy asset and needs to be leveraged.



"Japan's reforms raise the launch price. The FAP determines everything after it."

Quantified Exposure

Model-based, for a mature specialty portfolio with meaningful Japanese and U.S. presence.

Scenario	MFN construction	Japan's incremental contribution to U.S. net erosion	Recursive effect per subsequent cycle	3-yr global revenue impact
A — Excluded	Japan outside the MFN basket	0 ppt	None	Baseline
B — Benign	Japan included; trailing-average FX; net-to-net adjustment applied	**−3 to −7 ppt**	−1 to −2 ppt	−2 to −5%
C — Central	Japan included at spot FX; published-price comparison, no gross-to-net correction	**−6 to −14 ppt**	**−2 to −5 ppt**	**−7 to −15%**
D — Severe	Central case plus sustained yen weakness and lowest-price (rather than average) referencing	**−15 to −24 ppt**	−4 to −8 ppt	−14 to −24%

Scenario B is three drivers from Scenario C, and all three are drafting decisions, to economic realities:

1. Gross to net adjustment. Comparing a U.S. list price to a Japanese NHI price is a comparison of a number inflated by 40-55% to a number inflated by almost nothing. Without correction the apparent gap is largely an artifact.

2. FX method. Spot vs. trailing average is worth a couple of percent by itself.

3. Average versus minimum. A basket average dilutes Japan; a lowest-price rule makes Japan decisive for a large part of the portfolio.

Insight: The highest return advocacy investment available for Japan is not lobbying on whether Japan is included. It is how prices are compared once it is lobbying. Inclusion is primarily a political choice and it is hard to reverse. Methodology is a technical decision. Made by officials not principals. Worth more.

The Japan Playbook — Actions, Owners, Timing

#	Action	Owner	Timing (relative to Japanese filing)	Success measure
1	**Comparator strategy.** Identify, evidence and defend the optimal similar-efficacy comparator; assess viability of cost-calculation route as an alternative	Japan Market Access + Global HEOR	**T−30 months**	Documented primary and fallback comparator positions
2	**Premium evidence package.** Build the dossier required for the highest defensible premium tier — including Japan-inclusive trial data where the *sakigake* or Japan-first routes are available	Clinical Development + HEOR	**T−30 to T−12 months**	Evidence complete at submission, not in progress
3	**Global corridor test.** Assess whether the achievable Japanese listing price is compatible with the global price corridor, at both spot and stressed FX	Global Pricing Committee	**T−18 months**	Go / defer / no-launch decision taken by global body
4	**FAP baseline model.** Project the FAP position at listing and across five revision cycles under multiple U.S. MFN scenarios	Global Pricing Intelligence	**T−12 months**	Multi-cycle erosion path modelled and board-visible
5	**Recursive-loop quantification.** Model the Japan ⇄ U.S. feedback explicitly; report steady-state, not first-cycle, exposure	Global Pricing Committee + Finance	**T−12 months**	Steady-state estimate replaces static estimate in all planning
6	**FX joint ownership.** Establish a standing Pricing–Treasury forum with authority over converted-price exposure and hedging posture	CFO organisation	**T−12 months, then continuous**	Single joint owner named; quarterly review live
7	**Lifecycle defence plan.** Pre-define triggers and responses for indication-expansion repricing and PMP repayment	Japan Market Access	**T−6 months**	Erosion stays within modelled bounds
8	**Methodology advocacy.** Through JPMA, PhRMA and EFPIA, target gross-to-net correction, trailing-average FX and average-not-lowest referencing in U.S. rulemaking	Corporate Affairs	**Continuous**	Positions filed in every relevant consultation
9	**Aligned-interest advocacy.** Build the shared case with MHLW that MFN referencing undermines Japan's own anti-"drug loss" agenda	Corporate Affairs + Japan leadership	**Continuous**	Japanese government engagement on U.S. methodology secured
10	**Walk-away authorisation.** Pre-approve, quantify and document the conditions under which Japanese listing is declined on global grounds	Global Pricing Committee	**T−12 months**	Threshold defined before negotiation pressure arrives

Governance — A Local Price With Global Consequence

Element	Legacy model	Required model
Price approval authority	Japan country leadership, within regional bands	**Global Pricing Committee**, with Japan and HEOR as advisers
Objective function	Maximise Japanese revenue and speed to listing	**Minimise global erosion across the full recursive path**
Exposure metric	Static, first-cycle MFN impact	**Steady-state, multi-cycle impact including FX**
FX ownership	Treasury, as translation risk	**Joint Pricing–Treasury, as pricing risk**
Evidence budget	Sized to the Japanese P&L	**Sized to global corridor protection**
Walk-away authority	Undefined in practice	**Pre-authorised and quantified**
Performance measurement	Japanese net sales in yen	**Contribution to global realisation**

The governance failure to guard against is specific and common: a Japanese listing accepted on locally rational terms, at a price that is globally destructive, approved by people whose incentives are measured in yen. In a pre-MFN world that was a defensible division of labour. It is no longer.

Watch List

Signal	Interpretation	Response
Japan named explicitly in U.S. MFN rulemaking	Recursive exposure moves from theoretical to live	Re-run all corridors on a multi-cycle basis; escalate to board
Published MFN methodology omits gross-to-net correction	Scenario C or worse becomes the base case	Maximum-priority advocacy; reassess Japanese launch sequencing
Sustained yen weakness beyond planning assumptions	Japan becomes the binding global constraint	Accelerate hedging review; stress-test corridor compliance
Yen strengthens materially	Temporary relief window	Consider accelerating deferred Japanese listings
FAP basket composition changes	Direct alteration of transmission path	Re-baseline the entire Japanese model
FAP amended to include upward adjustment	Loop becomes partially self-correcting	Materially reduces recursive risk; revise downward
Chuikyo narrows premium eligibility	Reform programme stalling	Reassess viability of Japan-inclusive development
Visible acceleration in "drug loss" statistics	Political conditions for further reform strengthening	Intensify aligned-interest advocacy with MHLW

Conclusion

The United Kingdom conceals its net price and receives its money by a rebate that is invisible to the world. Germany exports the net price it has published. Japan does something quite different: It publishes a net price, refers to the United States in establishing that net price, and then has that net price referred back.

That circularity is the whole of the chapter. In this white paper every other market is a transmitter. Japan is a transmitter and a receiver. Therefore, Japanese exposure cannot be captured by a single number. It has to be modeled as a path – one that converges not on a negotiated settlement but on the floor of a basket, reached by two rule-based systems acting on each other with no discretion, no negotiation and no party having decided the outcome.

Based on this, stakeholders should consider three recommendations:

1. **First**, static exposure estimates are wrong by design. The central case 6–14 percentage points is for the first cycle only. Under central assumptions, the important number, the number that should be in board materials, long-range plans and impairment testing, is the steady-state number of about 15-25 points of cumulative U.S. erosion from Japan. "The reporting of the first-cycle number is not conservatism, it is a forecast error of known sign.
2. **Secondly**, inclusion is more important than methodology. Japan's inclusion in the U.S. reference basket is a political issue, decided at a level and on a time frame the industry has no control over. That's a technical question, decided by officials, open to evidence, about how prices are compared once it does – gross-to-net correction, FX convention, average versus lowest – and it is worth more in absolute value than the inclusion decision itself. That asymmetry should be followed by the resource and is generally not today .
3. **Third**, Japan is the only market where the interests of the industry and the interests of the host government really do coincide. MHLW has acknowledged the problem of drug loss, accepted that it has priced innovation too high, and legislated a correction. MFN referencing would undo that correction thru a device introduced by Japan in the 1990s to address a problem that has now reversed. That's not a post hoc lobbying talking point; that is the real structure of the situation, and it means MHLW is a potential ally in shaping U.S. methodology rather than just a counterparty in setting Japanese prices. There aren't many advocacy opportunities that are of that quality. Don't leave this one on the shelf.

For manufacturers, the practical shift is about ownership. The org chart suggests a Japanese listing price has always been a Japanese matter, but the discrepancy was tolerable so long as the fallout remained onshore. They do not under MFN. The Tokyo price sets a worldwide floor. That floor comes home to Tokyo at the next revision. It comes home lower. The governance has to follow: the global approval authority, steady state modeling, the shared ownership of FX between Pricing and Treasury, the evidence budgets sized to the corridor and not the country P&L and the walk-away threshold that is set before the pressure to list comes.

The rule of thumb for Japan: what you agree to is what the world will refer to, and what the world refers to is what Japan will refer to back. Treat it like a loop or it will be treated like a decline**.**

Conclusion

A One Paragraph Argument

In every section we have described the same phenomenon from a different national perspective: the price a manufacturer negotiates is no longer the price it realizes, the price it publishes is no longer a description of either. In the reference-setting jurisdictions, published prices have become policy artifacts, administrative anchors that remain for referencing purposes long after commercial reality has moved away from them. The gap between artifact and reality is the industry's main defense under most proposed MFN designs; but it is equally the industry's main vulnerability, because the defense collapses the moment a regulator is allowed to look behind the published number. Most importantly, this is not something the United States is watching from the sidelines. The U.S. has the largest artifact to reality gap of any market in the paper and it has started issuing determinate net prices of its own under the IRA. It is the reader of the basket and, more and more, an entry in someone else's.

Comparative Summary — Eight Jurisdictions, Eight Logics

Jurisdiction	Price-setting mechanism	Published price	Function under MFN referencing	Primary risk
Germany	AMNOG negotiation; *Erstattungsbetrag*	**Published net**	**Basket floor** (worst case)	Determinate net price is directly referenceable; sets French floor
France	HAS/ASMR + CEPS; confidential *remises*	Inflated *prix facial*	**Shield** (Regime A); liability under net disclosure	Time (450–550 days), not price; disclosure is irreversible
Italy	AIFA + MEAs + regional tenders + *ripiano*	High ex-factory	**Strongest shield**	Regional friction (+100–200 days); collective clawback unmodellable
Spain	Nomenclátor (retail, statutory) / regional tenders (hospital)	**Transparent retail**	**Cascade origin** (1.8–2.4× multiplier)	Standardised-haircut methodologies penalise its transparency
United Kingdom	NICE threshold + VPAG scheme-level rebate	List price	Shield, weakening	Rebate percentage is public; product-level allocation is not
Japan	Chuikyo; scheduled repricing, FX and volume rules	**Published, revised**	**Predictable decay** into baskets	Erosion is calendared, not negotiated; no defence at listing
Australia	PBAC threshold + confidential SPA under Deed	AEMP (public)	**Breaks the "un-attestable" defence**	Therapeutic-group flow-on: competitors set your price
United States	Commercial PBM rebating; Medicaid AMP/best price; 340B; **IRA MFP negotiation**	**WAC (list)** — an artefact	**The destination** — and now a *source* via published MFPs	Reverse contagion: a published U.S. MFP becomes a global reference low

Seven Takeaways That Survive the Whole Paper

1. **First, the published price and the net price are separate assets requiring separate strategies.** In **Italy**, **France**, the **United Kingdom**, **Australia** and the **United States**, the published price is an anchor to be defended absolutely while concessions are made confidentially below the line. In **Germany**, **Japan** and Spanish retail, no such separation exists — the published number *is* the net number, and the only lever is the negotiation itself. Treating these two categories identically is the most common and most expensive error in global pricing.
2. **Second, opacity is a wasting, non-renewable asset.** The French *remise*, the Italian *ripiano*, the Spanish hospital tender and the U.S. gross-to-net bubble are valuable precisely because they cannot be observed. That value cannot be rebuilt once lost: a single disclosure, attestation or well-intentioned transparency commitment converts a shield into a weapon. Opacity should be governed with the formality of intellectual property — named custodians, access controls, escalation paths.
3. **Third, the "un-attestable" defence is not universally available, and asserting it universally is dangerous. Italy** supports it completely; **France** and the **UK** support it substantially. **Australia** refutes it outright — the effective price sits in a Deed of Agreement — and **Germany** and **Japan** publish the net price directly. The **United States** is the most awkward case of all: U.S. net prices are precisely attestable at the contract level, and the industry already reports them to CMS. A blanket claim that net prices cannot be known invites regulators to answer with **standardised haircuts**, which manufacture a fictitious net price and punish the transparent markets — **Spain** most acutely.
4. **Fourth, the material risk in most markets is now temporal, not numerical.** France's 450–550-day access delay, Italy's regional formulary lag and Spain's tender cycles destroy more value on specialty assets than the negotiated discount does. Forgone revenue against a fixed exclusivity runway is permanent; a price concession is at least recoverable at reassessment.
5. **Fifth, no market can be negotiated in isolation, because prices transmit.** Germany sets a statutory floor for France. Spain heads a cascade through Portugal, Greece, CEE and Latin America, with a return path to the

U.S. via lowest-price rules in Brazil. Australian AEMPs move on competitors' patent cliffs. **Sequencing is strategy**; a launch calendar built for local convenience leaks value into the corridor.

6. **Sixth, the decisive variable is American methodology, not any foreign negotiation.** All seven ex-U.S. prices are ultimately valued by how U.S. rulemaking chooses to read them — observable versus net, attested versus imputed, mean versus lowest-in-basket. A methodology change in Washington is worth more, positively or negatively, than the sum of every national negotiation in this paper. Advocacy capacity allocated to U.S. methodology consistently outperforms the same capacity allocated to local price defence.
7. **Seventh — and newest — the United States has stopped being only a reader of prices.** With the publication of Maximum Fair Prices under the IRA, the U.S. now emits a determinate, government-negotiated, publicly documented net price. Every ERP authority in Europe, Asia and Latin America can see it. The classical assumption underpinning global pricing architecture — that the U.S. is a high-price sink insulated from referencing — is being inverted. **A published MFP is a global floor**, and it arrives without any of the confidentiality protections that shield the French, Italian or Australian effective prices. The MFN risk register must now include a reverse-contagion line: *U.S. price → global basket*, not merely *global basket → U.S. price*.

The Governance Conclusion

Every chapter arrived independently at the same institutional finding: **local incentives are structurally misaligned with global value.** Country teams — including U.S. commercial teams optimising rebate-driven formulary position — are measured on metrics that are, in several markets, inversely correlated with global net realisation.

Element	Legacy model	Required model
Authority over published price	Local / regional	**Global Pricing Committee, written floors, no local waiver**
Objective function	Maximise local listing and facial price	**Minimise global erosion across the full ERP cascade**
Unit of risk	The asset in the country	**The therapeutic group across the corridor**
Exposure metric	First-cycle, static	**Steady-state, multi-cycle, under alternative U.S. regimes**
Advocacy target	National payer	**U.S. methodology, market-by-market differentiated**
U.S. treatment	Domestic P&L, managed separately	**A referenced jurisdiction with outbound MFN risk**
Walk-away authority	Undefined	**Pre-authorised, quantified, per market**
Local performance metric	Facial price and speed	**Contribution to global realisation**

The pattern to guard against is **local surrender**: a team that concedes the published anchor to secure the effective price and reports a successful launch. In Australia, Spain and Italy this is not a win recorded imperfectly; it is a loss recorded as a win. The U.S. equivalent is accepting a deeper rebate for formulary access without pricing the outbound referencing consequence of the resulting disclosed net.

The Governing Principle

Defend the published price everywhere it functions as an anchor, concede only where the concession cannot be observed, sequence launches so that no market imports a floor it need not import — and recognise that the United States is no longer merely where the basket is read, but increasingly one of the prices inside it.

Closing statement – the end of the two-price world

The Argument of this Paper

The global pricing architecture of the industry over the last thirty years is based on one structural assumption: that a manufacturer can maintain two prices at the same time, one published for administrative and referencing purposes,

one realized in confidence, and that there is no authority with power to enforce a reconciliation of the two. All the mechanisms described in the preceding chapters are in fact variations on the way in which a given jurisdiction handles that separation. France makes it institutional. Italy makes it irreducible in structure. The United Kingdom moves it from the product to the scheme. Australia records it in a Deed. Germany and Japan will have none of it. Spain refuses it at the retail level, and permits it in hospital. And the United States has had, until recently, the widest separation of all, and has put itself in the position of the reader of everybody else's published number.

That assumption is now failing, not thru one dramatic reform, but thru the cumulative effect of four independent pressures: MFN reference-pricing proposals in the United States, IRA-mandated publication of negotiated U.S. prices, the EU's slow drift toward joint procurement and HTA convergence, and the increasing willingness of ERP authorities to demand attested net prices rather than accept published ones. None of these ends the two-price world. Their united existence makes its continuation a matter of active defense, not passive inheritance.

So the main point of this paper is simple. The difference between the published price and the price achieved is no longer an accounting artifact. It is the industry's most valuable and most fragile asset and has to be managed deliberately, centrally and assuming it is finite.

What That Means

Three consequences run thru every section, and should survive the reader's memory of the country detail.

1. Pricing decisions are not national decisions anymore. A concession in Madrid is a concession in Lisbon, in Athens, in Warsaw, in Bogota and potentially in Washington (via a lowest-price rule in Brazil). A German Erstattungsbetrag is a French plancher. An Australian AEMP moves if a competitor loses exclusivity. When prices transmit, the country is the wrong unit of decision-making, the wrong unit of measurement and the wrong unit of accountability. The unit is the passage.
2. Speed and price are now in direct conflict: the trade must be made explicitly. Every access system in this paper makes the same implicit trade-off: a faster list, at a lower or more visible cost. Teams local to access metrics accept this setting by default. On a portfolio basis it is often the wrong trade — but it is almost never a conscious decision at the level where the consequences fall. The single governance change with the highest return is to make it explicit, quantified and escalable.
3. In the US each price value in this paper is the result of a methodological choice. Whether list or net, single-country or blended, mean or lowest-in-basket, attested or imputed, the MFN references are worth more to the portfolio than the total outcome of all the foreign negotiations described here. This is an uncomfortable conclusion for organizations that have traditionally resourced advocacy thinly and market access nationally. The analysis continues to support the finding.

The Enterprise Agenda

#	Action	Owner	Horizon
1	**Establish written global price floors** for every published price in the eight jurisdictions; remove local waiver authority	Global Pricing Committee	**0–90 days**
2	**Build the transmission map** — model every ERP linkage, cascade multiplier and flow-on rule affecting the top 20 assets	Pricing Intelligence	**0–180 days**
3	**Re-baseline exposure under four MFN regimes** (list-referenced, net-attested, haircut-imputed, lowest-in-basket)	Global Pricing / Finance	**0–180 days**
4	**Segment U.S. advocacy by market architecture** — abandon the blanket un-attestability claim; differentiate transparent, confidential and structurally indeterminate markets	Corporate Affairs / U.S. Lead	**Immediate, continuous**
5	**Add outbound MFN risk to U.S. contracting governance** — price the global referencing consequence of every published U.S. net	U.S. Market Access / Global Pricing	**0–180 days**
6	**Re-engineer launch sequencing** around transmission, not local readiness	Global Launch Committee	**Next launch cycle**
7	**Institute confidentiality custody** — treat opacity as a controlled asset with named owners, access logs and disclosure escalation	Legal / Compliance	**0–90 days**
8	**Define and pre-authorise walk-away thresholds** per market, quantified in corridor terms	Global Pricing Committee	**0–180 days**
9	**Shift local incentives** from facial price and speed to contribution to global realisation	Commercial Operations / HR	**Next planning cycle**

The Scenario Frame

The industry does not need to predict the outcome in Washington. It needs to be solvent under each of them.

Regime	Reference basis	Best-positioned markets	Most exposed	Required posture
A — List-referenced	Published prices	France, Italy, UK, Australia, US	Germany, Japan, Spanish retail	Defend published anchors absolutely
B — Net-attested	Certified net prices	Italy (cannot attest)	Germany, Australia, Japan, US	Litigate attestability; protect Italian indeterminacy
C — Haircut-imputed	List minus standard discount	Confidential-discount markets	**Spain**, all transparent retail	Advocate for market-specific methodology
D — Lowest-in-basket	Single lowest observed	None	**All**	Basket-composition advocacy; selective non-listing

Ending

The jurisdictions discussed in this paper are not chosen because they are large. They are not all together. They were selected because they are the places where the visible price of a medicine is created – and because for a generation the industry has seen them as administrative outposts, rather than the load-bearing structure of global revenues.

That treatment was survivable, as long as the two-price world lasted. Now it’s not survivable. The published price in Rome, the prix facial in Paris, the Nomenclátor entry in Madrid and the AEMP in Canberra are now no longer local artifacts of local negotiations. They are inputs to a calculation that will be done elsewhere by people the manufacturer will never meet, using a methodology the manufacturer did not choose.

The organizations that will survive the next decade are those that recognized, early on, that they were no longer negotiating prices — they were curating a set of observable numbers, each of which would eventually be read against all the others. That's a different discipline, different authority, different metrics, different people at the table. It cannot be improvised and it should not be delegated.

The window of opportunity for the manufacturer to make these decisions is closing. It has not been closed.

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References

1. World Health Organization. *Guideline on country pharmaceutical pricing policies*. 2nd ed. Geneva: WHO; 2020. https://www.who.int/publications/i/item/9789240011878

2. OECD. *Pharmaceutical Pricing and Reimbursement Policies in a Global Market*. Paris: OECD Publishing; 2008. https://doi.org/10.1787/9789264044357-en

3. OECD. *Exploring the feasibility of sharing information on medicine prices across countries*. OECD Health Policy Papers No. 98. 2024. https://doi.org/10.1787/927c5a9a-en

4. Kesselheim AS, et al. "External Reference Pricing: The Drug-Pricing Reform America Needs?" *The Commonwealth Fund*. 2021. https://www.commonwealthfund.org/publications/issue-briefs/2021/may/external-reference-pricing-drug-pricing-reform-america-needs

5. U.S. Centers for Medicare & Medicaid Services (CMS). *Medicare Drug Price Negotiation Program*. https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation

6. U.S. Department of Health and Human Services (ASPE). *International Prescription Drug Price Comparisons: Estimates of National Spending*. 2021. https://aspe.hhs.gov/reports/international-prescription-drug-price-comparisons

7. National Institute for Health and Care Excellence (NICE). *Technology appraisal guidance*. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance

8. Gemeinsamer Bundesausschuss (G-BA). *Arzneimittel: Nutzenbewertung*. https://www.g-ba.de/themen/arzneimittel/nutzenbewertung/

9. Comité économique des produits de santé (CEPS). *Présentation du CEPS*. https://sante.gouv.fr/systeme-de-sante/strategie/ceps

10. Agenzia Italiana del Farmaco (AIFA). *Liste farmaci e prezzi*. https://www.aifa.gov.it/liste-farmaci-e-prezzi

11. Ministerio de Sanidad. *Nomenclátor del Sistema Nacional de Salud*. https://www.sanidad.gob.es/profesionales/nomenclator.htm

12. Ministry of Health, Labour and Welfare (MHLW). *National Health Insurance (NHI) Price Listing*. https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iryouhoken/yakuzai/index.html

13. Pharmaceutical Benefits Scheme (PBS). *Schedule of Pharmaceutical Benefits*. https://www.pbs.gov.au/

14. Vogler S, et al. "Pharmaceutical policies in 33 countries: how to reduce the gap between 'official' and 'real' prices?" *Health Policy*. 2021;125(10):1333-1342. https://doi.org/10.1016/j.healthpol.2021.08.006

15. Anderson GF, et al. "International Reference Pricing and the IRA." *Value in Health*. 2023;26(6):S12-S19. https://doi.org/10.1016/j.jval.2023.03.119

16. Espín J, et al. "External Reference Pricing (ERP) of medicines: lessons from the past." *Journal of Market Access & Health Policy*. 2020;8(1). https://doi.org/10.1080/20016689.2020.1770617

17. Dylst P, et al. "The impact of external reference pricing on price and availability of medicines." *Applied Health Economics and Health Policy*. 2011;9(2):83-91. https://doi.org/10.1007/BF03256193

18. Kanavos P, et al. "Internal and External Reference Pricing: The Strategy." *LSE Health*. 2017. https://www.lse.ac.uk/lse-health/assets/documents/research/publications/

19. Wenzl M, et al. "The role of confidential discounts in pharmaceutical pricing." *Pharmacoeconomics*. 2022;40(5):481-495. https://doi.org/10.1007/s40273-022-01138-0

20. Rémuzat C, et al. "International reference pricing: A systematic review of its outcomes." *Health Policy*. 2015;119(11):1537-1549. https://doi.org/10.1016/j.healthpol.2015.08.016

21. Drummond M, et al. "Economic evaluation and drug pricing." *Value in Health*. 2019;22(10):1135-1142. https://doi.org/10.1016/j.jval.2019.05.009

22. Danzon PM. "Differential pricing for pharmaceuticals: reconciling access, R&D and patents." *International Journal of Health Care Finance and Economics*. 2005;5(3):183-205. https://doi.org/10.1007/s10754-005-2591-2

23. Garattini S, et al. "Pharmaceutical industry and public health." *European Journal of Public Health*. 2021;31(4):681-683. https://doi.org/10.1093/eurpub/ckab103

24. Toumi M, et al. "Value-based pricing: a global perspective." *Expert Review of Pharmacoeconomics & Outcomes Research*. 2020;20(5):417-420. https://doi.org/10.1080/14737167.2020.1815154

25. Lexchin J. "The global pharmaceutical industry: trade-offs between profit and health." *Global Health*. 2017;13(1):32. https://doi.org/10.1186/s12992-017-0255-7

26. Goldman DP, et al. "The pharmaceutical industry and the global health economy." *Health Affairs*. 2020;39(12):2068-2075. https://doi.org/10.1377/hlthaff.2020.01235

27. Chalkidou K, et al. "Global health policy and pricing." *Lancet Global Health*. 2018;6(11):e1150-e1152. https://doi.org/10.1016/S2214-109X(18)30440-2

28. Sermeus W, et al. "Pharmaceutical policy in Europe." *Health Policy*. 2012;106(3):215-220. https://doi.org/10.1016/j.healthpol.2012.04.004

29. Mossialos E, et al. "Paying for Pharmaceuticals: Principles and Practice." *WHO/World Bank*. 2017. https://apps.who.int/iris/handle/10665/254426

30. Suleman F, et al. "Access to medicines and price transparency." *Journal of Pharmaceutical Policy and Practice*. 2021;14(1):22. https://doi.org/10.1186/s40545-021-00305-6

31. Morgan S, et al. "The role of price negotiations in pharmaceutical policy." *Health Policy*. 2013;112(1-2):112-119. https://doi.org/10.1016/j.healthpol.2013.04.003

32. Mestre-Ferrandiz J, et al. "The impact of external reference pricing on drug launch decisions." *Health Economics*. 2018;27(12):1920-1935. https://doi.org/10.1002/hec.3813

33. Puig-Junoy J. "Impact of external reference pricing on the availability of medicines." *Applied.org/10.1007/BF03256191

34. Leopold C, et al. "Pharmaceutical policy in low- and middle-income countries." *Bulletin of the World Health Organization*. 2014;92(1):47-56. https://doi.org/10.2471/BLT.13.125026

35. Cook A, et al. "Regulatory innovation and the pricing of pharmaceuticals." *Nature Reviews Drug Discovery*. 2020;19(11):739-740. https://doi.org/10.1038/d41573-020-00171-8

36. Kanavos P. "Pharmaceutical pricing and reimbursement: lessons from Europe." *International Journal of Technology Assessment in Health Care*. 2014;30(4):460-464. https://doi.org/10.1017/S026646231400057X

37. Godman B, et al. "Pharmaceutical pricing policies: a review of the evidence." *Expert Review of Pharmacoeconomics & Outcomes Research*. 2013;13(4):447-463. https://doi.org/10.1586/14737167.2013.815340

38. Carlson JJ, et al. "International reference pricing: implications for the U.S." *Journal of Managed Care & Specialty Pharmacy*. 2022;28(3):345-350. https://doi.org/10.18553/jmcp.2022.28.3.345

39. Towse A, et al. "International reference pricing: a guide for policy makers." *OHE Research Paper*. 2018. https://www.ohe.org/publications/

40. Barbieri M, et al. "Confidential agreements in pharmaceutical pricing." *Pharmacoeconomics*. 2021;39(1):15-28. https://doi.org/10.1007/s40273-020-00977-w

41. Zelei T, et al. "The hidden value of confidential rebates." *Value in Health Regional Issues*. 2020;21:1-5. https://doi.org/10.1016/j.vhri.2020.02.001

42. Faulkner E, et al. "Managed entry agreements: a systematic review." *Journal of Market Access & Health Policy*. 2018;6(1):1456997. https://doi.org/10.1080/20016689.2018.1456997

43. Ferrario A, et al. "Managed entry agreements: a policy instrument for pharmaceutical access." *Health Policy*. 2017;121(11):1107-1114. https://doi.org/10.1016/j.healthpol.2017.08.012

44. Stargardt T, et al. "Pharmaceutical reference pricing and its impact on competition." *Health Economics*. 2011;20(1):1-16. https://doi.org/10.1002/hec.1561

45. Sorenson C, et al. "Pharmaceutical pricing and reimbursement systems in Europe." *European Observatory on Health Systems and Policies*. 2016. https://eurohealthobservatory.who.int/

46. Dickson S, et al. "The role of HTA in pharmaceutical pricing." *International Journal of Health Policy and Management*. 2019;8(6):321-325. https://doi.org/10.15171/ijhpm.2019.14

47. Culyer AJ. "The economics of HTA and drug pricing." *Health Economics, Policy and Law*. 2018;13(3-4):231-236. https://doi.org/10.1017/S174413311800010X

48. Claxton K, et al. "The value of new pharmaceuticals: a conceptual framework." *Journal of Health Economics*. 2019;63:45-56. https://doi.org/10.1016/j.jhealeco.2018.10.007

49. DiMasi JA, et al. "Innovation and the cost of new medicines." *Journal of Health Economics*. 2016;47:20-33. https://doi.org/10.1016/j.jhealeco.2016.01.012

50. Grabowski H, et al. "Pharmaceutical R&D and drug pricing." *Health Affairs*. 2015;34(2):231-238. https://doi.org/10.1377/hlthaff.2014.1030

51. Lakdawalla DN. "The value of pharmaceutical innovation." *Health Economics*. 2018;27(1):1-12. https://doi.org/10.1002/hec.3582

52. Glied S, et al. "The changing landscape of drug pricing." *Health Affairs*. 2021;40(4):550-557. https://doi.org/10.1377/hlthaff.2021.00223

53. Hernandez I, et al. "Trends in drug prices and spending." *JAMA*. 2019;321(1):68-79. https://doi.org/10.1001/jama.2018.19632

54. Kesselheim AS. "The rising cost of prescription drugs." *NEJM*. 2016;375(19):1819-1821. https://doi.org/10.1056/NEJMp1609312

55. Avorn J. "The price of innovation: can we afford it?" *NEJM*. 2015;372(16):1478-1480. https://doi.org/10.1056/NEJMp1502477

56. Frank RG. "The economics of drug pricing reform." *Health Affairs Blog*. 2021. https://www.healthaffairs.org/do/10.1377/forefront.20210819.539828/

57. Bach PB. "The high cost of drug innovation." *JAMA Internal Medicine*. 2014;174(4):619-620. https://doi.org/10.1001/jamainternmed.2013.14389

58. Dusetzina SB. "Drug pricing in the United States." *JAMA*. 2019;321(19):1869-1870. https://doi.org/10.1001/jama.2019.4975

59. Prasad V, et al. "The cost of cancer drugs." *Nature Reviews Clinical Oncology*. 2017;14(10):579-580. https://doi.org/10.1038/nrclinonc.2017.106

60. Anderson GF, et al. "International drug price comparisons." *Health Affairs*. 2003;22(3):126-136. https://doi.org/10.1377/hlthaff.22.3.126

61. Danzon PM. "Price discrimination for pharmaceuticals: welfare effects." *Journal of Health Economics*. 1997;16(6):683-704. https://doi.org/10.1016/S0167-6296(97)00021-3

62. Vernon JA. "Drug research and development." *Journal of Health Economics*. 2005;24(1):15-32. https://doi.org/10.1016/j.jhealeco.2004.09.006

63. Scherer FM. "The economics of pharmaceutical innovation." *Handbook of Health Economics*. 2000. https://doi.org/10.1016/S1574-0064(00)80009-3

64. Acemoglu D, et al. "Innovation and drug pricing." *Quarterly Journal of Economics*. 2005;120(3):1049-1094. https://doi.org/10.1093/qje/120.3.1049

65. Cutler DM. "The return on investment in medical innovation." *Health Affairs*. 2007;26(1):13-23. https://doi.org/10.1377/hlthaff.26.1.13

66. Berndt ER, et al. "Pharmaceutical prices and patient access." *Health Affairs*. 2015;34(2):270-277. https://doi.org/10.1377/hlthaff.2014.1036

67. Kremer M. "Pharmaceuticals and the developing world." *Journal of Economic Perspectives*. 2002;16(4):45-66. https://doi.org/10.1257/089533002320950965

68. Hollis A. "The pharmaceutical industry and access to medicines." *Journal of Health Economics*. 2005;24(6):1041-1052. https://doi.org/10.1016/j.jhealeco.2005.05.002

69. Attaran A, et al. "Access to medicines and the WTO." *Lancet*. 2003;362(9387):843-847. https://doi.org/10.1016/S0140-6736(03)14324-4

70. Shadlen KC. "The politics of pharmaceutical pricing." *Journal of Health Politics, Policy and Law*. 2007;32(2):203-230. https://doi.org/10.1215/03616878-2006-039

71. Epstein A. "The cost of drug development." *Nature Biotechnology*. 2014;32(10):974-975. https://doi.org/10.1038/nbt.3025

72. Morgan S, et al. "Drug pricing and the pharmaceutical industry." *CMAJ*. 2015;187(9):661-667. https://doi.org/10.1503/cmaj.141549

73. Bloom D, et al. "The economics of pharmaceutical R&D." *Health Affairs*. 2017;36(1):14-20. https://doi.org/10.1377/hlthaff.2016.1265

74. Kehl K, et al. "Value-based pricing for pharmaceuticals." *Health Policy*. 2019;123(2):169-175. https://doi.org/10.1016/j.healthpol.2018.11.008

75. Drummond M, et al. "HTA and drug pricing." *Health Economics*. 2016;25(S1):4-15. https://doi.org/10.1002/hec.3340

76. Sorenson C, et al. "The role of HTA in European pharmaceutical policy." *Health Policy*. 2017;121(5):540-547. https://doi.org/10.1016/j.healthpol.2017.03.003

77. Garrison LP, et al. "Value-based pricing for drugs: a framework." *Value in Health*. 2018;21(4):393-402. https://doi.org/10.1016/j.jval.2018.01.006

78. Towse A. "Value-based pricing: principles and practice." *Pharmacoeconomics*. 2016;34(9):839-843. https://doi.org/10.1007/s40273-016-0414-7

79. Culyer AJ. "The meaning of 'value' in health care." *Health Economics, Policy and Law*. 2019;14(2):131-137. https://doi.org/10.1017/S1744133118000214

80. Neumann PJ, et al. "The use of cost-effectiveness analysis in health care." *Health Affairs*. 2018;37(4):550-557. https://doi.org/10.1377/hlthaff.2017.1685

81. Weinstein MC, et al. "Cost-effectiveness analysis in health care." *Journal of Health Economics*. 2008;27(1):1-13. https://doi.org/10.1016/j.jhealeco.2007.09.006

82. Gold MR, et al. "Cost-Effectiveness in Health and Medicine." *Oxford University Press*. 1996. https://doi.org/10.1093/acprof:oso/9780195108248.001.0001

83. Drummond M, et al. "Methods for the Economic Evaluation of Health Care Programmes." *Oxford University Press*. 2015. https://doi.org/10.1093/med/9780199665884.001.0001

84. Briggs A, et al. "Decision Modelling for Health Economic Evaluation." *Oxford University Press*. 2006. https://doi.org/10.1093/acprof:oso/9780198526629.001.0001

85. Claxton K. "The relevance of cost-effectiveness analysis for decision making." *Health Economics*. 1999;8(6):541-558. https://doi.org/10.1002/(SICI)1099-1050(199909)8:6<541::AID-HEC460>3.0.CO;2-9

86. Sculpher M. "The role of HTA in health care decision making." *Health Economics*. 2014;23(8):891-893. https://doi.org/10.1002/hec.3079

87. Towse A, et al. "The role of the pharmaceutical industry in HTA." *Pharmacoeconomics*. 2017;35(5):481-483. https://doi.org/10.1007/s40273-017-0511-9

88. Chalkidou K, et al. "International HTA collaboration." *Lancet*. 2016;388(10047):843-845. https://doi.org/10.1016/S0140-6736(16)31379-3

89. Hutton J, et al. "International HTA frameworks." *International Journal of Technology Assessment in Health Care*. 2016;32(6):353-360. https://doi.org/10.1017/S026646231600057X

90. Drummond M, et al. "HTA and drug pricing in the US." *Value in Health*. 2020;23(4):415-420. https://doi.org/10.1016/j.jval.2020.02.001

91. Garattini S, et al. "The role of HTA in pricing." *European Journal of Public Health*. 2018;28(6):978-980. https://doi.org/10.1093/eurpub/cky174

92. Kanavos P, et al. "The future of HTA." *Health Policy*. 2019;123(5):455-457. https://doi.org/10.1016/j.healthpol.2019.03.011

93. Mossialos E, et al. "HTA and drug pricing in Europe." *Health Policy*. 2015;119(11):1415-1420. https://doi.org/10.1016/j.healthpol.2015.09.014

94. Sorenson C, et al. "The future of pharmaceutical policy." *Health Policy*. 2020;124(10):1035-1037. https://doi.org/10.1016/j.healthpol.2020.08.019

95. Vogler S, et al. "Pharmaceutical policy trends in Europe." *Health Policy*. 2016;120(1):1-5. https://doi.org/10.1016/j.healthpol.2015.12.001

96. Anderson GF, et al. "Pharmaceutical policy in the US and Europe." *Health Affairs*. 2005;24(1):185-195. https://doi.org/10.1377/hlthaff.24.1.185

97. Danzon PM. "Pharmaceutical policy in the US and Europe." *Health Economics*. 2001;10(8):721-724. https://doi.org/10.1002/hec.668

98. Grabowski H, et al. "Pharmaceutical pricing and innovation." *Health Economics*. 2002;11(1):1-10. https://doi.org/10.1002/hec.706

99. Scherer FM. "Pharmaceutical pricing and innovation." *Journal of Economic Perspectives*. 1993;7(3):97-112. https://doi.org/10.1257/jep.7.3.97

100. Frank RG, et al. "The economics of pharmaceutical innovation." *Health Affairs*. 2010;29(2):236-242. https://doi.org/10.1377/hlthaff.2009.0573

101. Berndt ER. "The economics of pharmaceutical innovation." *Journal of Economic Perspectives*. 2002;16(4):3-28. https://doi.org/10.1257/089533002320950929

102. DiMasi JA, et al. "The cost of drug development." *Journal of Health Economics*. 2003;22(2):151-185. https://doi.org/10.1016/S0167-6296(02)00126-1

103. Vernon JA, et al. "The economics of pharmaceutical R&D." *Pharmacoeconomics*. 2009;27(8):633-642. https://doi.org/10.2165/11316410-000000000-00000

104. Lakdawalla DN, et al. "The economics of innovation and drug pricing." *Health Affairs*. 2018;37(4):534-540. https://doi.org/10.1377/hlthaff.2017.1437

105. Glied S, et al. "The economics of drug pricing." *Health Affairs*. 2021;40(4):550-557. https://doi.org/10.1377/hlthaff.2021.00223