The Rise of Geopolitics in Health Policy: "*Most Favored Nation*" Policy in the United States and International Reference Pricing

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FUNCAS Social and Economic Studies, 11

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CONFLICT OF INTEREST:

The author is vice-president of the Advisory Committee for the Financing of Pharmaceutical Provision (CAPF) of the Spanish Ministry of Health.

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ABBREVIATIONS USED

Acronyms	Description
CAPF	Spanish Advisory Committee for the Financing of Pharmaceutical Provision
CBO	Congressional Budget Office
DDD	Defined Daily Dose
EU	European Union
FDA	Food and Drug Administration
GCEA	Generalized Cost-Effectiveness Analysis
GLP-1	Glucagon-Like Peptide-1
GLOBE	Global Benchmark for Efficient Drug Pricing
GPO	Group Purchasing Organization
GUARD	Guarding U.S. Medicare against Rising Drug Costs
HTA	Health Technology Assessment
IPB	International Pricing Benchmark
IRA	Inflation Reduction Act
IRP	International Reference Pricing
MDPNP	Medicare Drug Price Negotiation Program
MDRP	Medicaid Drug Rebate Program
MFN	Most Favored Nation
NPLB	No Patient Left Behind
OECD	Organisation for Economic Co-operation and Development
PBM	Pharmacy Benefit Manager(s)

Acronyms	Description
PPP	Purchasing Power Parity
PMPRB	Patented Medicine Prices Review Board (Canada)
POLI	Global Data Pharmaceutical Prices (POLI)
QALY	Quality-Adjusted Life Year
R&D	Research and Development
URA	Unit Rebate Amount
US	United States
VA	Veterans Health Administration
VBDP	Value-Based Differential Pricing
VBP	Value-Based Pricing
VPAG	Voluntary Scheme for Branded Medicines Pricing and Access (UK)
ZCTA	ZIP Code Tabulation Area

ABSTRACT

This document deals with the economics of the new drug pricing policy measures in the United States (US) generically known as "*Most Favored Nation*" (MFN) and their expected impact in the US and in the European Union (EU). The main, though not the only, component of the MFN policy consists of the adoption of an international reference pricing (IRP) system in the US. Other components of the recent pricing policy in the US, such as tariff and trade policy, are not addressed here. The first part of this text describes the economic lessons learned from several decades of IRP implementation in Europe: the advantages of this type of policies, the design elements and problems, and the implications for the United States of the evidence on its application in Europe. The second part reviews the evidence on the growing price differential between the US and Europe that has served to justify the new policy in the US. The third part analyses the theoretical and empirical arguments on the free riding of ex-US prices and whether there really is an appropriate level of price differential. The fourth part describes the background and MFN policies in the US according to details known to this date (05/31/2026). The fifth part describes and analyses the expected impact of the MFN policies on prices, access, and R&D from both the US and European perspectives, emphasizing the economic logic and limitations of the reactive policies initially adopted in Europe as of this date (05/31/2026) to address the impact of the US MFN measures. Finally, the last section presents brief recommendations for Spain.

Executive summary

Lessons from the experience in the application of international reference prices (IRPs)

1. The main attractions of the application of IRPs have been the speed in achieving price reductions in the short term with very low transaction costs, avoiding costly investments in resources and time in HTA-type evaluation agencies and procedures.

2. The basic design of an IRP policy is based on four elements: the extension of the medicines included, the basket of comparator or reference countries, the choice or calculation of the reference price and the criteria for dynamic updating.

3. In the medium term, IRPs lead to a trend towards international price convergence, making it difficult for countries to pay prices inversely related to price elasticity, and with possible delays in the entry of new medicines and higher prices in the reference countries ("beggar thy neighbor").

4. Net prices tend to become confidential and non-observable prices through strategies of dual prices, invoice prices with non-transparent rebates and discounts, which leads to the announced "death" of IRPs as an effective instrument of price policy.

5. International launch strategies become interdependent and may affect patient access: delays and even renunciation of launch in large markets that aim to apply strictly an IRP observed in smaller and lower-income countries; faster launch in countries with higher prices.

6. The impact of IRPs on innovation is more controversial since the reduction in prices and expected future profits may affect R&D investment decisions; although, in the opposite direction, the reduction of own resources to finance R&D may have a positive effect on the productivity and efficiency of new medicines.

The differential in medicine prices between the United States and Europe

7. In the United States there has for years been a bipartisan consensus when interpreting the fact that the prices of new patented branded

medicines are much higher than in Europe as a way in which the rest of the world benefits from the United States paying most of the cost of R&D (global free riding).

8. The only international price indices available on medicine prices are invoice price indices and come from non-verifiable private information sources. There is no public information on net price indices, that is, on the level of discounts, rebates and returns applied to invoice prices in the United States and the rest of the world. It can be reasonably presumed that the difference between invoice prices and net prices is higher in the United States than in Europe. An assumption used by various researchers places the net price in the United States more than 37% below the invoice price.

9. The international comparison of invoice price indices in 2022, using the United States consumption basket, indicates that the price of patented branded medicines in the United States is more than double the same price in any of the five large European markets and that, instead, invoice prices of generic medicines are systematically quite higher in Europe.

10. The differences observed in 2018 and 2022 in the invoice price index of patented branded medicines in the United States and in the countries of the rest of the world with a GDP per capita equal to or higher than 60% of that of the United States, once adjusted by the purchasing power parity of GDP, have no statistically significant relationship with the GDP per capita of these countries, with the United States price index representing an abnormally high observation, or extreme in statistical terms.

The end of "taking advantage" of United States investment in R&D?

11. The economic literature provides two theoretical arguments in favor of the existence of differential prices in the pharmaceutical market in very different contexts: price discrimination by the monopolist in a free-price market (Lerner rule) and the contribution to optimal financing (ideal situation) of global R&D investment as a global public good (Ramsey rule). A price elasticity inversely related to the level of per capita income of countries makes differential prices desirable instead of uniform international prices both in terms of efficiency and equity, which could be the result towards which a global IRP system would tend.

12. The higher prices in the United States have their origin in the absence of price regulation within a framework of a higher willingness to pay and

of a policy of incentivizing innovation through prices, the United States being the largest world market and with a high capacity to influence global R&D. The exercise of purchasing power in the United States has been quite weak since the market is not centralized in a single purchaser, PBMs as intermediaries may have incentives not aligned with lower prices for insurers and patients, and the public Medicare program was legally prohibited from negotiating prices until 2023. This is an element of renunciation in the previous price policy in the US. The volume of purchases of public programs is not small at all and the comparison with the institutions that do exercise it, the VA, is very important.

13. Financing and pricing decisions in some of the largest European markets are based on centralized regulation and negotiation processes that have long been using health technology assessment (HTA), the imposition of internal reference prices with pharmacological and/or therapeutic equivalence, international reference prices, decision of exclusion or restrictive inclusion in insurance coverage, maximum willingness to pay per quality-adjusted life year gained, etc. Commonplace, very debatable, in United States policy is the fact of considering that Europe uses HTA as an excuse to pay less.

14. The contribution of each country to global R&D should be measured not only through price differentials but taking into account the quantity consumed, that is, through the volume of expenditure or sales of new patented branded medicines. The estimate of each country's per capita contribution to R&D highlights, as does the comparison of invoice prices, that the contribution of the United States is more than 100% higher than that of the largest European markets. This per capita contribution also has no statistically significant relationship with the income level of countries with a GDP per capita equal to or higher than 60% of that of the United States, the contribution of the United States being an abnormally high value, an extreme observation in statistical terms.

15. There is no theoretical evidence nor foundations from economic theory to sustain that the current value of investment in R&D as a global public good is the socially optimal one nor that the optimal per capita value of this contribution is closer to that of the United States than to that of the rest of high per capita income European countries. In particular, it is not clear that the observed allocation of resources maximizes health outcomes on a global scale, nor that it adequately reflects unmet medical needs, the burden of disease and the marginal social value of innovation.

"Most favored nation" (MFN) pricing policy in the United States

16. The first official proposal for the application of international reference prices can be situated in 2016 with the Obama administration. In 2020, already under the name of "most favored nation" (MFN), the first Administration introduced an international reference price-type proposal that ended up being annulled by the courts. With similar objectives aimed at reducing prices, the Biden administration approved in 2022 a law that meant the start of a negotiation process for a limited number of medicine prices in the Medicare program. In May 2025, an Executive Order of the second Trump administration reintroduced MFN price policies and announced that it would resort to voluntary agreements with the main pharmaceutical companies, with price reductions and investment commitments in the United States in exchange for exemption from tariffs.

17. The deployment of MFN pricing policies has been based on bilateral and voluntary government/industry agreements and three programs that affect publicly funded programs. As of 05/31/2026 the United States government has signed confidential agreements with 17 pharmaceutical companies, this being the preferred instrument for applying MFN prices: GENEROUS (Medicaid) with voluntary participation; and GUARD and GLOBE (Medicare), which are experimental in nature (25% of the population) and have mandatory participation. A political interpretation of the form of deployment of MFN prices interprets this instrument not so much as a policy but as a negotiation strategy based on tariff exemptions and softer criteria for applying the MFN price as a counterpart.

18. The known application framework (The Council of Economic Advisers, April 2026) of MFN pricing policies in confidential agreements with industry and the GENEROUS program (voluntary) is characterized by being able to be applied to all or most new medicines, a basket of reference countries composed of the G-7 countries, except the United States, plus Denmark and Switzerland; the reference price for the US will be the second lowest net price of this group of countries, reported by industry, adjusted by the purchasing power parity of each country's GDP.

19. The GLOBE and GUARD programs apply to certain therapeutic groups (18 groups in GUARD and only 7 in GLOBE), including in both cases oncology medicines; the basket of reference countries is expanded to 19 countries with a GDP per capita equal to or higher than 60% of that of the United States; and the reference price is the second lowest price observed in these countries, which may be the net price reported

by industry or the invoice price, also adjusted by the purchasing power parity of GDP.

Expected impact of MFN policies in the United States and in Europe

20. The main limitations related to the evaluation of the expected impact on prices and health benefit in the United States of MFN policies have to do with: (a) limitations in the diagnosis of the price problem in the United States and its institutional context (comparison of MFN with price negotiation; non-aligned incentives of PBMs; absence of criteria related to added therapeutic value and the incremental cost-effectiveness ratio); (b) limitations derived from the strategic reactions of industry and the reference countries (anchoring in the changing net price of other countries; increase in the probability of initial launch in the United States); and (c) limitations related to the practical implementation of this form of price regulation (absence and confidentiality of information on net prices, verification capacity, cost of auditing the information reported by companies; mandatory confidentiality clauses in other countries; regulatory weakness of confidential agreements in the medium term; lack of information on the detail of the criteria for calculating and updating product-by-product adjusted net prices).

21. In the short term, an increase in the net price in the reference countries is expected, as well as delays in launch in these countries, an increase in the mechanisms that increase confidentiality and that increase, at the same time, the difference between the invoice price and the net price in the reference countries; likewise a decrease in net prices in the United States in the short term and a moderate reduction in the medium and long term are expected.

22. A scenario of greater international price compression with a strict application of MFN prices and with observed net prices would still allow product-by-product international price differences according to the purchasing power parity of GDP and the frequency of updating the exchange rate to variations in net prices in each country, with different results according to the breadth of the number of countries included in the reference basket.

23. There is a certain consensus on the fact that the retrospective application of MFN prices to net prices of medicines that are already on the market in Europe will be a scenario still little compatible with an important international price compression. This may be due to regulatory downward inflexibility in price, to the budgetary impact on public accounts and to a

possible difference in net prices, when discounts and rebates on invoice prices are taken into account, much smaller than expected between the United States and Europe.

24. In the prospective application of MFN prices to new medicines launched on the market after the start of application of this policy in the United States, the impact on prices and access in Europe may be potentially important: higher entry prices in Europe together with an increase in the use of financing and purchasing instruments based on variable and scarcely transparent prices, as well as delays in commercialization in the reference and lower-price countries, combined with more restricted or conditioned coverage decisions in these countries, including coverage exclusions or non-launches.

25. The prediction of the expected impact on global innovation is really uncertain and the intuition of economic models is still too uncertain to translate into reasonable evidence. The Congressional Budget Office of the United States estimated that the reduction in expectations about future revenues may translate into a reduction in the entry of new medicines. The economic models that assume a reduction in global profits because of MFN prices go in the same direction. The marginal reduction in R&D investment could mean an increase in the productivity and efficiency of innovation from the social perspective, especially if European governments orient R&D through prices towards new medicines with greater added therapeutic value and better cost-effectiveness ratio.

26. The strategic response strategies of European governments and health systems to the prospective application of MFN prices may be based on different combinations of instruments and of heterogeneous objectives (health, budgetary, economic and commercial) according to pharmaceutical company and even according to indication or therapeutic group: (a) adjustment via net prices and pharmaceutical expenditure without affecting patient access (adaptive or accommodative strategy); (b) adjustment via net prices and patient access conditions (and willingness to pay per QALY gained) without affecting pharmaceutical expenditure; and, (c) delay of any adjustment in prices, expenditure and access (status quo while awaiting better information and less uncertainty) and adoption of evasive measures that hinder the effective application of MFN prices by the United States.

27. The initial response of new launches by the pharmaceutical industry in the first ten months after the first MFN Executive Order in the United

States indicates that the prospective application of MFN prices is leading the industry to have as its preferred objective entry and price setting in the United States and to delay launch in the reference countries. Well-designed empirical analyses will have to confirm this behavior and isolate the contribution to it of MFN prices from the rest of factors.

28. The agreement signed between the government of the United Kingdom and that of the United States is situated within the framework of the adaptive or accommodative strategy. This agreement means the acceptance by the United Kingdom of an increase in net prices of 25%, of the percentage of GDP devoted to medicines, of the percentage of public health expenditure devoted to medicines and an increase in the maximum cost threshold per QALY gained. As a counterpart, the United States government commits to exemption from the application of tariff measures to the United Kingdom and to not using the net price of this country as a reference price (with some limitations). The opportunity cost of this agreement in terms of life years renounced by the NHS may amount to an important figure of QALYs sacrificed annually.

29. The most important pharmaceutical markets of the European Union have introduced proposals for legislative changes (France, Spain, Germany and Italy) in the line of making transparency of net prices difficult as an instrument to mitigate the possible externalities of MFN prices in Europe. At the same time, a trend is already observed in some countries towards an increase in financing and purchasing policies based on variable prices (price-volume agreements, outcome-based agreements, etc.) and confidential discounts (Germany).

Recommendations for Spain

30. Pharmaceutical price and expenditure policy must be recognized not only as an instrument of health policy, but also, increasingly, as an instrument of industrial, commercial and economic geopolitics. Given that national measures may have a limited path, especially when the counterpart is the United States, it would be advisable to develop a joint European policy in which Spain has an important specific weight. Any strategy must evaluate the Spanish macroeconomic situation and avoid having the objectives of industrial, commercial and economic policy load their opportunity cost on the health budget.

31. Financing and price regulation/intervention decisions should preserve confidentiality before third parties of net prices and of other purchasing mechanisms equivalent to variable prices, preferably through a

confidentiality clause at European level. For new medicines with reduced or null added therapeutic value, it is recommended to establish prices with therapeutic equivalence criteria, supported by European tools for measuring added therapeutic value. Price premiums with respect to the comparator must be justified in a reasoned manner and preferably supported by evidence, especially when the incremental cost-effectiveness ratio exceeds a reference value. Likewise, it is recommended to consider a state virtual budgetary fund, preferably multiannual, compatible with the budgetary restriction of the Autonomous Communities, and to adopt decisions informed by the incremental cost per life year gained, risk-sharing agreements and dynamic reviews of financing and price.

32. The evaluation of efficacy, effectiveness and efficiency must clearly separate the transparent and independent evaluation of added therapeutic value and of the incremental cost-effectiveness ratio from decision-making on financing and price. Applications for financing and price of new medicines with a price higher than that of the comparator should mandatorily be accompanied by a budget impact analysis, an economic evaluation and, where appropriate, an economic impact study. These reports should be presented in accordance with periodically updated official good practice guidelines. An independent body should review the methodological quality of the studies submitted by industry, guarantee acceptable quality levels, synthesize the clinical and economic information, and report clearly and in a structured way on the main sources of uncertainty and on the type of appropriate risk-sharing agreements.

Chapter 1

WHAT HAVE WE LEARNED FROM INTERNATIONAL REFERENCE PRICING IN EUROPE?

This chapter analyzes the European experience with international reference prices, their economic foundations and their design problems. The arguments on differential prices, Ramsey rule, market separation and effects on launches are presented. The relationship between prices, incentives to innovation and alignment of R&D with social priorities is also introduced.

1.1. INTERNATIONAL REFERENCE PRICES: BEGGAR-THY-NEIGHBOR?

Since the 1990s, it has been a common practice in European health systems to use the price of patented medicines observed in other countries to inform price negotiations, regulation and/or also to establish maximum limits. A review of the literature and consultation with national decision-makers in 2015 (Rémuzat et al., 2015) already documents that only 2 of 31 European countries did not use international reference pricing (IRP) (international or external reference pricing or cross-reference pricing): United Kingdom and Sweden. In 23 countries IRPs were used as the most important criterion and in 6 countries as supporting information to negotiate and/or regulate prices.

Some obvious attractions of IRP are rapid implementation, apparently low transaction costs, potential reduction of new prices in the short term and regulatory simplicity compared with systems that require an effective and well-organized health technology assessment system[1] (HTA) such as value-based pricing (VBP). On the other hand, adopting as reference the price of countries with small economies and a low income level has been described by some authors as a policy of the "beggar-thy-neighbor" type (Rand et al., 2021): taking advantage of wealth inequalities between countries giving rise, probably, to higher prices for poorer countries, generating even more inequalities when prices from much poorer countries are adopted and also generating delays in access. In reality, an IRP-type regulation creates externalities for the reference countries in the form of higher prices, with a price that, if IRPs become globalized, tends towards the uniform price that maximizes the global profit of the monopoly, without this

[1] Health technology assessment: a systematic process for evaluating the characteristics, effects, and impacts of a health technology, including its clinical, economic, organizational, social, and ethical dimensions, in order to inform health-related decision-making.

meaning that it is necessarily a zero-sum game since some countries pay more and others pay less and others may be left out of the market.

1.2. DIFFERENTIAL PRICES VERSUS (ALMOST) UNIFORM PRICES

The most serious economic problem of IRPs, assuming that it is still possible to apply them (Persson & Jönsson, 2016), is not only that they are based on beggar thy neighbor in a zero-sum game, but that it may be that they impoverish us all by moving us away from the maximization of global health (optimal prices): "a zero-sum scenario in which nobody obtains any benefit" (Bohnet & Chilazi, 2025). Globalizing IRPs, as the adoption of this system in the US implies, may be equivalent to making it still more difficult to differentiate prices that would allow each country to pay according to its income level as an imperfect approximation to the inverse elasticity pricing rule (Ramsey prices[2]; Danzon, 2018); that is, differential prices instead of (almost) uniform prices. In reality, the Ramsey price solution would correspond to an ideal situation in which a global regulator maximizes joint social welfare (consumer and producer surplus).

With countries that differ in income level and willingness to pay (for example, higher cost thresholds per quality-adjusted life year -QALY-), the optimal way to finance the joint and sunk costs of R&D at the moment of reaching the market is, in theory, through differential prices: the countries that are less price-sensitive pay more and even so all countries gain, while the monopolist can maximize profits; all countries maximize access to innovations (static efficiency) and there are strong incentives to invest in R&D (dynamic efficiency). This may justify the existence of international price differences (Schmidt et al., 2001). The application of economic theory on optimal prices and financing of global R&D, following Ramsey prices, does not justify proposals for single and uniform international prices for all higher-income OECD countries, as is the case of the proposal by Ho and Pakes (2025), since even among these countries there are important differences in the level of per capita income.

[2] Ramsey pricing has its origins in the work of the British mathematician and economist Frank P. Ramsey, particularly in his 1927 article on optimal taxation. Ramsey's central insight was that, when a government needs to raise revenue while minimizing distortions in economic behavior, the highest tax rates should be applied to goods for which demand is least sensitive to price changes. This idea was later adapted to pricing in regulated industries and public services, where companies typically need to recover fixed costs while avoiding excessive welfare losses. In this context, Ramsey pricing became a rule for setting markups on marginal cost based on demand elasticities: services with inelastic demand carry higher markups, while services with elastic demand carry lower markups.

1.3. RAMSEY RULE AND SEPARABLE MARKETS

Differential prices require separable markets, that is, the prices of one country must be independent of the price in the other countries: arbitrage through parallel trade must not be possible (Oxera, 2008) or, as an equivalent policy, the lowest price observed in low-income countries must not be used in high-income countries, that is, without IRP policies. There is consensus on this in economic theory. Disagreement appears in the fact that the Ramsey rule of 1927 does not by itself provide a normative guide on how differential prices between countries should be from the point of view of equity. The rule establishes that margins over marginal cost must vary inversely to the price elasticity of demand: markets with less elastic demand would bear higher margins, while those with more elastic demand would bear lower margins. In the case of medicines, this may translate into higher prices in higher-income countries if their demand is less price-sensitive, but Ramsey theory does not directly determine what "fair" proportion of the fixed and sunk costs of R&D each country should bear. That question requires additional criteria of equity, ability to pay or health policy. Ramsey prices ignore the existence of insurance, which in practice weakens price elasticities; in addition, Ramsey prices are optimal prices for an objective of efficiency, not of dynamic efficiency as is the case of global financing of R&D (Danzon, 2018). Hence economic theory helps little in this case to determine the fair proportion of these costs that each country should bear.

Health economics has provided a useful tool to approximate this proportion that must influence how differential prices should be between countries: value-based differential prices[3] (VBDP) (Danzon et al., 2013; Danzon, 2018). VBDP are based on the principle that the prices of each country, with different income levels, should be a reflection of its willingness to pay for defined improvements in health, for example, through the controversial maximum limits or thresholds per QALY (Puig-Junoy, 2026).

1.4. IRP DESIGN: IS "GOOD PRACTICE" POSSIBLE?

The details of an IRP system, as shown by the heterogeneity of the evidence of the comparative system (Gill et al., 2019), notably influence its

[3] Value-based pricing is an approach to pricing medications, medical devices, or health technologies in which the price is linked to the therapeutic, clinical, and economic value provided by the technology, typically in comparison with available alternatives. This value can be measured using health outcomes, quality-adjusted life years (QALYs), cost-effectiveness, disease severity, unmet medical need, and budgetary impact. Differential value-based pricing involves applying different prices for the same health technology based on the value that technology provides in different contexts, countries, indications, patient groups, or health care systems. These differential prices may reflect differences in comparative effectiveness, avoided costs, willingness or ability to pay, disease burden, available therapeutic alternatives, cost-effectiveness thresholds, or budget constraints.

impact and make the design of this policy itself difficult and may dilute it to almost a fiction in practice. To assess the adoption of an IRP system in the United States (US), it is necessary to know the main basic parameters (Frank et al., 2022) for the design and evaluation of good practices (Gill et al., 2019) of a pricing policy of this type.

- First, which medicines are subject to the IRP system (new, brands, non-hospital, all, etc.)?
- Second, how is the list of countries defined to obtain comparator prices (global, countries of similar income, type of health system, geographical proximity, market size, etc.)?
- Third, what are the prices observed in each country that are adopted as reference (official catalogue or list prices[4], purchase or invoice prices, net prices after discounts, confidential rebates, payback clauses, volume-based or outcome-based agreements, etc.)?
- And, fourth, how is the product-by-product reference price calculated and dynamically updated (definition of product at the level of same active ingredient, presentation form, dosage, package size, defined daily dose, etc.; lowest, average, median, weighted average price, etc.; fixed or dynamic exchange rate; adjustment by income level or purchasing power parity, PPP; periodicity of calculations and adjustments; etc.)? Belgium and France, in Europe, appear as the countries with the best IRP practices (Gill et al., 2019).

1.5. LESSONS FROM THE EUROPEAN EVIDENCE ON PRICES AND LAUNCHES

The evidence from several decades of IRP application in Europe may help to predict (prevent?) the consequences of a globalization of the system (Frank et al., 2022) with the adoption of IRP in the US. Prices of new medicines are reduced in the short term in those countries with prices higher than the average; however, in the medium term there is a trend towards international price convergence, the greater the number and market of comparator countries, with anchoring in the prices of higher-income European countries (Grueger et al., 2025). International interdependence increases, and all this implies higher prices for lower-income countries and delays in the entry of innovations in lower-price countries. Delays derived from strategic behavior of the companies that market

[4] For consistency, the term list price is used throughout this article.

the medicines. These delays may or may not have an impact on health and efficiency, but they respond to a clear logic of incentives for companies.

IRPs limit the capacity of industry for price discrimination between countries (Maini & Pammolli, 2023). The introduction of IRP in Germany in 2011 has meant an average increase of 6.6% in the prices of the countries included in the reference basket compared with those not included (Gamba et al., 2022).

Prices become interdependent (Fontrier et al., 2019): IRPs alter price incentives in comparator countries, as well as the timing and place of initial product launches; they increase prices in the countries that form the comparison set, at least the prices communicated or notified by payers. Net or actually paid prices tend to be confidential through dual/triple prices as a strategy to re-establish differential prices (Grueger et al., 2025):

- list or public prices,
- invoice prices with rebates and discounts,
- and confidential discounts and non-observable net prices (after payback clauses, confidential price-volume agreements, outcome-based agreements, maximum expenditure ceilings by product or by company sales, supra-product and supra-company agreements, etc.).

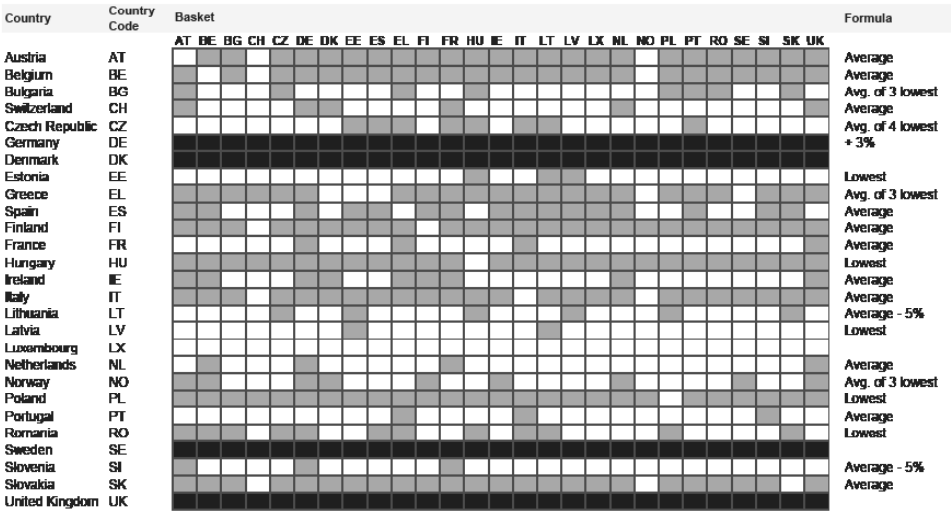
Today there is no robust evidence of a significant contribution of IRPs (direct and indirect effects) to the global reduction of prices of new medicines in Europe (Persson & Jönsson, 2016; Grueger et al., 2025). Even more important: the effective return to differential prices through net prices below invoice and list or official prices may both improve efficiency and further distort price differences with respect to the Lerner rule or the ideal Ramsey rule depending on the details of their application (Danzon, 2018).

Launch strategies also become interdependent (sequential entry conditioned by the details of the IRP system): larger markets and more binding IRPs increase delays in launches (or even non-launch) in countries with lower medicine prices and that others frequently use as a reference (Fontrier et al., 2019). As a counterpart, faster and strategic launches occur in countries with higher prices (for example, Germany). Complementarily, increases have been observed in industry efforts to make products less comparable between countries (forms of administration, dosage, number of units, etc.). A study (Maini & Pammolli, 2023) for 481 medicines in the period 1995-2012 in Europe has estimated the impact of IRPs with their absence as counterfactual: IRPs increase delays in the launch of new medicines in lower-income countries that are reference for

higher-income countries (Figure 1) by up to one year per medicine. Figure 1 includes countries with a GDP per capita equal to or higher than 60% of GDP per capita in the US:

FIGURE 1

COUNTRIES ADOPTED AS REFERENCE AND PRICE CALCULATION FORMULA



Source: Maini and Pammolli (2023).

1.6. IMPACT ON INNOVATION: HOW TO ALIGN R&D AND SOCIAL PRIORITIES?

The dynamic impact on incentives to innovation, on which there is less consensus and evidence, may also be very important (Kanavos et al., 2019). The argument on the relationship between reduction of prices/sales/profits and innovation, associated with IRPs, is based on the conventional assumption that investment in R&D will be reduced and this will have as a consequence a reduction in the new medicines that reach the market. This will be so if prices and global revenues of pharmaceutical companies are reduced as a result of IRPs, which is not always or entirely evident if the compensating strategic responses of industry are successful. It is important to remember that prices must constitute a signal (Kyle, 2025) not only for the level of innovation (volume of R&D), but they must provide information on the socially desirable direction of innovation (induced technological change). Adopting the price of another country or countries is

no guarantee that one is contributing to aligning the benefits of the innovator with added therapeutic value or with the cost-effectiveness ratio or other equity criteria of each national health system.

First, investment in R&D, if capital and investment markets are efficient, must depend on future prices and profits, not past ones (Rebitzer & Rebitzer, 2023; Shaikh et al., 2021), except insofar as these are a proxy for future prices and profits; the rules and criteria of evaluation and financing in large pharmaceutical markets must decisively influence and signal the expected future profits, that is, the direction of technological change.

Second, a reduction in R&D may incentivize greater efficiency and productivity (Schuhmacher et al., 2025), currently decreasing, in investment. Third, the evidence indicates that a reduction in profits reduces R&D and innovation (Kyle, 2025), but the set of medicines whose commercialization is deterred by potentially lower revenues may not coincide with the medicines of greatest social value (Woods, 2025). That is, we have little evidence on the marginal (health) value of the innovation that is abandoned. And, finally, in theory, a loss of innovation in the private sector could be compensated through investments in public financing, unlikely in the short term in the United States despite the importance it has had until now, and also one of the recommendations of the Draghi Report for Europe (European Commission, 2024).[5]

[5] The Draghi Report recommends strengthening public funding for pharmaceutical R&D in Europe, but directing it in a more strategic and coordinated manner: concentrating European and national resources on areas of high scientific and industrial value, reducing the fragmentation of public programs, supporting common health data platforms and multicenter clinical trials, and making better use of European funding instruments to attract private investment toward biotechnology, innovative medicines, and advanced technologies. The central idea is not to replace private investment, but rather to reduce risk during critical phases of research, create a European scale, and prevent discoveries funded or generated in Europe from being developed and commercialized primarily outside the EU.

Chapter 2

WHAT DO WE KNOW ABOUT THE LEVEL AND EVOLUTION OF THE PRICE DIFFERENTIAL BETWEEN THE UNITED STATES AND EUROPE?

This chapter analyzes the available evidence on the level and evolution of the differential in medicine prices between the United States and Europe. Comparisons based on list prices, invoice prices and net prices are reviewed, pointing out the limitations of each source. The chapter pays special attention to the difficulty of measuring real and comparable net prices between countries.

2.1. ARE PRICES IN THE UNITED STATES SO HIGH?

The adoption of an IRP policy in the United States (US) is nothing new or recent in American policy (see Chapter 4), being a bipartisan proposal (Morgan Lewis, 2025) supported by two arguments with broad popular support in the US (Kearney et al., 2026):

- that prices in the United States are much higher than in Europe (ASPE, 2024);
- and, that the rest of the world benefits from the US paying most of the cost of R&D of new medicines without contributing appropriately to its cost (the global stowaway problem or global free riding) (Kolchinsky & Xie, 2025).[6]

Both arguments have been used in proposals for MFN (Most Favored Nation) pricing policies in the US to justify the need for the rest of the world to increase the proportion of its contribution to financing the fixed costs of R&D on the basis of the political valuation that judges that the current contribution is not "fair" (Katebi, 2025).

[6] The *free-rider* problem: a situation in which an individual or organization benefits from a good, service, or effort provided collectively without contributing fairly to its cost or production. This is particularly important in the case of public goods, where it is not easy to exclude people from their benefits and where one person's use does not necessarily reduce another's use. In health economics, a classic example is vaccination: a person can avoid the costs or risks of vaccination and still benefit from the herd immunity generated by the vaccination of others. In that case, that person is engaging in free-riding with respect to others' contributions to public health.

The evidence on international differences in medicine prices is scarce, of low quality (Danzon, 2018) and based on private data sources that are neither verifiable nor reproducible. Let us look at the evidence from data on the level and variation of prices including the US, and the (controversial) assessment of it. The two relatively recent and more rigorous reports that we adopt here as sources of information are that of the Canada Patented Medicine Prices Review Board, PMPRB (2022) and that of RAND Corporation (Mulcahy et al., 2022 and 2024a), financed by the US Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. A review of the previous literature on international price comparisons can be found in Mulcahy et al. (2024).

Both reports are based on private data and ex-factory prices. The first (PMPRB, 2022), for the US and some European countries, compares list or official prices (different from invoice prices and net prices) of branded medicines (under patent). PMPRB uses Canada's consumption basket of prescription medicines for bilateral comparisons and has published indices adjusted by purchasing power parity (PPP). The PPP adjustment makes it possible to take into account differences in the standard of living of each country in a way that approximates a response to the opportunity cost of medicines in terms of the rest of goods and services. The RAND Corporation reports (Mulcahy et al., 2022 and 2024a) use 2018 and 2022 data relating to manufacturer gross or invoice prices from IQVIA's MIDAS® database[7]; they do not include off-invoice reductions down to the net price according to reported information nor any PPP adjustment. In the present study, bilateral relative prices from this report are also presented adjusted for PPP estimated from the Price level ratio (PPP vs exchange rate) of the World Bank. The ASPE report (US Assistant Secretary for Planning and Evaluation, 2024) is also based on IQVIA MIDAS, which is why the RAND Corporation report (Mulcahy et al., 2022 and 2024) is used here. The main limitations in the data and in the method used by IQVIA for price estimates in each country can be consulted in ASPE (2024).

Tables 1, 2 and 3 present comparative indices of prices adjusted for PPP of the US (base 100) with the price in several European countries from the two information sources cited. These indices have been calculated from the indirect comparison of the various bilateral indices published in various editions of each report. The method, the medicines and the countries included in each

[7] IQVIA MIDAS is a private international database on the pharmaceutical market that provides standardized information on drug sales, volumes, and prices by country, product, therapeutic class, and distribution channel. In pharmaceutical price analysis, MIDAS is commonly used to compare invoice prices or observed/estimated list prices in the commercial chain, market shares, and spending patterns across national markets. However, it generally does not capture confidential discounts, risk-sharing agreements, ex post reimbursements, or effective net prices paid by payers or public purchasers.

TABLE 1

BILATERAL COMPARISON OF PRICES[a] (INDEX NUMBERS) ADJUSTED FOR PPP AND VOLUME OF MEDICINE SALES IN THE US AND IN 5 EUROPEAN COUNTRIES IN 2018[b]

Country	*Patented brand*	*Generics[c]*	*Whole market*	*Sales share[d] (%)*	*Volume share[e] (%)*
United States (US)	100	100	100	58.4	24.0
Germany	41	187	51	5.0	5.7
Spain	45	232	55	2.9	4.4
France	32	194	43	3.9	4.9
Italy	39	211	51	3.9	4.3
United Kingdom	31	160	43	3.0	5.9

Notes: a. Quarterly prices paid in 2018 to the pharmaceutical industry by wholesalers or distributors reflected in invoicing and adjusted by quarterly exchange rate, without adjustment by net prices. b. Own calculation from Mulcahy et al. (2021) with the weight of consumption in the US adjusted for PPP and without adjustment by net prices. c. Unbranded generics, which account for most generic sales in the US in 2018. d. Sales share (%) in monetary units in the 32-country market. e. Sales share in physical units (standard unit) in the 32-country market. A standard unit is one tablet or capsule for solid oral pharmaceutical formulations; 5 ml for liquid oral formulations; and a count of vials, syringes, autoinjectors or another count unit for injected or infusion-administered formulations, as well as other prespecified count units for each other formulation. Price level ratio adjustment according to data from: World Bank. World Development Indicators: Price level ratio of PPP conversion factor to market exchange rate (PA.NUS.PPPC.RF). [Internet]. Washington (DC): World Bank; c2024 [accessed Apr 20 2026].

of the two reports are not directly comparable with each other, nor entirely comparable internally between their different editions, so the data must be interpreted with caution.

The information available in the last two decades on prices in the US versus Europe yields two conclusions (Tables 1, 2 and 3): first, the price level of new branded medicines is considerably higher in the US than in Europe while the price level of generics is considerably lower in the US; and, second, during the first two decades of this century the differential in brand prices in the US has increased notably with respect to Europe.

The US pharmaceutical market in 2022 represents more than 60% of all sales in the 33 countries of the Mulcahy et al. (2024) report, while the volume of consumption in physical units is less than one fourth (Tables 1 and 2). The US market share in sales has increased by 4 percentage points compared with 2018, despite the fact that the volume share remains constant. And all this despite the fact that the volume of consumption of generics in the US exceeds 90%. In the tables of this document, the US market is compared with that of the five largest European pharmaceutical markets in sales volume: Germany, France, Italy, United Kingdom and Spain.

TABLE 2

BILATERAL COMPARISON OF PRICES[a] (INDEX NUMBERS) ADJUSTED FOR PPP AND VOLUME OF MEDICINE SALES IN THE US AND IN 5 EUROPEAN COUNTRIES IN 2022[b]

Country	*Patented brand*	*Generics[c]*	*Whole market*	*Sales share[d] (%)*	*Volume share[e] (%)*
United States (US)	100	100	100	62.4	23.8
Germany	36	244	47	4.7	5.8
Spain	47	382	60	2.8	4.4
France	31	265	43	3.8	4.6
Italy	45	349	60	3.3	4.0
United Kingdom	33	274	47	3.2	6.1

Notes: a. Quarterly prices paid in 2022 to the pharmaceutical industry by wholesalers or distributors reflected in invoicing and adjusted by quarterly exchange rate, without adjustment by net prices. b. Own calculation from Mulcahy et al (2024) with the weight of consumption in the US adjusted for PPP and without adjustment by net prices. c. Unbranded generics, which account for most generic sales in the US in 2022. d. Sales share (%) in monetary units in the 33-country market. e. Sales share in physical units (standard unit) in the 33-country market. A standard unit is one tablet or capsule for solid oral pharmaceutical formulations; 5 ml for liquid oral formulations; and a count of vials, syringes, autoinjectors or another count unit for injected or infusion-administered formulations, as well as other prespecified count units for each other formulation. Price level ratio adjustment according to data from: World Bank. World Development Indicators: Price level ratio of PPP conversion factor to market exchange rate (PA.NUS.PPPC.RF). [Internet]. Washington (DC): World Bank.

According to the data from the Mulcahy et al. (2024) report, the invoice price index of patented branded medicines adjusted for PPP for Germany in 2022 (Table 2) is equivalent to 36% of the list price in the US, a figure similar to that of the United Kingdom (33%). The invoice price index of patented branded medicines for Germany in 2018 was equivalent to 41% of the invoice price in the US (Table 1), a figure higher than that of the United Kingdom (31%). For Spain this figure is slightly higher in 2022 (47%), and similar to the 2018 level (45%). For the 7 European countries included in Tables 1 and 2: between 2018 and 2022 the relative level of brand prices with respect to the US remains quite stable in 5 countries, while it decreases in Germany and increases in Italy.

The invoice price index of generic medicines (non-branded) adjusted for PPP for Germany is 2.44 times and 1.87 higher than in the US in 2022 and 2018, respectively (Tables 1 and 2); and 2.74 and 1.60 times higher in the United Kingdom. For Spain this price index in 2022 is 3.82 times higher than the US (2.32 times in 2018)[8]. For the 5 European countries of Tables 1 and 2,

[8] The Spanish case illustrates that the mere existence of generic drugs does not, in and of itself, guarantee intense price competition. The design of the reference pricing system, the alignment of prices between brand-name and reimbursed generic drugs, and the incentives for prescribing and dispensing all influence the degree of market penetration and the savings attributable to generic drugs (Puig-Junoy, 2010)

TABLE 3

BILATERAL COMPARISON OF PRICES OF PATENTED BRANDED MEDICINES IN THE US AND IN 4 EUROPEAN COUNTRIES (INDEX NUMBERS) ADJUSTED FOR PPP[a]

Country	*2006*	*2011*	*2016*	*2021*
United States (US)	100	100	100	100
Germany	56	56	39	33
France	46	36	26	25
Italy	43	39	35	37
United Kingdom	53	40	31	32

Notes: a. Own calculation from Canada Patented Medicine Prices Review Board, PMPRB (2007, 2012, 2017, and 2022), Canadian consumption weights and prices adjusted for PPP. This study does not include Spain. Prices for non-Canadian markets are based on publicly available gross prices (list or official prices), specifically ex-factory price information reported by patentees to the PMPRB.

the relative price of generics is not only higher than in the US but it has increased notably between 2018 and 2022.

Despite the high market share in volume of generics in the US and the lower price compared with European countries, the invoice price index adjusted for PPP of all medicines (under patent and off patent) for Germany and the United Kingdom in 2022 is equivalent to 47% of the price in the US (60% in Spain and Italy, the highest of the 5 countries) (Table 2).

According to the data from the PMPRB report (2022), between 2006 and 2021 the differential in list prices of patented branded medicines adjusted for PPP between the US and Europe has increased very importantly (Table 3): in 2006 the price in Germany was equivalent to 56% of the price in the US and that of the United Kingdom was 53%; in 2016 this relative proportion decreased significantly for the 6 countries of Table 3. And, in 2021 both figures were, respectively, notably lower: 33% for Germany and 32% for the United Kingdom.

The international differences in prices of patented branded medicines in high-income countries in the previous tables do not seem justified by the Ramsey rule. The US price index, unadjusted and adjusted for PPP, appears as an extreme observation at the upper end: What would happen if the United States, instead of starting from the premise that prices in the rest of the world are too low or incorrect, provisionally accepted their validity and required an explicit justification of its own higher prices? (Mulcahy, 2026).

2.2. WHAT MATTERS IS THE DIFFERENTIAL IN NET PRICES

International price comparisons US versus Europe, even adopted as approximations to levels and trends of price differentials, must be interpreted taking into account the limitations derived from the fact that:

- net prices are not available either for the US or for Europe, which leaves us with approximations that depend on the heterogeneous and confidential difference across countries and products, between net price and list or invoice prices;
- there are reasonable indications (Persson & Jönsson, 2016) that, at least in Europe, the distance between list price, invoice price and net price may be growing because of the spread of the use of IRP systems (Espín et al., 2018);
- the differential in net prices between Germany (Berkemeier et al., 2019), with price negotiation policies based on comparative efficacy/effectiveness, and the US has been 29.2% between 2007 and 2011 and 28.9% between 2012 and 2018;[9]
- price differentials should take into account not only the net entry or launch price on the market but its evolution throughout the full life cycle of the product including prices of periods under patent, but with therapeutic competition and the successive entry of generics when the patent expires;
- product differentiation between countries constitutes an added difficulty for the calculation of price indices;
- details on differences in methods and data inter- and intra-reports may affect the calculated price indices in directions difficult to determine;
- and, it cannot be overlooked that the databases used to construct the indices are private and confidential, not being freely accessible to researchers.

[9] The net prices come from two different administrative/commercial sources. For Germany, the authors use the Lauer-Taxe database —specifically, a version maintained by the IGES Institute— which compiles the net prices paid by German insurers, including applicable discounts and rebates. For the United States, they use the Average Sales Price (ASP) data published by CMS for drugs covered by Medicare Part B; the ASP is calculated based on the net prices reported by manufacturers, after discounts and rebates granted to private insurers, PBMs, wholesalers, specialty distributors, medical practices, hospitals, and other purchasers. The authors emphasize that these prices reflect net amounts actually received by manufacturers, not list prices, although they exclude Medicaid, the Veterans Administration, and other federal programs with specific mandatory discounts.

From a conceptual perspective, the differential prices observed in list and invoice prices must be interpreted in light of:

- the point information available on the differential between net prices and invoice or list prices;
- and, the analysis of the causes of the level and temporal trend of the observed price differential between the US and Europe.

2.3. WHAT (LITTLE) DO WE KNOW ABOUT THE NET PRICE DIFFERENTIAL

List prices are more accessible for international comparison, more comparable, but in most cases they have little to do with invoice prices, estimated and less accessible, and much less with net prices.[10] The scarce literature on net prices in the US is based on assumptions or on point observations for certain medicines. Knowledge about net prices in Europe and their hypothetical distancing from list and invoice prices in recent decades is equally or even less known.

The already cited RAND Corporation report (Mulcahy et al., 2024) presents a sensitivity analysis adjusting net prices downward by 37.2% with respect to invoice prices in retail sale. Even with this discount on the invoice price in the US and a net price equal to the invoice price in Europe, the price differentials observed in Tables 1 and 2 would remain very important. This figure is based only on the review of the results of two previous studies (grey literature) for the US that have reported: a) discounts of 23% (Roehrig, 2018) from the insurer perspective in 2018; b) discount of 37% (IQVIA, 2023) on industry invoice prices (and of 52% on list prices). As is to be expected because of the very nature of the information, in both cases these are private and confidential information sources. The same report admits that this differential down to net prices is variable between medicines and therapeutic groups and that this estimate includes a "substantial measurement error". In the case of the US it is important

[10] List price: the official or publicly disclosed price of a medication before applying confidential discounts, rebates, mandatory rebates, risk-sharing agreements, or other price concessions. It is typically used as a reference price for regulatory purposes, public financing, or international comparisons, but may differ substantially from the amount actually paid. Invoice price: the price recorded on the invoice for a transaction between a seller and a buyer at a specific point in the supply chain, for example, between a manufacturer and a wholesaler, a wholesaler and a pharmacy, or a supplier and a hospital. It may include explicit discounts applied on the invoice, but typically does not include off-invoice discounts, retroactive discounts, confidential rebates, or reimbursements resulting from risk-sharing agreements. Net price: the actual price received by the manufacturer or paid by the buyer after deducting discounts, rebates, mandatory rebates, confidential agreements, and other price concessions.

to distinguish whether we refer to the net price for industry, Pharmacy Benefit Management (PBMs)[11] or health insurers (see Chapter 3). ASPE (2024) cites discounts on invoice prices in the US according to the literature of 23%-28% and proposes applying these rebates to the US price as a lower limit of the price in this country and comparing it with that of other countries without any rebate, despite the fact that it is known that also in the rest of the world there are differences between invoice prices and net prices, although it is presumed that these differences are lower than those of the US.

However, to estimate the price differential between the US and Europe it would also be necessary to know the discounts applied in Europe on invoice prices, information that is not available. If these discounts were greater in the US, the differential estimated from invoice prices would be overestimated. However, there is currently not enough evidence to determine whether the differential based on net prices would be greater or smaller than that based on invoice prices. Therefore, the differential in net prices can only be approximated through the available estimates of invoice prices. Even so, some authors, such as Kolchinsky and Xie (2025), have assumed a 20% discount on invoice prices outside the US, supposedly from publications on Canada, the European Union and the United Kingdom, although those sources do not seem to empirically confirm that percentage.

[11] In the United States, a PBM is an intermediary organization that manages pharmaceutical benefits on behalf of health insurers, employers, and public programs. PBMs negotiate price reductions and discounts with pharmaceutical manufacturers, design and administer drug formularies, process prescriptions, establish reimbursement terms for pharmacies, and may operate mail-order or specialty pharmacies.

Chapter 3

IS GLOBAL FREE RIDING ON THE PRICE OF MEDICINES IN THE UNITED STATES OVER?

This chapter analyzes whether the international price differential can be interpreted as a problem of global free riding. Possible causes of the differential are reviewed, including the United States institutional structure. Different approaches to estimating a "fair differential" in prices and the optimal contribution to global pharmaceutical R&D are also presented.

3.1. WHAT ARE THE CAUSES OF THE PRICE DIFFERENTIAL?

The economic literature provides two foundations in favor of the existence of differential prices in the pharmaceutical market: price discrimination by the monopolist and Ramsey prices (Danzon, 2012; 2018). If price elasticity is inversely related to the income level of countries, then differential prices, instead of uniform prices, may be desirable not only in terms of efficiency (static and dynamic) but also in terms of equity (Berndt and Newhouse, 2012).

First, in the absence of price regulation and arbitrage, conventional economic theory predicts that a firm with market power (monopoly) such as that granted by patent protection for a new medicine will maximize profits (producer surplus), subject to the constraint of covering total costs, by applying differential prices if it can segment the market (Danzon, 2012; 2018): higher prices to those individuals or populations with greater willingness to pay and less sensitive to variations in price and lower prices to those with lower willingness to pay and more sensitive to changes in price (Lerner rule or condition) (Lerner, 1934). Here the monopolist maximizes its surplus and not the social surplus that also includes consumer surplus and not only producer surplus. Probably, the distance between the sale price and marginal cost will be higher with the Lerner rule than with Ramsey prices in markets with less price elasticity, leaving aside the rest of factors that influence demand in each country. The high fixed and sunk costs and low marginal costs in the pharmaceutical sector further incentivize price discrimination (Berndt and Newhouse, 2012). Second, the logic of Ramsey prices (Chapter 1) indicates that joint and sunk fixed costs such as those of pharmaceutical R&D should ideally be distributed optimally among heterogeneous countries (individuals) inversely to per capita income (Danzon, 2018). It is worth qualifying that this would require perfect information on justifiable costs and should be applicable to the optimal regulation of a

multinational monopolist firm operating globally, a situation different from that originally analyzed by Ramsey (1927).

In the empirical field, it seems logical to find price differentials between countries with quite different income levels, as may be the case between some European countries and the US. With 2016 data, the relationship between per capita income and prices was positive but the association was weak (Danzon, 2018). However, this is not an indication that the size of this differential in reality is optimal, far from it. Hence the need, first, to know the possible causes of price differentials between the US and Europe. The main causes of this price differential (Chapter 2) in the US can be classified for conceptual purposes into two groups:

- higher willingness to pay for new medicines and lower price elasticity in the US;
- and, incentives of some agents of the US health system poorly aligned with obtaining lower prices for patients and insurers.

In the literature on international prices, the following explanations can be distinguished for the differential in prices of patented medicines related, directly or indirectly, to greater willingness to pay and lower price elasticity in the US:

- use of prices as an incentive to innovation;
- renunciation of exercising purchasing power;
- prices based on the behavior of a profit-maximizing monopoly in a market with high willingness to pay;
- the price elasticity of aggregate demand at the level of public programs is lowest in Medicare, which renounced negotiating discounts until 2023, and somewhat higher, though still low, in Medicaid and VA;
- and, price control and negotiation policies in the rest of countries with potential global free riding of smaller and lower-income countries.

First, the willingness to pay of the US is not only higher because of the higher income level but also because of a policy of incentivizing innovation through prices by being a large market with capacity to influence global R&D: willingness to pay higher prices in exchange for a higher level of innovation (Kyle, 2025; Robinson, 2025a). A review of the economic literature reports a long-term elasticity of innovation with respect to revenues of the biopharmaceutical

sector situated between 2.5% and 15%: a 10% reduction in expected revenues would give rise to a fall of between 2.5% and 15% in the number of new medicines in the US (Filson et al., 2025). The evidence on the impact of higher prices on the level and direction of innovation is still somewhat controversial in the economic literature (Frech et al., 2026; Kesselheim et al., 2016; Kyle, 2025; Moreno & Epstein, 2019; Rebitzer and Rebitzer, 2023), although it is not part of the object of this document. It is known that this does not necessarily translate into health improvements. Two examples: (i) crisis of opioid derivatives (fentanyls and others) in the US; (ii) in a system where there is a non-irrelevant proportion of the population without insurance or with basic insurance, patient copayments for a new medicine (*e.g*. an oncology medicine) whose price doubles the previous one may drive the patient's family finances into bankruptcy.

Second, on the demand side, the US market is not centralized in a single purchaser, but is fragmented, and, moreover and even more important, the exercise of purchasing power is scarce in public programs and in the hands of organizations (PBMs) with scarce incentives to reduce prices in private health plans. By contrast, in most European countries there is a single central negotiator with purchasing power (Robbins, 2024). Nevertheless, the size of US public and private programs should be sufficient to exercise purchasing power without becoming a monopsony. Instead, the US has opted until recently for renouncing the exercise of purchasing power in public programs. The perverse or biased incentives of PBMs regarding price reduction of patented branded medicines are analyzed in the following section.

In the case of US public programs:

- Medicare, which covers an adult population of 68 million people (University of Kansas, 2024) in 2024, was legally prohibited from negotiating prices from 2003 until 2023; the consequence is that Medicare has been paying higher prices than other US public programs and than other countries and that it finances new medicines regardless of their incremental efficacy and cost-effectiveness ratio (Conti et al., 2024).

- By contrast, Medicaid (and Children's Health Insurance Program, CHIP), which covers more than 79 million people in 2024 (Centers for Medicare & Medicaid Services, 2026), must finance almost all medicines approved by the Food and Drug Administration (FDA); unlike Medicare, Medicaid can negotiate discounts on the average industry sale price (therefore linked to prices in the private sector) and is subject to limits on price increases above inflation.

- Veteran Health Administration (VA), which covers a population of 6.2 million people (2018-19 data) (Agency for Healthcare Research and Quality, 2026), can also negotiate prices with a discount on the average price and make decisions of inclusion or exclusion from insurance coverage, achieving lower net prices than Medicaid and Medicare (Kesselheim et al., 2016).

Third, the US is the only country with almost free prices (there are no price controls). France uses internal and international reference prices, as does Germany although this country uses them once they have already entered the market (12 months). For its part, the United Kingdom regulates the rate of profit (Kyle, 2025; OECD, 2013). In this context, the level of prices of patented medicines in the US will be what the market is willing to bear (Kesselheim et al., 2016), which tends to exhaust consumer surplus in the absence of restrictions on profit-maximizing monopoly behavior.

Fourth, in the US uninsured patients cannot afford the prices of new medicines, while insured patients have quite inelastic demand due to high insurance coverage and maximum limits on copayments (Danzon, 2018).

And, fifth, in financing and pricing decisions other countries use technology assessment, negotiation of internal and international reference prices (IRP), exclusion or partial inclusion in insurance coverage, criteria related to the incremental cost-effectiveness ratio, etc. These price control and negotiation policies contain potential free riding by smaller and lower-income countries. That is, other smaller countries may artificially widen the price differential, to some extent, by reducing their real willingness to pay through price control policies (free-riding) (Kyle, 2025; Kolchinsky, 2020; Kolchinsky and Xie, 2025).

3.2. ECONOMICS OF PHARMACY BENEFIT MANAGEMENT (PBMs)

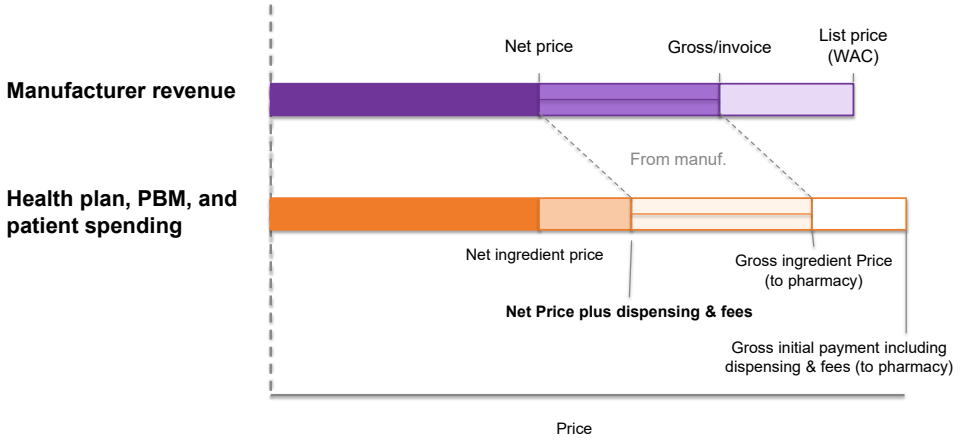
In the US, in the absence of a centralized health system and single payer as in most European countries, new patented medicines can be sold at different prices for each purchaser. Pharmacy Benefit Managers (PBM) are organizations that negotiate prices with the biopharmaceutical industry for insurers and carry out the assignment of medicines to different levels of preference and copayment (tiered copayments), the requirement of prior authorization and reviews of medicine utilization. The functions of PBMs are somewhat broader since they include the processing of prescription medicine claims and the negotiation of plan savings with other actors in the health care supply chain (Mulligan, 2022).

PBMs are private profit-maximizing organizations and, in theory, should operate in a competitive market with other PBMs offering services to health plans and patients. Likewise, in theory, PBMs face the possible loss of market share if they exclude pharmacological treatments valued as important by patients (Kyle, 2025). Reality is characterized rather by weak competition and important market power (monopsony) of PBMs operating in a highly concentrated market (Berndt and Newhouse, 2012): in 2024 the first three PBMs (Express Scripts, Caremark and Optum Rx) concentrate 80% of the market and the first 6 concentrate 95% (Fein, 2025).

The discounts (rebates or returns) that PBMs obtain on net prices are confidential and usually take the form of a transfer from industry to the PBM (Danzon, 2018). These discounts depend on the market share achieved by PBMs for each medicine or group of preferred medicines. This allows industry to sell to distributors at the list price offering discounts directly to PBMs. The degree of pass through of these discounts to lower premiums for health plans and their members depends on the degree of competition in the market (see Figure 2): a low level of competition and confidentiality of discounts allows one to suppose that pass through is only partial and that an important part of them is retained by PBMs, although the evidence is scarce and inconclusive (Danzon, 2018). Transparency in discounts is unlikely to improve this pass-through to insurers since it could facilitate, counterproductively, price collusion by reducing competition for industry (Danzon and Chao, 2000; Cabrales et al., 2013). On

FIGURE 2

RELATIONSHIPS BETWEEN LIST, INVOICE AND NET PRICES FOR BRANDED MEDICINES AND COMMERCIAL PBMS OR PAYERS IN THE US



Source: Mulcahy et al. (2024b), page 3.

the other hand, it is noteworthy that the copayment borne by patients, while it does not exceed ceilings or maximum limits, is calculated on the list price and not on the net price, which implies a higher effective copayment rate on the net price of medicines (Kolchinsky, 2020).

In this economic context in which PBMs operate, competition is distorted, giving rise to incentives poorly aligned with social welfare (Rebitzer, 2024; Robbins, 2024): a) PBMs have a preference for medicines with higher list prices and larger discounts down to the net price compared with other medicines (Danzon, 2018); b) and, the confidentiality of discounts incentivizes industry to increase list prices, in the absence of restrictions on pricing freedom, and to increase discounts (Hiltzik, 2017).

3.3. DOES GLOBAL FREE RIDING EXIST?

The existence of an important differential in prices of patented medicines between the US and the rest of the world (Chapter 2) has been used, from various economic and political sectors, expert groups and pressure groups in the US, in the political direction of the slogan "Put Americans First" that characterizes many of the sectoral policies (defense, trade, industry, etc.) of the second presidential term of Donald J. Trump. From this perspective, price differentials have been used as proof of the fact that other rich countries are taking advantage of the willingness to pay of the US. In this way a so-called "global freeloading" would be incurred that would harm sick US citizens who are forced to pay much higher prices for medicines (Katebi, 2025; Gonzalez López-Valcárcel, 2026). This argument suffers *a priori* from severe limitations from the economic and health perspective.

- First, information on internationally compared prices is deficient for precisely measuring the magnitude of the differential because of the lack of knowledge, imprecision and weakness of information on net prices and on the net price throughout the life cycle of the medicine (Chapter 2).

- Second, according to economic theory, the existence of any important price differential is not sufficient evidence of free riding behavior but this differential, according to the magnitude and heterogeneous direction by comparator country and medicine, may constitute both proof of efficiency and of distortion in price allocation (Danzon, 2018).

- Third, the impact of causes of the price differential between the US and Europe related and/or attributable to the existence of inadequate

incentives of the organization and incentives of the health system in the US (see previous section) cannot be considered free riding behavior by European countries but weaknesses within the US health system: for example, the perverse incentives of PBMs or willingness to pay monopoly prices unrelated to the added therapeutic value of innovations.

- Fourth, that part of the price differential is attributable to a greater willingness to pay for new patented medicines in the US, regardless of their added therapeutic value (or incremental effectiveness) and their cost-effectiveness ratio (for example, cost per quality-adjusted life year gained), may be precisely an indicator of inefficient price setting compared with price regulation systems whenever they are based on rigorous systems of evaluation of medicines and health technologies (HTA) in various European countries. More explicitly, a high willingness to pay for any innovation unrelated to incremental effectiveness and the cost-effectiveness ratio will distort the direction of incentives to innovation and may imply a high opportunity cost in terms of health (years of life and quality of life) for the US population.

- And, fifth, the reduction in the contribution to financing R&D through prices that the price differential in Europe implies, if these prices are established according to an appropriate measure of the added therapeutic value of new medicines, may imply an orientation of R&D with more value in terms of health; at the same time, it may imply an improvement in the health of US patients, instead of the development of more new medicines with a lower incremental improvement in health.

The attribution of part of the price differential between the US and Europe to a good exercise of evidence-based HTA (as in the case of the two last previous limitations) has also been questioned by expert groups close to the pharmaceutical industry in the US (for example, the organization No Patient Left Behind, NPLB; or RA Capital), and may come to be regarded as free riding if it is based on biased information and has as its objective the negotiation and/or regulation of artificially low prices. It has been argued that outside the US, middle- and high-income countries use HTA agencies to systematically undervalue new medicines (NPLB 2025; Kolchinsky and Xie, 2025).

The methods most commonly used in HTA agencies and that may lead to the setting of arbitrarily low prices outside the US according to the guide of the self-styled generalized cost-effectiveness analysis (GCEA; Shafrin et al., 2024). GCEA is nothing more than a variant of the economic evaluation guidelines existing in many countries which, as main distinctive aspects with respect to most guidelines

of HTA agencies: a) adopts the social perspective (instead of that of the health payer) including all indirect costs (productivity) and non-health direct costs; b) takes into account the price throughout the entire life cycle of the medicine, which includes the generic phase; c) estimates option value, hope value and scientific externalities; d) estimates the dynamics of the evolution of disease prevalence (for example, the expected increase in the prevalence of Alzheimer's disease); etc. It is assumed that considering these aspects would result in incremental cost-effectiveness ratios than those estimated by most European evaluation agencies using the more limited perspective of the health payer.

If the HTA methods used outside the US undervalue the true social value of new medicines this would lead to artificially lower prices and to a greater price difference since the US price is determined by a free market in the absence of HTA. However, European countries such as the United Kingdom and Germany have HTA agencies that use evaluation methods with well-established transparent criteria based on the comparative clinical and economic evidence of new medicines, but always restricted to the perspective of the health payer, which excludes indirect costs and benefits.

3.4. CAN THE FAIR PRICE DIFFERENTIAL BE DETERMINED?

This section examines the most recent works that have tried to calculate or estimate the measure of free riding in the price differential or, in similar terms, the correction that should be applied to the currently observed differential in order to arrive at a fair price differential. Three types of measures of the degree of taking advantage behavior or free riding by the rest of countries are analyzed:

- measures based on statistical adjustments of the observed price differential;
- measures based on re-estimations of economic evaluation exercises carried out by HTA agencies that estimate the social value of the new medicine;
- and measures based on estimates of the optimal contribution to R&D from economic models.

3.4.1. Free riding indices

Although it is entirely inappropriate to confuse observed price differential with free riding behavior, some proposals of free riding indices based directly on

the observed price differentials (Section 2) have become popular in the political arena in the US.

Kolchinsky & Xie (2024), in a publication without an evaluation process, have estimated a free riding index based on net prices: the measure of what other high-income countries fail to pay, adjusted for GDP per capita corrected according to purchasing power parity (PPP) compared with invoice prices in the US. The adjustment is simply linear: for example, if the US pays a net price of $100 and the adjusted PPP relative GDP per capita between country A and the US were 43.2%, then the net price in A should be $43.20. The free riding index of country A, if the net price is $25 for this medicine, would be 42.1% [(43.20 - 25) /43.20]. That is, the normative assumptions, without further theoretical or empirical justification, that this calculation adopts are that: a) the appropriate price differential must be equal to the GDP per capita differential according to PPP for all countries; and, b) the price elasticity of aggregate demand for medicines is the same for countries with different levels of per capita income adjusted for PPP.

From the Mulcahy et al., 2024 report on international prices and data on GDP per capita adjusted for PPP from the World Bank, in this work these indices have been recalculated for 2018 and 2022 for the 5 European pharmaceutical markets with the greatest sales volume (Table 4) adopting the correction by net prices of Kolchinsky and Xie (2024): taking into account confidential discounts and rebates that reduce the invoice price down to the net price under the assumption that these discounts represent 37.7% in the US and 20% in the rest of the countries.

The results in Table 4 allow observing that: a) the free riding indices are positive for the 5 countries both in 2018 and in 2022 with a minimum value of 27.7% (all medicines in Italy in 2022) and a maximum value of 62.4% for the United Kingdom (patented branded medicines in 2018); b) the free riding indices for branded medicines are higher than those for all medicines as a whole in the two years for all countries due to the higher prices of generics in Europe with respect to the US; c) the free riding indices for all medicines in 2022 are lower than those of 2018 in 3 of the 5 European countries, ranging between a little less than 28% in Italy and Spain and 48.6% in France. The normative interpretation proposed by the authors of this index would imply, for example, that the prices of all medicines should have been 43.4% higher in Germany, 42.7% in the United Kingdom or 27.9% in Spain in 2022.

TABLE 4

FREE RIDING INDEX IN THE PRICES OF ALL MEDICINES IN 2023 IN 5 EUROPEAN COUNTRIES (Percentage)

Country	*Patented brands 2018*	*Patented brands 2022*	*All medicines 2018*	*All medicines 2022*
Germany	50.3	57.0	38.3	43.4
Spain	45.6	43.3	34.0	27.9
France	61.2	62.2	47.6	48.6
Italy	52.4	45.5	38.5	27.7
United Kingdom	62.4	59.8	48.5	42.7

Sources: Own calculations from Rand Corporation, and from World Bank. GDP per capita, PPP (current international $) [Internet]. Washington (DC): World Bank; 2022 [cited 2026 Apr 27]. Available from: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD, according to the method of Kolchinsky & Xie (2024).

3.4.2. HTA in Europe as an excuse to pay less

A report commissioned and disseminated by NPLB in 2024 compares the prices of an unidentified small group of medicines in two countries with HTA agencies, Canada and Germany, with those prices that would derive from taking into account social value fully through a re-estimation of their social value by means of GCEA (Shafrin et al., 2024). The exercise is carried out only for 10 new drugs in Canada and 5 in Germany corresponding to 6 therapeutic areas (cancer, cardiovascular diseases, diabetes, cystic fibrosis and obesity) and without information on the criteria for selecting the treatments.

This report does not provide any other information on the particular differences in the application and assumptions of the GCEA method compared with the use of evaluation guidelines by the HTA agency of each country. The results of this report state that Canada and Germany would be undervaluing the value of new medicines by approximately 90% in Canada and 94% in Germany. That is, the ratio between the observed price and the price according to their true social value in Canada for these treatments is only 10% and 4% in Germany.

The authors of the report attribute this high underestimation of value to the fact that HTA agencies apply "obsolete and outdated" criteria: a) a more limited perspective than the social one; b) an assessment based on the short term of health budgets (launch price, for example, instead of the price throughout the life cycle of the medicine); c) defective estimation of quality-adjusted life years (QALYs) gained; d) and, patient preferences on future health outcomes.

There is a range of arguments for and against adopting the social perspective versus the health perspective and a renewed debate in the applied economic literature (Koh and Sha, 2026; Radu et al., 2026). Some authors have examined the impact of considering the social perspective instead of the health perspective, more restricted, in economic evaluations of medicines published up to 2018 (Oliva et al., 2020) in five therapeutic areas as case studies: Alzheimer's disease, diabetes, rare diseases, multiple sclerosis and depression). The conclusions reached by these authors after reviewing these five case studies indicate that the variations in the cost-effectiveness ratio when introducing the perspective are heterogeneous, but, in general, are modest, reaching variations between 4% in rare diseases and 15% in multiple sclerosis. These estimates are not very consistent with those of the NPLB report, although broadening the perspective is not the only change introduced in GCEA (Shafrin et al., 2024).

Likewise, the estimation of the price of the new medicine throughout its life cycle (long-term cost), including the generic phase in the US, has estimated that the brand price at launch was 11% higher than the long-term cost (Lakdawalla et al., 2017).

This NPLB report (2024) and other authors (Kolchinsky & Xie, 2025) have interpreted the previous results as evidence that these agencies systematically undervalue the social value of new medicines and that they use HTA "as a negotiation tool to deny coverage and/or obtain lower prices, and benefit for free from R&D investments made outside their countries". That is, HTA as an excuse to pay less and as a vehicle of free riding behavior. It is worth remembering that these are, therefore, conclusions of a non-transparent and non-reproducible GCEA economic evaluation exercise, which has not been subjected to any peer review process, and whose internal and external validity is unknown.

Finally, beyond the aspects regarding the method and the questionable validity of the results, it must be pointed out here that if the price paid to industry in Canada and Germany were equal to the price according to the social value calculated in this report, this would be equivalent to extracting the totality of consumer surplus (welfare) and delivering it to industry, which lacks theoretical support and is not applied in any other good. One may wonder, by way of example, what the price of water or electricity or telecommunications or transport or artificial intelligence should be according to this same criterion.

3.4.3. Optimal contribution to R&D

The contribution to the fixed costs of R&D, as a global public good, does not depend only on the level of prices of patented medicines in each country.

Nor does it seem an appropriate measure of the existence of global free riding to point out that 46% of sales and 78% of profits of the pharmaceutical industry occur in the US (The Council of Economic Advisers, 2018). A more appropriate approximation to the estimation of the global contribution of each country must take into account the aggregate measure of payments made to pharmaceutical companies above marginal cost: that is, it should be estimated from the difference between the net price paid and marginal cost multiplied by the volume of sales in each country. The measure of global free riding should be based on this measure and not only on the price differential.

The study by Skinner (2026) compares the prices of 87 new active ingredients sold in 2020 in Canada, the United States and 12 reference countries used by the Canadian regulator PMPRB. This work estimates the measure of free riding in Canada by comparing list prices with the average of 14 countries, including the US, and multiplying the difference with respect to the average by the volume of sales to estimate the "fair" contribution to sales. That is, this measure assumes as normative value of the appropriate price the average observed list price in the other countries (uniform price equal to the international average price, including the US monopolist price) and Canada's consumption basket. Attributing normative value to the observed uniform average price lacks theoretical and empirical justification, but this study improves the limitation of free riding indices based only on the price differential. The use of the uniform average price is equivalent to assuming a unit income elasticity of price, invariable with the income level.

The results of Skinner (2026) indicate that the expenditure made on patented medicines in 2020 in Canada is equivalent to 43.6% of the expenditure it should have made paying the average price observed in the rest of countries. Or, in other terms, Canada should have made an expenditure on patented medicines 130% higher to reach a "fair" contribution to the share of R&D that would correspond to it.

Frech et al. (2026) use as measurement variable of global free riding the global amount paid by each country for branded medicines above marginal cost from the data on price differentials of 2018 published by Rand Corporation (Mulcahy et al., 2021). These authors adopt the lowest price index observed in the set of countries of the RAND Corporation report (Turkey, with an index of 14.2%, US being 100) as an approximation to marginal cost. The contribution of each country to R&D will be the product of the percentage represented by the differential between the net price and marginal cost over this net price and multiplied by the volume of sales of patented medicines in each country. The per capita contribution indices of the US and 5 European countries are presented in Table 5, adjusted for PPP, for the base case and for a sensitivity analysis assuming that marginal cost is 24% of the US price index.

TABLE 5

AVERAGE CONTRIBUTION PER PERSON TO GLOBAL R&D ADJUSTED FOR PPP THROUGH SALES OF PATENTED MEDICINES IN THE US AND 5 EUROPEAN COUNTRIES IN 2018

Country	*Per capita contribution ($) (base case)*	*Index (base case)*	*Per capita contribution ($)(sensitivity analysis)*	*Index (sensitivity analysis)*
United States (US)	998	100.0	884	100.0
Germany	304	30.5	228	25.8
Spain	374	37.5	272	30.8
France	244	24.4	160	18.1
Italy	344	34.4	242	27.4
United Kingdom	182	18.3	120	13.5

Sources: Own calculations from Frech et al. (2026) and adjusted for PPP (World Bank Open Data).

The index of per capita contribution to global R&D of the 5 European countries in Table 5 is in all cases below 40% of the US index: it ranges between 37.5% and 18.3% in the base case, and between 30.8% and 13.5% in the sensitivity analysis. Of these six countries, the highest index of contribution of each country adjusted for PPP corresponds, in both cases, to Spain and the lowest to the United Kingdom. As in invoice prices, the per capita contribution to R&D adjusted for PPP of the United States appears as an extreme observation.

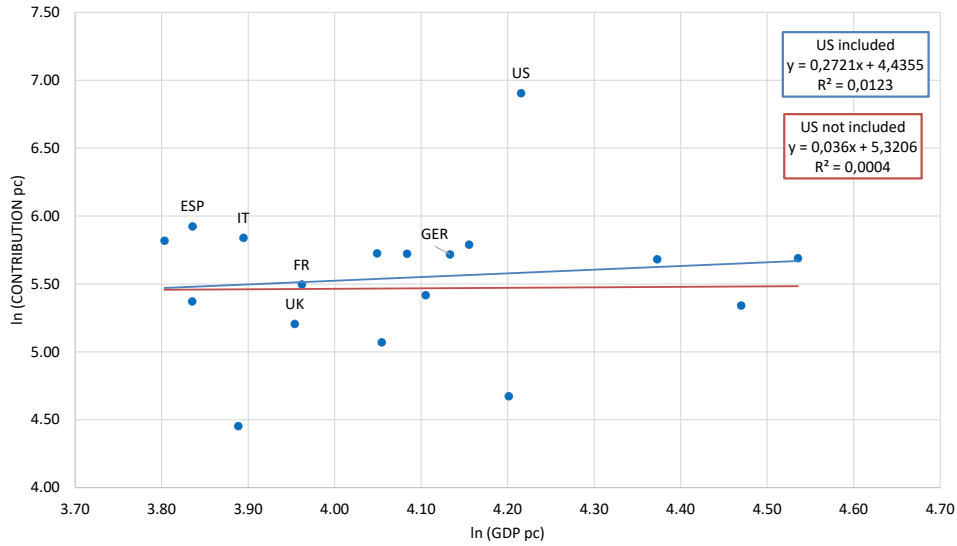
The estimated arc elasticity of the total contribution of each country to unadjusted R&D in the sample of 32 countries of the study by Frech et al. (2026) in relation to GDP is 1.23: a 10% increase in GDP correlates with a 12.3% increase in the contribution. This elasticity is compatible with the "exploitation hypothesis" from lower-income countries to higher-income countries (Frech et al., 2026): countries with higher GDP contribute more than proportionally, free riding behavior not being complete. Likewise, this estimated elasticity is compatible with a greater willingness to pay for innovation and for health outcomes as the global income of countries increases. It should be noted that the Ramsey rule on the optimal price difference (Section 2) does not allow establishing any normative value on price elasticity with respect to income nor that this must be unitary. However, a more appropriate measure of Frech et al.'s (2026) "exploitation hypothesis" should take into account the purchasing capacity of each country and its dimension in population terms for those countries of an income more similar than that of the 32 included in their study.

As an alternative estimate to that of Frech et al. (2026), here the relationship is analyzed between the adjusted per capita contribution to R&D, not the global contribution of each country, with respect to GDP per capita also adjusted for PPP and for countries of relatively similar income: OECD countries

with an adjusted GDP per capita equal to or higher than 60% of that of the US, which is precisely the group of reference countries of some of the Medicare programs of the US MFN pricing policy (see Chapter 4). Denmark and Israel are excluded for lack of data and Luxembourg for being an extreme observation. For this group of countries and when corrected for purchasing power capacity, the elasticity between per capita contribution to GDP with respect to GDP per capita has no statistical significance: the total contribution to global R&D of each country appears simply as proportional to the volume of population and is, in the income interval of the selected countries, rather inelastic with respect to GDP, the United States likewise being an extreme observation. This result does not confirm the so-called "exploitation hypothesis" for these high-income countries but rather detects the existence of an empirical "norm" of adjusted per capita contribution to R&D from which the US departs markedly at the upper end (see Figure 3).

FIGURE 3

RELATIONSHIP BETWEEN PER CAPITA CONTRIBUTION TO R&D AND GDP PER CAPITA (VARIABLES ADJUSTED FOR PPP)



Source: Own elaboration from the data of Frech et al. (2026).

The various measures of global "free riding", more or less precise or appropriate, highlight a more than proportional contribution, above 50%, of the US to innovation in R&D in medicine as a global public good (Murphy, 2026). The per capita contribution adjusted for PPP of the first 5 European

markets is much lower than that of the US. Considering the global level of the US per capita contribution to global R&D, the differences observed in Table 5 could be interpreted as an implicit subsidy from the US to the rest of the world. However, this conclusion must be qualified, beyond the details on data and method highlighted in this Section and the previous one, by some implicit hypotheses and relevant considerations.

- First, these measures adopt as implicit hypothesis the fact of considering that the current global volume of recovery of R&D by industry, as well as the corresponding global profit rate, and R&D investment itself correspond to the level of efficiency and are aligned with their contribution to global social welfare. The evidence in this regard is insufficient.

- Second, all the measures presented in this Section also adopt the implicit hypothesis, by using observed net prices in the US as reference value, that the current willingness to pay in the US for biopharmaceutical R&D represents an adequate measure of its incremental contribution to health and social welfare. Likewise, this implicit hypothesis lacks, in the absence of an HTA system in the US, sufficient empirical support.

- Third, the evidence points to a heterogeneous and rather moderate impact at the aggregate level on incremental cost-effectiveness thresholds when the health perspective is broadened to the social one or when the long-term price is used and not the entry price. Therefore, if the willingness to pay based on HTA used in various European countries through the indicative use of explicit or implicit cost-effectiveness thresholds (see Chapter 5) were relatively close to the real one (or even somewhat close to the opportunity cost of adopting new medicines in public health systems) of these countries, the measure of European "free-riding" would be much smaller or moderate assuming greater social welfare and opportunity cost for these countries. Instead, in the US there would be a very high transfer of social welfare from patients to industry or simply an income transfer associated with R&D, in the absence or with reduced added therapeutic value, that would impoverish US patients.

- Fourth, this high transfer of consumer surplus to producers through the price differential of new medicines in the US is carried out almost without any guarantee that it bears an appropriate relationship with the incremental benefit and the incremental cost-effectiveness ratio of R&D. This could be so, whether for current R&D or for future R&D induced by a price differential, and the corresponding expected profit

rate, whose orientation to health outcomes has not been proven in the US.

- Fifth, it should be noted that the measures of "free riding" reviewed refer to price per package or physical unit of medicine and not to the true relevant price in the health sector. What the patient and the health system purchase when financing R&D is the social utility of new patented medicines: incremental outcomes in individual and population health.

- And, finally, in line with the points previously set out, it must not be overlooked that the price per unit of measurement of health improvement in terms of survival related to quality of life (for example, the cost per QALY) should be the relevant reference to estimate the possible existence of free riding, as well as its effects not only on the level of current and future R&D but on the alignment of this towards innovations with greater global incremental benefit in terms of health. This argument suggests that the global level of R&D should tend to adjust towards the declared willingness to pay of each country, the inverse situation to that in which countries' willingness to pay adjusts to investors' expectations about the appropriate global level of R&D.

Chapter 4

"MOST FAVORED NATION" (MFN) PRICING POLICY IN THE UNITED STATES: GLOBALIZATION OF INTERNATIONAL REFERENCE PRICING?

This chapter analyzes the evolution of the United States "Most Favored Nation" pricing policy applied to medicines. Its background is presented, from proposals for Medicare and the Inflation Reduction Act to the 2025-2026 measures. The chapter describes Executive Order 14297, voluntary agreements with pharmaceutical companies and the GENEROUS, GLOBE and GUARD programs.

4.1. BACKGROUND: A BIPARTISAN CONCERN

Publicly financed health care programs in the US, Medicare and Medicaid, have had legislative restrictions that have prevented direct price negotiation with industry until 2022 (Sullivan, 2023). The only exception in these two programs has been the Medicaid Drug Rebate Program (MDRP): this program requires the medicine manufacturer to agree and keep in force a National Drug Rebate Agreement (NDRA) in exchange for the state Medicaid program covering most of the manufacturer's medicines. The result is that Medicare pays much higher prices than other public programs in the US that allow price negotiation, such as the Veterans Administration (VA) and Medicaid's Unit Rebate Amount (URA). Both internal price comparisons in the US constitute confidential information not accessible to Medicare and call into question the real magnitude of the net, effective and potential price differential in the US with respect to other countries (Chapter 2). A question without sufficient evidence is whether the VA and URA (Medicaid) programs have had negative externalities resulting in higher prices for Medicare.

VA obtains high discounts and prices much lower than those of Medicare through direct price negotiation for inclusion in insurance coverage. A 2020 report indicates that the net prices paid by VA for almost 400 medicines are on average 54% lower (GAO, 2020) than the net prices paid by Medicare Part D (medicines dispensed in pharmacy and covered by private plans approved by Medicare).

An additional federal program in the US (340B Program) requires manufacturers participating in Medicaid to offer substantial discounts on medicine prices to organizations (for example, hospitals) that provide medical care to underserved populations. The maximum price in this case is determined from the Average Manufacturer Price reported by the manufacturer to which a Unit Rebate Amount (URA) is applied. The URA establishes a minimum discount percentage of 23.1% for branded medicines, 17.1% for branded pediatric medicines and clotting factors, and 13% for generic and over-the-counter medicines (Sullivan, 2023). There is the possibility that states may negotiate additional discounts generally related to the type of coverage within the formulary when there is therapeutic competition.

In this context of prices paid by public programs in the US, the first proposal for the application of IRPs in the US dates back to the Obama Administration in 2016. Quite a few years before President Trump's second term, both the Republican administration (2020), under the first term of President Trump, and the Democratic administration (2022), under President Biden, introduced different policy measures (international reference prices versus price negotiation) but both aimed at reducing the differential in prices of patented medicines in the US compared with the rest of the world.

Despite the widespread concern about the international differential of observed prices, the recent evolution of pharmaceutical expenditure in the US highlights an important moderation both in the price of patented branded medicines and in overall pharmaceutical expenditure in the US (Cutler and Klarnet, 2026). This analysis helps to contextualize the expected impact of a potential reduction in the price differential between the US and the rest of countries, taking into account not only brand prices but also sales volume. Using IQVIA invoice data and estimates of net prices based on assumptions about discounts and rebates, for the period 1998-2024 in the US, Cutler and Klarnet (2026) find a very important deceleration in the growth rate of pharmaceutical expenditure: 1.3% annually in the period 2010-2024 compared with 7.8% between 2000 and 2005. The explanatory factors of this deceleration correspond to factors related to utilization management more than to prices (effectiveness of prior authorization policies and increases in copayments), which especially affects demand and price elasticity of new medicines with high net price. On the price side, the growing patent loss of medicines with high sales figures has contributed significantly to this deceleration.

4.1.1. MFN for Medicare Parts B and D (2020)

In 2016 the administration of President Obama had already introduced a proposal for the application of international reference prices in Medicare Part B

(Kirschenbaum, 2025; CMMS, 2016). Two years later, in October 2018, President Trump promised to reduce the prices of medicines paid under Medicare Part B to match them to international prices in Europe.

The formal beginning of the policies called "Most Favored Nation" (MFN) in the US can be identified with Executive Order 13048 (September, 2020) of the first term of President Trump. The declared objective of this policy was that Medicare Part B (in physician office or outpatient hospital consultation) and Part D (retail, outpatient) would not pay higher prices than the lowest observed price, adjusted by magnitude and differences in GDP, in countries with comparable GDP per capita. 50 high-cost medicines selected each year had to have prices based on those of other countries. This policy was annulled by the courts in December 2020 for issues mainly related to the approval and implementation procedure. Finally, the Democratic government of President Biden repealed the legislation based on the MFN price criterion in December 2021 (Kirschenbaum, 2025) in favor of price negotiation procedures.

4.1.2. The Inflation Reduction Act (2022)

The Inflation Reduction Act (IRA) signed in August 2022, under a Democratic presidency, marks the start of a negotiation process for a limited number of medicine prices in the Medicare program (Parts B and D) directly with industry (Sullivan, 2023; Conti et al., 2024), which in principle is not so different from MFN-type policies. The basic elements of this legislation (Medicare Drug Price Negotiation Program, MDPNP) to compare with the MFN policies of 2020 and 2025 are the following:

- Medicines included. It would apply from 2026 to the 10 patented branded medicines (15 in a second negotiation cycle) with the highest sales volume in Part B, selected in 2024; those of Part D would be applied from 2028.

- Medicines excluded. Those with less than 7 years on the market and biological medicines without biosimilar[12] with less than 11 years on the market. Exclusion from the entry of generics or biosimilars.

[12] A biosimilar medicine is a biological product that demonstrates, through analytical, preclinical, and clinical comparability studies, a high degree of similarity to a previously authorized reference biological medicine, such that any differences observed in its quality attributes do not have a clinically significant impact on its safety, efficacy, or immunogenicity.

- Negotiation criteria. Information on current regulation and patent; R&D, production and distribution costs; federal financing of R&D, sales forecasts, unmet medical need and comparative effectiveness.[13]

- Maximum price (Maximum Fair Price, MFP). Decreasing scale on the AMP (Average Manufacturer Price, average manufacturer invoice price, once discounts and rebates on the list price have been applied); decreasing invoice price according to time since marketing approval: a) 75% of AMP when between 9 and 12 years have elapsed since approval; 65% when between 12 and 16 years have elapsed, and 40% when more than 16 years have elapsed.

- Price updates. Price increases are limited to inflation variations, as in Medicaid.

- Resolution of disagreements. Companies that did not accept this negotiation would be subject to a special tax of 65% and 95% on sales from previous years, with the option of voluntarily renouncing inclusion in the financing of Medicare and Medicaid programs.

According to an estimate by the US Congressional Budget Office (CBO, 2022), the application of this policy could initially imply a fairly moderate average saving, of 5.4%, in Medicare pharmaceutical expenditure (Parts B and D) over 10 years, a figure expandable with extension to more medicines, although susceptible to possible strategic responses by industry with upward changes in list prices. On the other side of the balance, comparative effectiveness as a criterion could be interpreted as a promising first step that would later open the door to HTA and to the incremental cost-effectiveness ratio. The same CBO (2021) estimated that, for the 176 most prescribed patented branded medicines, the average price per defined daily dose (DDD) of Medicaid was equivalent to 34.4% of what Medicare paid in 2017, which gives an idea of the potential reduction through price negotiation in Medicare. Nevertheless, the selection of products makes extrapolation of results difficult.

4.2. MFN POLICIES 2025-2026 (as of May 31, 2026)

From the start of Trump's second presidential term, the US government withdraws support for the measures to expand Medicare price negotiation, announcing, instead, that it will resort to voluntary agreements with

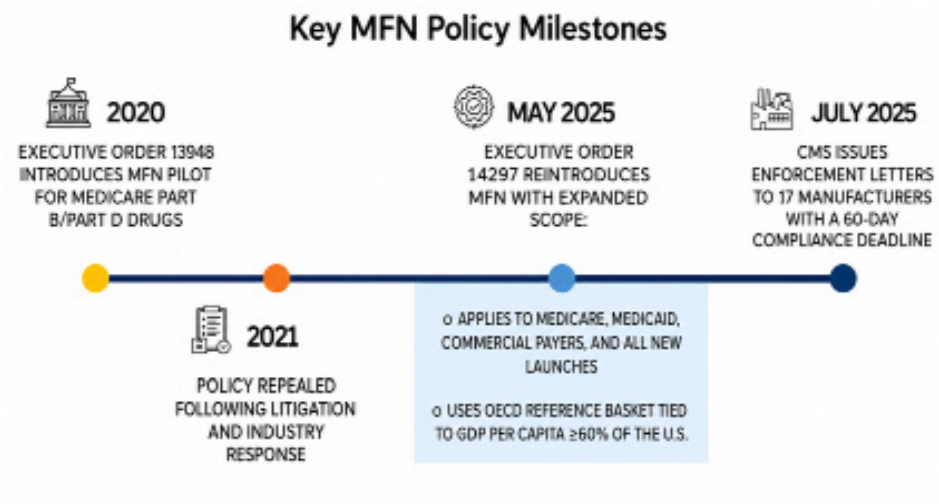
[13] An unmet medical need exists when a patient population lacks satisfactory treatment options, or when existing options leave a clinically significant margin for improvement in relevant health outcomes.

pharmaceutical companies, with price reductions and increased investments in R&D and industrial production in the US.

MFN-type policies are reintroduced, although in a much broader way than in 2020 (see Chronology in Figure 4), from April 2025, with Executive Order 14273. This order recovers the objective of the previous term of President Trump to reduce the costs of prescription medicines for patients and taxpayers. Already more explicitly, an MFN pricing policy is established in May 2025 through Executive Order 14297 and, subsequently, with the letters addressed in July of the same year to 17 large pharmaceutical companies. These letters have given rise, to date, to 17 confidential bilateral agreements between each company and the US government. These measures are complemented by the announcement, at the end of 2025, of three more formalized MFN-type pricing programs: GENEROUS for Medicaid, and GUARD and GLOBE for Medicare.

FIGURE 4

CHRONOLOGY OF MFN POLICY IN THE US



Source: Gwatkin N, Nzenza E, Freemyer K. Policy Brief: Most Favored Nation (MFN) and the future of pharmaceutical pricing and access. Decisive Consulting; 2025. Available at: https://herspiegel.com/white-paper/most-favored-nation-policy-pricing-and-access/

4.2.1. Executive Order 14297 (May 2025)

Executive Order 14297 establishes the general terms, although very imprecise, of the framework of the so-called MFN policy of Trump's second

presidential term in 4 main lines (general objective; generic policy chosen; imprecise application; extensive sanctions/threats) that will characterize the following Executive Orders issued to this date.

- First, the logic of the diagnosis of the problem starts from the declared intention to end the "generosity" of the US that is paying excessively high prices (see Chapter 2) that finance global innovation while the rest of countries take advantage of this effort ("free riding") (see Chapter 3).

- Second, the policy to achieve this objective must be to ensure access in the US to the most favored nation price (MFN price) without indicating any limitation in its scope of application and pointing out that patients must be able to access MFN prices in direct-to-patient sale programs.

- Third, within a maximum period of 30 days it establishes that the government will communicate the MFN targets, which are not identified or defined, to pharmaceutical companies in order to achieve prices comparable to those of developed countries.

- And, finally, it establishes that in case of not observing "significant progress" towards MFN prices, sanctions of various kinds will be adopted: a) plans to impose MFN prices; b) import policies from low-price countries; c) sanction anticompetitive actions; d) review exports that are facilitating global price discrimination; and, e) review and modify or revoke marketing authorizations.

On July 31, The White House addressed a letter to the 17 main pharmaceutical companies: AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, EMD Serono, Genentech, Gilead, GSK, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Regeneron and Sanofi. In these letters they are granted a 60-day period in order to comply voluntarily with four mandates:

- Initial claim for extension of MFN prices to the entire portfolio of products to Medicaid patients.

- Guarantee MFN prices at the launch of any new medicine and thereafter through a contract with the US government that guarantees these prices to Medicare, Medicaid and private payers.

- Return of the higher revenues obtained abroad to US patients and taxpayers, for which companies must commit to negotiating with foreign governments that take advantage ("freeloading") of the US;

these revenues must be repatriated in order to reduce prices in the US through an agreement with the government; US tariff trade policy will support this objective.

- Offer MFN prices in direct purchase by patients by participating in distribution of high-consumption products in direct-to-consumer and direct-to-company sales with high discounts so that all American citizens can access MFN prices similar to those that industry offers in third countries.

If these requirements are rejected, the letters indicate that the US government will deploy the entire possible arsenal of measures to put an end to "abusive" pricing policies in the US. This is a statement that recalls that of the president of the European Central Bank in 2012 when he declared that he was willing to do whatever it takes to save the euro (Robinson, 2026).

4.2.2. Voluntary agreements

Annex I details the scarce information available on the confidential bilateral agreements reached with all of these 17 companies between September 2025 and April 2026. These companies represent 86% of the US branded medicines market (Pines, 2026). To date, these agreements remain confidential. In general terms, the agreements contain provisions on four main known elements:

- Industry commits to offering MFN prices to the public programs Medicaid and/or Medicare for most of its patented medicines.
- Industry commits to offering MFN prices through the centralized TrumpRx direct sale channel for some of its patented medicines.
- Industry commits to certain investments in production and in R&D in the US.
- The US government commits to exemption from future trade measures (tariffs) and mandatory MFN programs for industry.

The White House has communicated, explicitly, tariff exemption for these companies as counterpart: "For companies that enter into most favored nation pricing agreements with the Department of Health and Human Services (HHS) and domestic production agreements with the Department of Commerce, a 0% tariff will apply until January 20, 2029" (The White House, April 2, 2026). Likewise, participation in voluntary agreements avoids formal MFN price

regulation through mandatory programs (see later in this Chapter). The tariff threat possibly weighs more than MFN prices in the decisions to relocate production of pharmaceutical companies in the US.

4.2.3. Framework for the application of MFN pricing policy

For the first time in May 2026, after the scarce concretion of the Executive Order of May 2025 and the confidentiality of the 17 agreements with the main pharmaceutical companies, a document from The Council of Economic Advisers has provided a conceptual framework of MFN prices in line with the main four elements (Section 1.4) of the known IRP-type policies (CEA, 2026).

- Medicines included: all medicines and biologics not subject to competition from generics or biosimilars; it excludes generics and biosimilars, with some possibility of exceptions regarding their inclusion in certain public programs. Details are pending on the level of application for each active ingredient: defined daily dose (DDD) for any presentation, distinction according to form of administration, number of units per package, dose of active ingredient, etc. The MFN programs GUARD and GLOBE (see later in this Chapter) define each medicine at the NDC-9 level: the same active ingredient, dosage, form of administration and concentration.

- List of reference countries: Germany, Canada, Denmark, France, Italy, Japan, United Kingdom and Switzerland; these are the G-7 countries adding Denmark and Switzerland following the criterion of including all countries that have the headquarters of the top 10 companies by market capitalization.

- Prices adopted as reference: net sale price excluding discounts, rebates and any other concession by industry to the payer, including claw back clauses such as the UK Voluntary Scheme for Branded Medicines Pricing, Access and Growth (VPAG); these net prices will be reported by companies and subjected to an audit procedure. Various European countries have adopted legislative measures that prohibit making public the net prices in their countries (see Chapter 5).

- Calculation of the reference price: the net price observed in each country will be corrected for differences in GDP per capita adjusting by PPP, adopting as reference the second lowest net price in the 8 comparator countries. The choice of exchange rates and the frequency in updating reference prices remain to be known.

Four important differences distinguish, initially and with the information available to this date, MFN prices from the application of IRPs in Europe: the

scope of application, the implementation instrument, the time horizon of the pricing system and the threats of trade sanctions.

- First, in Europe the reference price is established for medicines under public financing, the scope of application of the MFN price is much broader in the US: all pharmaceutical markets in the US, including in addition to those publicly financed programs, also private insurance markets and direct sales to patients.

- Second, in Europe IRPs are used as a formally established criterion among the various pricing criteria or else are used implicitly. However, the main instrument of the MFN price is being set as the sole criterion through voluntary agreements directly between the US government and pharmaceutical companies, accompanied by the threat of trade sanctions in case of no agreement. The effects of non-compliance with these agreements are unknown for now. In addition to the 17 voluntary and confidential agreements already signed to this date with a duration of three years, the US government states that it expects to reach similar agreements with most companies producing branded medicines and biologics without competitors that market in the country. The CEA document (2026) reports that "the Administration is working with Congress to incorporate those voluntary agreements into legislation". Approval in Congress does not seem easy since the government has the opposition not only of Democrats but also of a platform of more than 50 Republican congressmen (Brooks, 2026).

- The time horizon of voluntary MFN pricing agreements has an expected duration of 3 years, pending regulatory formalization. The use of international prices as one of the pricing criteria in Europe, whether explicitly or implicitly, has been adopted continuously during the last two decades in most European countries.

- The voluntary agreements have as counterpart exemption from possible tariffs and mandatory MFN policies in the following 3 years (Robinson, 2025b).

The framework for applying MFN prices distinguishes retrospective application (medicines that are already on the market) from prospective application (new launches). In the application to medicines that are already on the market, the CEA document (2026) only defines, for now, the scope of application of three components: Medicaid MFN, direct sales to patients (TrumpRx) and coverage of anti-obesity medicines (GLP-1s) in Medicare Part D.[14]

[14] GLP-1 medications are drugs that mimic or enhance the action of *glucagon-like peptide*-1 (GLP-1), an incretin hormone involved in the regulation of glucose and appetite.

- *Medicaid MFN.* CEA (2026) recognizes that *Medicaid* already obtains very important discounts through the MDRP, some of which may even be lower than the MFN price (340B program). Despite this, *Medicaid* net expenditure is concentrated in a small number of patented medicines whose net price is above the MFN price by two or three times according to CEA (2026) (62% of *Medicaid* net medicine expenditure corresponds to 150 products). The voluntary MFN scheme in this case is based on the commitment to provide medicines whose price exceeds the MFN price at this price. There is insufficient information to determine the scope of those medicines whose MFN price will be lower than that of *Medicaid* with discounts.

- *TrumpRx.* TrumpRx.gov is a website that allows patients access to discounted prices in direct purchase under all voluntary agreements signed with 16 of the 17 pharmaceutical companies. CEA (2026) highlights access through this channel to two types of treatment with reduced insurance coverage: anti-obesity GLP-1s (indicated for diabetes) and fertility treatments. The impact of *TrumpRx* on the price paid by consumers should be considered taking into account that: a) many of the drugs initially marketed through this channel are at a stage close to the entry of generics or biosimilars; b) this platform could be of little relevance for patients with private insurance since the copayments borne by them will hardly be lower than the MFN price offered in *TrumpRx*; c) possibly the results of this direct sale channel will depend on approval of the inclusion of these purchases at MFN price within the purchase conditions of private insurance (Cohen, 2026).

- *GLP-1s in Medicare Part D.*- MFN policy has also facilitated access to GLP-1s in the Medicare Part D program from which they were excluded. According to CEA (2026), price negotiation allows expansion of this coverage without fiscal risks from July 1, 2026 with reduced copayments. A first estimate of the effect of the reduction in the price of Semaglutide through voluntary agreements estimates that it is equivalent to providing coverage for treatment of half a million more Medicare beneficiaries (Dusetzina et al., 2026). Nevertheless, observation of the price of GLP-1s in pharmacies of other high-income countries in March 2026 shows prices lower than those offered by *TrumpRx* (Robbins, 2026).

Pharmaceutical companies have committed in the voluntary agreements to apply MFN prices in new launches (prospective MFN): second lowest net price observed in the reference countries. CEA (2026) has assumed that net prices will be reduced by 30% at the end of a decade of MFN policy with a forecast of price convergence. Likewise, CEA (2026) adopts the hypothesis of savings of $600 billion within 10 years, without further information on the

counterfactual adopted or details on the models used in this estimate (Cohen, 2026). Likewise, the CEA document (2026) and the documents issued by The White House, for now, do not indicate how they will set the MFN price for new launches when the new medicine has been launched only in one or in no reference country (Maini et al., 2026). More than 70% of new medicines are approved first in the US (Brooks, 2026). 5 of the 7 reference countries have HTA agencies, which influences a longer time to regulatory approval. And, in addition, the strategic behavior of industry itself may lead to not launching or to postponing launch in certain countries in order to avoid the MFN price. None of these assumptions seems to have been incorporated in the CEA model (2026).

Still lacking important details on the application of MFN prices, two implementation difficulties of this policy can be highlighted: obtaining reliable information on net prices in the reference countries and setting the MFN price when the medicine has not yet entered any or only one of the reference markets. For this second difficulty, for the moment, the criterion adopted by the prospective MFN policy is unknown. Regarding information on net prices of medicines already marketed in other countries, MFN policy requires this information from industry, proposing a procedure for information transfer and audit (CEA, 2026) similar to the German Arbitration Board. In this case, if industry cannot disclose the discounts down to the net price in the reference countries, or if the GKV-Spitzenverband (German public insurance system) does not consider credible the net prices reported by industry, then the Arbitration Board estimates the discounts based on its own information (Rodwin & Gerke, 2021). Nor can the existence of more than one net price in each reference country with the possible existence of extreme observations be ignored.

The potential impact on the role and activity of PBMs in the US could be potentially important (Ankura, 2025), although this will depend on the details of implementation of the measures. The revenues of PBMs and GPOs[15], which act on behalf of health plans, may be affected through the reduction of the capacity to negotiate discounts on invoice prices, which could potentially modify the form of payment towards fixed prices and the negotiating functions themselves of these organizations.

A preliminary estimate of the impact on expenditure on Semaglutide (GLP-1) of voluntary and bilateral MFN price agreements compared with the scenario of prices resulting from negotiation allowed by the IRA, and taking into account the future loss of exclusivity, concludes that the reduction in expenditure will

[15] GPOs (*Group Purchasing Organizations*) in the U.S. are organizations that pool the purchasing power of hospitals, healthcare organizations, and other providers to negotiate better prices, discounts, and contract terms with manufacturers and distributors for medications, medical devices, and other healthcare supplies.

be 148% higher under MFN (middle scenario) (Sullivan et al., 2026). These results cannot be extrapolated to other medicines and also do not take into account the increase in expected consumption associated with the expansion of insurance coverage and the price reduction itself.

The fact that the preferred implementation instrument by the US government is confidential agreements with the main pharmaceutical companies gives this policy a character of diffuse risk and uncertainty about its scope in the market and temporal continuity given the absence or scarce regulatory formalization. All this together with doubts about the capacity to enforce the agreements and the medium-term viability of threats of trade sanctions (tariffs). The fact that financial markets have reacted positively to the confidential agreements may be indicative, among other things, that the market has already anticipated the infeasibility of high prices in the US since the measures adopted previously and that industry has mitigated the effects of MFN pricing policy with net prices that may already be quite closer to those of other countries of similar income than what available statistics on invoice prices reflect, gaining in predictability through the agreements, and also the possibility that the market interprets MFN prices as a "temporary shock".

4.2.4. GENEROUS (Medicaid)

Retrospective and prospective MFN policies associated with voluntary agreements between the government and pharmaceutical companies constitute voluntary MFN. In November and December 2025, the Centers for Medicare & Medicaid Services announced three MFN-type programs: GENEROUS for Medicaid, also voluntary in character, and GUARD and GLOBE for Medicare, mandatory in character (Table 6). However, if we consider the market volume of the companies that have signed these agreements for 3 years and if the counterpart of these agreements that would free these companies from mandatory MFN is fulfilled, the scope of application of these programs could become quite limited.

GENEROUS ("GENErating cost Reductions fOr U.S. Medicaid") is a program of voluntary participation by the pharmaceutical industry and is directed to the Medicaid population of those states that join this program. The program affects prices of outpatient patented branded medicines and adopts the second lowest price adjusted for PPP in the previously mentioned countries and is superimposed on the Medicaid Drug Rebate Program (MDRP). Industry is expected to make participation decisions taking into account the differential in net price and also the legal risks regarding confidentiality of these prices (see Chapter V). The program represents a framework of centralized negotiation in addition to MFN

TABLE 6

COMPARISON OF THE GENEROUS, GUARD & GLOBE PROGRAMS

Program	*GENEROUS*	*GUARD*	*GLOBE*
Public insurance	*MEDICAID*	*MEDICARE Part D*	*MEDICARE Part B*
Start date	1/01/2026	1/01/2027	1/10/2026
Duration	5 years	5 years + 2 years	5 years + 2 years
Type of participation	Voluntary	Mandatory	Mandatory
Eligible companies	All those with an MDRP agreement, which is maintained	Companies that market GUARD medicines and are subject to the Medicare Part D inflation rebate program	Companies that market GLOBE medicines and are subject to the Medicare Part B inflation rebate program
Population included	Medicaid population of each state adhering to the program	Medicare population of a random selection of 25% of small areas (ZCTAs)	Medicare population of a random selection of 25% of small areas (ZCTAs)
Medicines covered	All outpatient patented branded medicines	Non-competitive medicines affected by Medicare Part D inflation rebates. 18 therapeutic groups	Subset of non-competitive Medicare Part B medicines. 7 therapeutic groups
Exclusions	No exclusions	Generics, biosimilars, those selected for Medicare MFP and with sales below $69 million in Medicare Part D	Generics, biosimilars, medicines with sales below $100 million in Medicare Part B, or subject to application of Medicare MFP
Reference price	Second lowest price adjusted for PPP	*International Pricing Benchmark* = higher price between the "Default Benchmark" (lowest list/invoice price in the 19 countries, adjusted for PPP) and the "Updated Benchmark" (weighted average net price in the 19 countries reported by the company and adjusted for PPP)	*International Pricing Benchmark* = higher price between "Method I" (lowest list/invoice price in the 19 countries adjusted for PPP) and "Method II" (weighted average net price in the 19 countries reported by the company and adjusted for PPP)
Type of price	Net price	List prices in IQVIA MIDAS, Eversana NAVLIN and POLI. Invoice and list prices, and net prices	List prices in IQVIA MIDAS, Eversana NAVLIN and POLI. Invoice and list prices, and net prices
Reference countries	Germany, Canada, Denmark, France, Italy, Japan, United Kingdom, Switzerland	19 OECD countries with PPP-adjusted GDP per capita >= 60% US and GDP >= $400 billion	19 OECD countries with PPP-adjusted GDP per capita >= 60% US and GDP >= $400 billion
Adjustments	PPP adjustment	PPP adjustment. 102% adjustment for "Default benchmark" and 104% for "Updated benchmark"	PPP adjustment. 102% adjustment for "Method I" and 105% for "Method II"
Counterpart	Common coverage criterion (prior authorization, preferred list)	None	None

MDRP: Medical Drug Rebate Program. MFP: Medicare maximum fair price. OECD: Organization for Economic Co-operation and Development. GDP: gross domestic product. POLI: Global Data Pharmaceutical Prices. PPP: Purchasing power parity. ZCTA: ZIP Code Tabulation Area.
Sources: www.thefdalawblog.com; www.cms.gov

prices (Maini et al., 2026) with the following most important characteristics (Table 6):

- (a) a coverage criterion common to all states adhering to the program (positioning on preferred list, prior authorizations, etc.),
- (b) centralized negotiation that can potentially reduce state-by-state negotiation costs especially for drugs that are candidates for new forms of market access such as outcome-based risk-sharing agreements, subscription models, etc.
- (c) contradictorily, anchoring and dependence on international prices may reduce the margin to experiment with these flexible forms of payment,
- (d) it suffers from the limitations already indicated on information relating to international net prices,
- (e) and selection bias may reduce the value of comparing the effective capacity of this program in the case of a hypothetical generalization. Maini et al. (2026) have suggested that mandatory participation and random implementation in a certain number of states would be a better option if the objective is to verify the impact of adopting MFN prices and centralized negotiation.

4.2.5. GLOBE & GUARD (Medicare)

The GLOBE (Global Benchmark for Efficient Drug Pricing) and GUARD (Guarding U.S. Medicare against Rising Drug Costs) programs correspond, respectively, to Medicare Parts B and D and are mandatory for pharmaceutical companies that market included medicines that are also subject to the Medicare inflation rebate program. Both programs have an experimental character since they are directed to a random selection of 25% of small areas called ZCTAs (ZIP Code Tabulation Area). These programs do not include non-competitive branded medicines from all therapeutic groups but a selection of broad use (7 therapeutic groups in GLOBE and 18 in GUARD) with exclusions based on global billing thresholds to Medicare.

The application of IRPs in these two programs is somewhat different from the so-called MFN price since it adopts as reference the price in 19 OECD countries with GDP per capita adjusted for PPP higher than 60% of that of the US (and an aggregate GDP of 400 billion or more). If pharmaceutical companies

do not provide international net prices, GLOBE and GUARD will automatically apply the list or invoice prices observed in the countries chosen as comparators. The reference price, with the details known so far, is a so-called "International Pricing Benchmark" (IPB) equal to the higher price of the two following cases:

- the lowest price in the 19 countries adjusted for PPP calculated from invoice (or list) prices observed in the MIDAS databases of IQVIA, NAVLIN of Eversana and/or POLI;
- or the weighted average net price in the 19 countries according to company communication and adjusted for PPP;
- to this IPB the application of an upward adjustment of 2% is foreseen if the higher price is the first of the previous ones and of 4% or 5% if the higher one is the second (low-intensity incentive to reveal net prices in other countries).

In general, the scope of application of these two programs is broader than that allowed by the IRA, which limited price negotiation, for example, to medicines for which 11 years had elapsed since their approval, while under these programs now only one year needs to have elapsed (Hwang et al., 2026). Likewise, they include medicines for rare diseases excluded from negotiation allowed by the IRA. However, none of these programs take comparative effectiveness into consideration in negotiation and price setting, which could have had some role with the IRA price negotiation model (Hwang et al., 2026).

Previous estimates on the expected impact of the price negotiation measures established by the IRA should allow evaluation of the incremental impact on net prices of the GUARD and GLOBE programs. An estimate of the impact of Medicare's Medicare Drug Price Negotiation Program (MDPNP) for the 10 medicines that were announced to enter under this model in 2026 estimated a reduction of 8.8% in net expenditure, taking into account the exclusions established in the IRA (Jeon et al., 2026). By contrast, another estimate of the impact on expenditure of the MDPNP regulated by the IRA for 15 medicines in 2027 has estimated a price reduction that would range between 16% and 56% of net prices when information on comparative effectiveness is used in price negotiation (Li et al., 2025) in a form partly comparable to a reference pricing system with therapeutic equivalence. On the other hand, a comparison of the price negotiated by Medicare with net prices in other countries for 10 medicines (Wouters et al., 2025), which would be implemented in 2026, finds net price reductions associated with price negotiation that for 9 of the 10 products are equal to or greater than 25%; however, these negotiated net prices continue to be higher than the average net prices in 6 other countries

(Germany, Australia, Canada, France, United Kingdom and Switzerland) except in the case of insulin with a net price very close to the average of these countries and lower than that of Germany, Canada and Switzerland.

The ambiguity about the potential exclusion of GUARD and GLOBE as mandatory programs for companies that have reached, or may reach in the future, bilateral agreements with the US government casts doubt on the effectiveness that these programs may come to have.

Chapter 5

EXPECTED IMPACT ON PRICES, ACCESS AND INNOVATION: TOWARDS A GLOBAL COMPRESSION OF PRICES?

This chapter analyzes the expected impact of MFN policies on prices, access and innovation. The limitations of the application framework, possible scenarios of international price compression and the intuitions of economic modelling are presented. Early strategic responses of European systems are also described, such as confidentiality of net prices and variable-price agreements.

5.1. LIMITATIONS OF THE FRAMEWORK FOR APPLYING MFN PRICES

The use of IRP, and of MFN prices as a particular case, has as an advantage the potential obtaining of price reductions in the short term. A positive factor of MFN prices is, in theory, the fact that the reference is based on net prices and not on invoice or list prices, which do not reflect the reality of prices actually received by industry in each country. Another notable positive factor lies in the adjustment of net prices in other countries by GDP PPP as a measure of differences in purchasing capacity so that the system admits "justifiable" price differences for countries of similar income.

The main problems related to the potential impact on prices of MFN policies in the US, in the known application framework, come from three types of limitations (Cookson, 2025; Cookson et al., 2025; Grueger et al., 2025; Megerlin, 2026; Robinson, 2025; Robinson, 2026):

- Limitations that derive from the diagnosis of the price problem in the US and its institutional context.
- Limitations derived from the strategic behavior of the pharmaceutical industry and of the health systems of countries with high income levels, especially European ones.
- And difficulties related to the practical application of MFN prices.

In the first group of limitations, it is worth citing the fact that MFN prices anchor US prices in international prices, a form of regulatory delegation, with scarce changes in:

- The criteria and mechanisms of price negotiation of public programs with an important capacity for price reduction as counterfactual scenario with which to compare the impact of MFN prices is not well established. The marginal contribution of MFN prices on net prices attainable with the price negotiation instruments already applied in VA and Medicaid, as well as those granted to Medicaid under the IRA of President Biden's government (Kelkar and Cliff, 2025), is unknown.

- The non-aligned incentives towards the reduction of list prices and the pass-through of discounts and rebates to final payers, public and private, by PBMs (Chen, 2025) remain with scarce changes, although the result will depend on the details of implementation and possible future complementary measures.

- MFN prices are not accompanied by nor related to indicators of comparative or incremental efficacy/effectiveness or to the incremental cost-effectiveness ratio (Hwang, 2026), *de facto* delegating the measurement of value to the HTA agencies of the countries that make up the reference basket by importing together with international prices, the criteria for setting them; this may not be the most appropriate for the US (local aspects of HTA) and may be vulnerable to strategic behavior by industry.

- The foreseeable attempt by the US to move away from an international differential compatible with optimal Ramsey prices if the MFN criteria are applied as they have been defined.

In the second group of limitations, related to the strategic behaviors of agents in response to MFN prices, we can highlight:

- The anchoring of US prices in the pricing policy of other countries, what has been called anchoring in a moving reference point (Barros et al., 2026; Robinson, 2026; Mulcahy, 2026) and which is susceptible to being influenced by strategic behaviors of industry and of other health systems (partially endogenous evolution related to the incentives generated by MFN prices themselves). In the European application of IRPs it is known that industry tries to increase the price in the reference countries and increases even more the opacity regarding net prices, potentially making the IRP system itself unviable.

- The probability of initial launch in the US is much greater than in other countries. Of the 287 new medicines introduced in 27 countries in the period 2017-2022, only 57% were launched in the US and in some other country; 17% only in the US; and 26% only outside the US (Mulcahy,

2024). More than half were launched first in the US, with a delay of roughly one year in launch in the main markets of OECD countries. In the absence of a well-established HTA system and clear criteria when the new medicine is launched first in the US or has only been launched in another country of the reference basket, MFN prices may lead to an increase in the probability that the US will be the country of first launch, trying to continue obtaining high prices that later industry will try to transfer to other reference countries according to their strategic responses.

- It is logical to expect that the application of most favored nation (MFN) treatment to existing branded medicines will successfully reduce their net prices in the US and increase them in other countries. The US may force companies to disclose their financial data (invoices and discounts) in other countries (whether through US legal means or through threats, regardless of laws passed in other countries requiring confidentiality, if the US market is too valuable to lose and other markets are not). It is very different to set MFN prices for new medicines, whose prices, by definition (public sector), have not been set outside the US. Other countries take months or even years to set prices financed by health technology assessment (HTA). Another major unknown about new medicines is that prices in the US tend to increase annually after launch, and how MFN policy will address this dynamic remains unknown.

And, in the third group of difficulties, those related to implementation of MFN prices, the following stand out:

- A complicated verification of increases in net prices in other countries outside the US that are scarcely transparent. This difficulty will be aggravated by the foreseeable increase in this opacity with instruments of creative accounting both by pharmaceutical companies and by European health systems (Mulcahy, 2026).

- The real impact on net prices of confidential agreements is very difficult, complex and costly to verify, so, at least in the short term, it seems expected that MFN policies will rely on other regulatory instruments. Among these instruments, threats of tariff impositions (Kolchinsky and Xie, 2025) and investment commitments in the US, or even favorable tax provisions (Mulcahy, 2026), stand out. The objective would be to achieve reductions in net prices in the US rather than to achieve very high increases in net prices outside the US.

- The almost absence, for the moment, of concretion and normative strength of this policy that is adopting confidential agreements of

the US government with pharmaceutical companies as the preferred instrument and with a three-year term may contribute to agents interpreting MFN prices as a one-off shock rather than a long-term structural policy. Robinson (2026) interprets MFN prices more as a negotiation instrument than as a commitment to follow a concrete and well-defined policy.

- The lack of knowledge of the counterparts of confidential agreements may notably limit the scope of MFN prices since these agreements are the preferred instrument of the new policy.

- The lack of definition about how the MFN price will be calculated when there are not enough reference points in the countries adopted as comparator (prospective application) constitutes a manifest weak point of this policy. A possible scenario is that companies decide not to launch their products in certain markets in order to avoid MFN prices. Many companies that have reached confidential agreements with the US government have been launching new medicines in the US and prefer to delay launch in the reference countries.

The set of these limitations casts serious doubt on the 10-year global estimate associated with MFN prices from the Council of Economic Advisers (CEA, 2026) and leaves the estimated saving of more than 500 billion dollars as a highly speculative figure that depends on many scarcely realistic assumptions (Cohen, 2025).

5.2. EXPECTED IMPACT ON PRICES AND ACCESS

5.2.1. Expected economic impact in the US

Classic economic impact studies of an activity or productive sector, based on input-output tables, highlight a high direct, indirect and induced impact of production and investment of the pharmaceutical sector on GDP and employment (Bosch et al., 2022; Juneja et al., 2024). If expenditure on medicines in the US is reinvested in R&D in the country itself, then paying lower prices thanks to MFN prices may have a negative economic impact on the overall US economy (Gandjour, 2025).

Gandjour (2025) starts from medicine sales in the US that correspond 50% to national production and 50% to imports. High prices increase the contribution to GDP, assuming a multiplier of 2, and at the same time imply a

high opportunity cost of imports if the assumption of identical reinvestment and productivity rates in the national pharmaceutical sector is accepted. However, if prices decrease, reinvestment in the US pharmaceutical sector will be reduced and if savings in import prices are redirected to sectors with a lower multiplier than the pharmaceutical one, then MFN prices may have a negative impact on US GDP. It is obvious to indicate here that the direction of the expected impact on GDP does not prejudge the same direction for the expected impact on health and social welfare.

Stock market reactions inform the interpretation of whether MFN policies are negative or positive for the pharmaceutical sector. Kirson et al. (2026) indicate that, for now, investors have interpreted the impact of MFN policies on pharmaceutical industry profitability positively. Data from the 16 publicly traded companies indicate that the negative impact of the MFN policy announcement and the communication of the letters sent to the 17 companies has been more than offset by a positive and statistically significant cumulative abnormal return (CAR) for most companies, which occurred with the signing of the first bilateral agreement by Pfizer. The market appears to have anticipated the signing of subsequent agreements with the first company (Pfizer). For most companies, the negative impact of the letters is more than offset by the positive impact on their share prices resulting from the agreements.

Three highly relevant points for interpreting the stock market reaction regarding Europe are not addressed in the analysis by Kirson et al. (2026): a) the differential impact on the European industry; b) the US-UK agreement that shields the UK from trade threats in exchange for concessions with a high opportunity cost; and c) the expected impact on the net prices of new medicines in Europe.

First, the most positive CAR (Compound Annual Cost) reaction to the signing of the confidential agreements is for US companies; the cumulative impact is negative for the valuation of European companies such as Novo Nordisk and Sanofi.

Second, the agreement signed by the US with the UK government commits the UK to increased spending on new medicines, higher prices, and an increased cost threshold per QALY (Quality-Adjusted Life Year). It is also known that the US government has opened negotiations to reach a similar agreement with Italy and has threatened to initiate trade sanctions proceedings against Germany if it does not increase the price of new medicines (information as of May 31, 2026).

Third, it is worth noting that the confidential agreements appear to contain a provision guaranteeing that the US government will defend the net prices of

their companies' new drugs against European health systems, especially those using HTA systems with more restrictive access and pricing conditions.

5.2.2. Expected impact on prices and access

The contrasted evidence on the application of IRPs in Europe (see Chapter 1) is the best available support for a forecast of the expected impact of MFN prices on prices and access in the US (Danzon, 2018; Frank et al., 2022; Maini and Pammolli, 2023; Grueger et al., 2025). The main conclusions of this literature applied to the US analyzing MFN prices as a case of IRP applied to net prices can be summarized as the following:

- Expected increase in the net price in the reference countries.
- Expected delay in the launch of new medicines in the reference countries (Ramagopalan et al., 2026).
- Expected increase in rebates, discounts and any other medicine purchasing mechanism that reduces transparency of net prices in reference countries.
- Expected decrease in net prices in the US in the short term and a moderate reduction in the medium and long term.

The international net price differentials of patented brands and MFN policies can be observed under three scenarios, with different assessments of the expected impact with the globalization of IRPs implied by the new US MFN policy (Mulcahy, 2026):

- Scenario 1: US prices are appropriate and prices outside the US are too low;
- Scenario 2: US prices are too high and prices outside the US are too low;
- Scenario 3: prices in the US are too high and prices outside the US are appropriate.

The initial reaction of the pharmaceutical industry to the launch price of new medicines points to the first scenario, as do those who accuse European HTA of being an instrument of free riding (Kolchinsky, 2020; Kolchinsky and Xie, 2025).

The report of The Council of Economic Advisers (CEA, 2026) and a significant part of the economic literature on international prices (Danzon, 2018; Frech et al., 2026; Robinson, 2026) are explicitly located in the second scenario, leaving open the question about the magnitude and criteria of both downward and upward adjustments. This second scenario is the one that Robinson (2026) has baptized as a scenario of "price compression".

Both scenarios 1 and 2 presuppose a reduction in net prices in the US, leaving aside the precise magnitude of this reduction. In February 2026, only a little more than half (52%) of the 62 experts of a panel convened by the Cornell Health Policy Center (Kakani et al., 2026) forecast a reduction in prices in the US, while 23.3% did not expect a reduction in net prices and 25% indicated that the impact on prices was uncertain.

And, the third scenario corresponds to the results of pricing policies based (approximately) on value practiced by HTA agencies of several European countries and founded on evidence on incremental efficacy or effectiveness and, in some cases, the incremental cost-effectiveness ratio, in addition to empirical estimates of the maximum willingness to pay for health gains (life expectancy and health-related quality of life) (Gondi et al., 2025). Among these agencies, NICE (National Institute for Health and Care Excellence) in the United Kingdom and IQWIG (Institute for Quality and Efficiency in Health Care) in Germany stand out.

HTA-type criteria based on evidence on comparative effectiveness were present in some of the price negotiation policies adopted under President Biden's mandate. However, in the current description, MFN prices are anchored to an external reference (which is not the same as an exogenous reference), international net prices, which means that evidence on efficacy, effectiveness and efficiency is not taken directly into account as a pricing criterion. However, anchoring to the net prices of countries that use evidence-based HTA criteria is also equivalent to the indirect importation of these criteria through prices into the US, although with the complication that the declared prices are not those actually applied in these countries that use HTA to inform their decisions.

The more independent (exogenous) these international prices are from US prices, the greater the indirect importation of HTA criteria may be. In the opposite direction, if international prices of new launches (prospective application of MFN prices) are increasingly dependent on the initial price in the US (a certain degree of endogeneity), then the importation of HTA criteria through MFN prices in the US will be less important. If companies prefer to delay the entry of new launches in the reference countries in the MFN basket and enter first in the US trying to obtain high prices to then transfer to the reference countries, we

will find ourselves in a situation that would be more similar to an approach to the first scenario. By contrast, a strict retrospective application of MFN prices on medicines that are already on the market in the reference countries, and that are not in the final stretch of the protection period, would be more similar to the third scenario.

5.2.3. Scenario of international price compression

In addition to seeking to reduce prices in the US, the objective of MFN prices is that net prices outside the US, and especially in Europe, be higher, reducing international price differences with high-income countries by adjusting for differences in purchasing power capacity (price compression scenario; Robinson, 2026; Megerlin, 2026). This objective, in theory and as has been made explicit in the logic of the application of MFN prices, would imply, assuming a strict application both in the short and medium term and under the hypothesis that net prices both in the US and outside the US become observable by the US government, that:

- International net prices product by product may continue to be different in monetary terms after dynamically applying the average exchange rate of each period and the evolution of average per capita income (frequency of updating to be determined), in high-income countries.

- These international net prices would be higher in countries with higher per capita income provided that the GDP price level index is positively correlated with GDP per capita. If this were so, net prices would continue to be higher in the US, although possibly with a smaller differential than the current one and which cannot now be quantified precisely because of uncertainty about current net prices both in the US and outside the US.

- The frequency of dynamic updating of the GDP PPP adjustment may influence future international differences in net prices importantly in view of the possible volatility of the exchange rate and variations in the GDP price level index.

- Without considering the possible dynamic mismatches that may occur, an application of MFN prices as described could still be apparently compatible with the recommendation of economic theory on optimal prices maintaining an inverse relationship with the price elasticity of each country, assuming that this is decreasing with income level (Ramsey prices).

- The only differences in international net prices between countries of considered high income included in the basket of reference countries could be that derived from differences in GDP PPP. Whether this is so depends, among other factors, on the comparative basket of countries included in the radar of MFN prices and on the form of choosing the MFN price among the net prices observed in these countries.

- In theory and without considering the criterion for choosing the MFN price within the comparison basket, that MFN prices being compatible with the Ramsey rule is more feasible when the criterion for choosing the comparator basket is based on relatively similar per capita income. *A priori*, the results will be different if a low cut-off point is used as criterion for inclusion in the basket taking as indicator the per capita income of the rest of countries with respect to the US (GUARD and GLOBE), adjusted by GDP PPP, than if only the G-7 countries plus two small countries that have the headquarters of some of the pharmaceutical companies with the largest market capitalization are chosen (confidential agreements and GENEROUS).

- However, the adoption of the second lowest price observed in the basket of reference countries no longer guarantees compliance with the Ramsey rule. The greater the differential of PPP-adjusted per capita income between these countries, with this second-lowest-price rule, the greater the probability that the theoretical resulting MFN net price in the US will be lower than that of countries with per capita income lower than the US (ordinality). This situation would breach the Ramsey rule of optimal prices and would result, potentially, in an objective of contribution to R&D strictly via price differential below that which would correspond to the US according to its income level.

Let us see the results of a simple numerical illustration as an example of this situation, resulting from a theoretical application of MFN prices with 2022 data, and without taking into account strategic behaviors of industry and of European health systems, either in the retrospective or in the prospective application. This illustration could approach a strict retrospective application without changes in the prices of the reference countries. The invoice prices from the Rand Corporation report are used (Mulcahy et al., 2024), which does not include Denmark or Israel.

With the G-7 countries plus Denmark and Switzerland as reference, the second PPP-adjusted price index would be that of France with a level equivalent to 31.3% of the current invoice price in the US: the US occupies second place in the group in PPP-adjusted GDP per capita and would occupy sixth place in the

PPP-adjusted branded price index. With the reference group formed by the 19 OECD countries with GDP per capita equal to or greater than 60% of that of the US, the price level should be equivalent to 22.7% of the current level in the US: the US occupies fourth place in PPP-adjusted GDP per capita and would occupy sixteenth place in the PPP-adjusted branded price index. Both situations seem unlikely in the reality of a retrospective application in which regulated prices in most reference countries are upwardly rigid after market launch. In any case, the objective of this simple illustration is to highlight that the framework for applying MFN prices is not initially coherent with the objective of prices in the US similar to those of a country with similar income, once adjusted for PPP, nor would it comply with Ramsey's optimal pricing rule.

The two most important regulatory elements in European countries tilt the balance towards the third scenario of expected prices (lower price compression): HTA and centralized negotiation of maximum prices with market power in the countries that represent the largest world markets after the US. In the retrospective application of MFN prices to prices of medicines that are already on the market in Europe, the already cited regulatory inflexibility and the budgetary impact on public accounts, with European limitations on deficit and public debt, as well as competition with other social expenditures and defense expenditure, lead to a status quo scenario for European prices (Mulcahy, 2026) scarcely compatible with very important price compression. For this case, the reduction of prices in the US associated with MFN prices may simply be:

- partially fictitious due to the possibility that the US versus other countries net price differential is much smaller than that reflected by the available reports on invoice prices;

- and/or, that industry is willing to make limited downward concessions in net prices similar to those it has already previously accepted in negotiation processes under the IRA.

In prospective application, the expected impact of MFN prices for Europe may be higher (Epstein, 2026). The regulatory framework in several European countries with an important pharmaceutical market supported by transparent HTA processes based on clinical and economic evidence is very likely not only to continue having a high influence on their decisions on entry net prices, but also that the reports of these agencies will be a mirror on which to rely for the other countries with less development of HTA (Kumar et al., 2025).

An upward modification of cost-effectiveness thresholds in some European countries, as in the case of the United Kingdom (see later in this chapter), may translate both into somewhat higher entry prices (adaptive or concession scenario of European countries), although not to the extent reflected by the

data on available price differentials, and an increase in the use of variable and scarcely transparent pricing instruments, such as risk-sharing agreements based on health or financial outcomes, subscription formulas, etc.

The foreseeable scenarios of already strained public finances, both in the EU and in the United Kingdom, make it difficult to foresee a notable increase in prices, such as that which would be required by an MFN price framework in which it is the US price that marks the entry price of new medicines in other countries. This situation may lead to a scenario characterized by greater restrictions on access for patients in the form of:

- Increase in delays in the public coverage decision, associated not only with European regulatory procedures but also with the entry strategies of industry itself in a credible scenario of MFN prices.

- A higher number of exclusions from public coverage associated with the application of stricter criteria on the value of new medicines or indications.

- Very restricted coverage decisions conditioned on those patient subpopulations with greater expected incremental effectiveness (Barros et al., 2026) and b) lower cost-effectiveness ratio in order to adjust to the modified thresholds of cost per QALY, whether explicit or implicit. The pharmaceutical industry itself will have incentives for launches with selective coverage in order to justify higher entry prices in HTA procedures (Barros et al., 2026).

The impact of these potential restrictions on patient access in the reference countries on health depends on the added therapeutic value of the new medicines and on their opportunity cost in terms of health. The balance for patients may not even be negative if the restrictions affect new treatments with reduced incremental efficacy or effectiveness (Naci et al., 2025) in favor of innovations with greater added therapeutic value and/or selective coverage for the population subgroups that can obtain a greater benefit in terms of health. As is evident, this requires transparent, independent, dynamic HTA procedures based on clinical evidence, as well as democratic, robust, solid and consolidated political governance.

5.2.4. Intuitions from economic modelling on expected prices under MFN policies

Modelling of the expected impact on prices of the adoption of a maximum price in the US referenced to that of other countries (MFN price) offers, for the

moment, limited and partially speculative results. The two main available works applicable to the new MFN policy in the US, although not yet published in a scientific journal with a peer-review process, are those of Dubois et al. (2022) and Barros et al. (2026). These two economic models provide information, under innumerable assumptions, on the expected impact of an MFN-price-type policy on the branded prices of new medicines launched after the application of this IRP-type policy both in the reference country and in the one that adopts the policy (prospective application).

In the scenario that represents the situation prior (status quo) to the introduction of MFN prices, both works share the modelling of the behavior of the pharmaceutical company as a profit-maximizing monopoly. The market of country A (which can represent the US) is initially a market of unregulated prices (free prices) without restrictions by buyers and in which, therefore, prices depend on the price elasticity of demand. The market of country B (which represents a market outside the US) is a market with a single public funder and with centralized negotiation in which prices are determined as the result of a Nash negotiation (Nash, 1950) between the company and the central funder of the country.

In the counterfactual scenarios (application in country A of a maximum price based on the price of country B, whether the latter represents a specific country or an average of the price of other reference countries), prices will also be determined in country B as the result of a Nash negotiation in which the company takes into account the effect on profits of price interdependence between country B and country A (internalization of externalities between countries caused by price regulation). In country A, in the counterfactual scenarios the company is constrained to apply the price of country B without a negotiation process (interdependent prices). In both cases, the models assume, among other hypotheses relevant to the interpretation of results, that in the two scenarios (status quo and counterfactual) there is perfect information, without costs of access to information and without time delays, on net prices for both countries and price decisions in the two countries occur simultaneously. Likewise, the assumption is adopted that the maximum IRP-type price adopted in country A can be strictly applied at any moment in time with stable exchange rates and perfectly homogeneous and comparable products in the two countries. Neither model coherently contemplates the possibility that the new medicine is not launched by industry or is excluded from financing by the insurer in either of the two countries.

Dubois et al. (2022) assume that country B (outside the US) has budgetary capacity to adapt to higher prices derived from the result of Nash negotiation. This situation would correspond to a scenario in which the reference countries

outside the US have an accommodating behavior that involves accepting price increases and revising upwards the budget constraint (scenario 2 of section 5.2.2. compatible with important global price compression). These authors estimate a structural demand model based on sales in the US and Canada in the period 2002-2013 with IQVIA data (invoice prices); an extension of the model also uses sales in the five main European markets (Germany, Spain, France, Italy and United Kingdom). The main results of Dubois et al. (2022) on the expected prices of new patented branded medicines under MFN- or IRP-type regulation are the following five:

- The price in the reference countries increases very importantly: for industry it is more costly to reduce the price by US$1 in the US than in Canada.

- The price in the US experiences a modest price reduction: between 0% and 21.2% with an average of 7.5%. The expected reduction in expenditure in the US is even lower because of the expected increase in the quantity consumed: a reduction of 5.5%.

- When the number of countries used as a reference is broader and when the size of the market of these countries is greater, the price reduction in the US is higher while the price increase in the reference countries is lower. With Canada and the 5 main European markets as reference, the expected average reduction in the US price is 14.8% and a reduction in expenditure of 11.5%.

- Changes in prices are heterogeneous between therapeutic groups depending, mainly, on differences in price elasticity and the marginal cost of the new medicine, in addition to the negotiating power of regulators in each market.

- Expected prices in the US will also depend on the behavior of the regulator in the US when industry decides not to launch the new branded medicine in the reference markets. In a scenario in which industry is obliged to launch the new medicine in the reference markets, the expected reduction in the average price in the US is 32.4% with a reduction in expenditure of 17.5%.

Dubois et al. (2022) introduce an additional counterfactual to that of the IRP scenarios, a scenario of price negotiation in country A (US) similar to that of country B (outside the US). In both cases, prices will be the result of a Nash negotiation under the conditions of each country. Now the price in the US will be independent of the price in other countries (absence of interdependence). The authors adopt the assumption of a price negotiator in the US who maximizes

consumer surplus. In this case, prices and expenditure in the US can be reduced very importantly and significantly more than in MFN-type policy scenarios: the expected reduction in the average US price would be 51.5% and expenditure could be reduced by 21.1%. Thus, the conclusion of this modelling is that a scenario of price negotiation in the US, that used HTA to determine willingness to pay for added therapeutic value, could be superior to MFN prices from the consumer perspective (Rodwin, 2020; Rodwin & Gerke, 2025; Sampson & Ollendorf, 2024; Kelkar & Cliff, 2025).

The main contribution of the model of Barros et al. (2026) consists of introducing a counterfactual for reference country B (outside the US) in which this country uses economic evaluation in an HTA framework to estimate the added therapeutic value (incremental benefit) of the new branded medicine under patent. This situation attempts to model the behavior of reference countries such as European ones that have HTA agencies that inform national financing and price decisions. The model assumes the absence of patient contribution or copayments.

In the negotiation process with the central funder of country B, industry may decide the patient subpopulation for which to obtain a favorable financing and price decision. That is, the model introduces the possibility of strategic decisions by industry on the degree of extension of the desired insurance coverage that influences compression or tendency towards convergence of international prices. If the company reduces the target population to that for which there is evidence that the added therapeutic value is greater, then it is possible that a Nash negotiation results in a higher price compatible with an MFN price in the US (Darrow et al., 2025). None of the scenarios considered are based on price negotiation in the US supported by HTA evidence. Barros et al. (2026) present an illustration of the quantitative impact of their model through a calibration based on parameters observed in the literature (Ho & Pakes, 2025).

The most notable results of the model of Barros et al. (2026) on prices and access in the two countries are the following:

- Population access to the new medicine in the reference country could be reduced if it maintains the HTA criteria prior to the adoption of MFN prices in the US and access would increase in the US. The model predicts that global therapeutic benefit increases by being redistributed from patients with lower benefit to patients with greater incremental benefit (global increase of 7.1%).

- The price in the US could be reduced by 47.4% compared with the previous situation without MFN prices if the reference country does

not modify its financing and price criteria. If the reference country "accommodates" these criteria by accepting higher prices, then the expected reduction in the US price could be somewhat lower, 38%.

- A scenario in which the reference country "accommodates" financing and price criteria to the adoption of MFN prices by the US could mean accepting an average price increase in the reference countries of 54.9% versus a 31.6% expected increase if it maintains the criteria prior to the new policy in the US.

In the model of Barros et al. (2026) it remains quite undetermined whether the increase in population with access to the new medicine in the US would correspond to the subpopulation for which industry has obtained the financing and price decision in the reference country with HTA criteria. The context of the US pharmaceutical market leads to forecasting that an extension to all patients with positive incremental benefit is more likely despite an unfavorable cost-effectiveness ratio. The difference between the average and marginal value of the added therapeutic value also plays an important role in the interpretation of the results of this model. The limitation of access in the reference country with HTA may be an efficient decision in terms of health outcomes, taking into account the opportunity cost, while the extension to marginal patients in the US may be an inefficient decision, which could question the value of the global increase in access predicted by the model. Finally, a price increase of 31.6% in the reference country or countries that do not modify their financing and price criteria based on HTA seems very unlikely in European health systems with public financing. Rather, it seems that a price increase for new medicines of this magnitude would require adaptation scenarios outside the US far above those foreseeable.

5.3. EXPECTED IMPACT ON GLOBAL INNOVATION

The preliminary estimate of the impact of MFN prices in the US states, without providing evidence, that prospective application of MFN will have a positive net effect on incentives for innovation due to the increase in the expected global value of new pharmaceutical products (CEA, 2026). This report assumes that MFN prices will not reduce the income available to invest in R&D but rather will redistribute the burden between countries more equitably thanks to the increase in prices in the reference countries. This situation would correspond to the scenario in which international prices converge towards US prices or in which price differentials are compressed and the effect of the price reduction in the US is more than compensated by the price increase in the reference countries and the increase in the quantity consumed in the US.

The previous literature on possible applications of IRP in the US, prior to the announcement of MFN prices in 2025, points to the risk that the reduction of prices in the US results in an important decrease in R&D investment (Sullivan et al., 2022). However, only 38.3% of the experts of the Cornell Policy Center panel (Kakani et al., 2026) thought in February 2026 that MFN prices would reduce innovation and 31.7% responded that the expected impact on innovation was uncertain.

R&D investment by pharmaceutical companies depends on the expected revenues from sales of the new medicine, the expected cost of development and expectations about changes in financing and price policies. The conventional approach to estimating the impact of a price regulation policy such as MFN prices on pharmaceutical innovation has consisted of estimating the elasticity of R&D expenditure or the elasticity of the number of new molecules that reach the market with respect to the variation in the current revenues of pharmaceutical companies as a result of the new price policy (Filson et al., 2025; Dubois, 2025; Corzo et al., 2026). Nevertheless, the proportion of R&D financed with own funds has decreased in recent years and R&D investment financed by research-oriented companies with few or no medicines on the market through external financing has increased (venture capital funds and collaboration agreements with large pharmaceutical companies) (CBO, 2021).

The estimate of the impact of the direct negotiation capacity opened by the IRA in 2022 in the US for Medicare on innovation offers a relevant precedent for knowing the possible effect of MFN prices on innovation. The US Congressional Budget Office (CBO) estimated that the reduction of expectations about future revenues of pharmaceutical companies due to this policy could mean the entry to the market of 8 fewer new medicines in the period 2020-2029 and 30 fewer in the following decade (CBO, 2021). Corzo Santamaria et al. (2026) have estimated the impact of a reduction in company sales produced by a hypothetical change in price regulation in the US through calibration of a valuation model using real options of pharmaceutical R&D that captures sequential clinical investment with clinical failures, stochastic costs, uncertain cash flows and optimal abandonment decisions. The quantitative results of this model indicate that a 30% probability of reducing cash flow by 25% means an average reduction in the value of a research project of 16.1% and also implies a reduction of the threshold for making optimal project abandonment decisions.

The economic models of Dubois et al. (2022) and Barros et al. (2026) have also estimated the expected impact on the reduction of global revenues or profits of pharmaceutical companies as a result of MFN prices. Dubois et al. (2022) estimate that global profits may be slightly reduced (-1.8%) when a single country is adopted as a reference (Canada) and may even increase slightly

when the 5 main European markets are also adopted as a reference (2.2%). In both cases, the expected impact on R&D and new medicines is expected to be scarce. It is important to remember that, in these two scenarios of the model, it is assumed that the reduction of profits in the US can be compensated by profits outside the US. The reduction of global profits is substantially greater in the scenario in which the pharmaceutical company is forced to launch the product also in reference markets (20.1%). And, when instead of MFN prices a price negotiation policy as in Canada or Europe is adopted in the US, the reduction of global profits is greater (27.6%).

In the quantitative results of the model of Barros et al. (2026) it is observed that a reduction in the global revenues of industry of 17.8% could occur in the scenario of application of MFN price (identical price in the US and outside the US) compared with the absence of MFN prices. In an alternative scenario with MFN prices but with adaptation of the reference countries (acceptance of changes in HTA criteria that allow higher prices, of the type agreed between the US and the United Kingdom) the variation in global revenues could even change sign and become an increase of 5.2% with an increase of 38.1% in the US and a reduction of 14.5% outside the US. Again, in the case of this model, the result of the adaptive scenario depends on the effective magnitude of the adaptation of prices and the budget constraint of the health systems of the reference countries (see Section 5.4).

Predictions about the way in which price variations in the US and outside the US, taking into account the compensation effect through changes in quantity, will affect innovations and, something more important, their added therapeutic value are, today, more a speculative art than a science (Mulcahy, 2026). Given the uncertainty about the details of MFN prices and the relative opacity about net prices in the US and outside the US, economics must humbly recognize that speculative results on the expected impact of this policy on innovation (dynamic efficiency) and health are still of scarce usefulness for decision makers.

The social assessment of the impact on dynamic efficiency of expected downward variations in prices in the US and of potential global reductions in the revenues and profits of pharmaceutical companies must take into account some precautions in its interpretation:

- First, the relationship between medicine prices (and the revenues and profits of companies) and the value of therapeutic innovation of new medicines remains an area where the evidence is inconclusive or it can even be recognized that it may be somewhat "nebulous" (Mulcahy, 2026). The relationship between the contribution to the variation in added therapeutic value and incremental health (survival and quality

of life) of the population and the launch of new medicines is also uncertain.

- Second, the evidence is not sufficient to sustain that the global level of R&D investment is adequate nor is it below the socially optimal level. For this reason, it is risky to assess the impact on dynamic efficiency and global health of short-term variations in the prices of new medicines and/or in the volume of sales and profits of companies. Under the untested hypothesis that the current situation in fact corresponded to a situation in which de facto a complete reimbursement of R&D investment occurred, with the corresponding profit rate adjusted by sectoral risk, this situation would be partially similar to that of a policy of recovery of investment costs and capital costs with low social control of the profit rate. In this scenario there would be incentives for overinvestment in R&D above the socially optimal level and absence of incentives for productive efficiency in research.

- Third, assuming that the shock of the MFN price policy will affect R&D decisions to some extent, the magnitude and social value of this impact will depend on the decisions adopted by companies and funders at the margin (Mulcahy, 2026). In this scenario, companies could have more incentives to efficiently reduce marginal R&D investment, that is: (a) to reduce R&D costs by improving the success rates of research projects (technical efficiency in production), (b) and to reduce that investment in new medicines with lower added therapeutic value and worse cost-effectiveness ratio, reducing investment in new medicines that entail reduced incremental improvements (allocative efficiency). In this same scenario of price increases outside the US, European funders supported by HTA evidence on comparative efficacy/effectiveness and the incremental cost-effectiveness ratio could have incentives to concentrate incremental expenditure on those indications and subpopulations of the new medicines that are more efficient. This could not only increase the efficiency of health expenditure in the short term, reducing the opportunity cost of financing treatments that do not pass the filter of the cost-effectiveness ratio (static efficiency), but could give signals and incentives to industry more aligned with the social value of new medicines, so that companies redirect the resources destined for investment towards R&D projects with greater value and expected benefit (dynamic efficiency) (Robinson, 2026; Mulcahy, 2026). Unlike what the adoption of MFN prices in the US assumes, this scenario implies adopting financing and price policies giving greater importance to HTA.

5.4. EARLY STRATEGIC RESPONSES OF EUROPEAN HEALTH SYSTEMS (AS OF MAY 31, 2026)

5.4.1. Application framework: Certainties and uncertainties

The initial response of new launches by the pharmaceutical industry, in an early context, with asymmetric and imperfect information, and with many uncertainties both in the US market and regarding the strategic responses of markets outside the US, can be analyzed based on expected behavior according to the experience of the European application of IRPs.

The initial response of the pharmaceutical industry, with prudence and waiting for better information and less uncertainty about the political scenario, is coherent with previous experience and economic theory. First, industry is adopting as its preferred objective entry and setting of launch price in the US. And second, the launch of new medicines in the reference countries is being delayed: a notable decrease in the number of pharmaceutical launches throughout Europe, with a total fall of 35% in the ten months after the introduction of IRP in the United States compared with the ten previous months (Gurung, 2026).

The current situation for European markets, especially that of the health systems of European countries with the 5 main pharmaceutical markets, can be characterized by the elements of the framework for applying MFN prices in the US that can be taken as foreseeably applicable with a high probability, and by important information problems and uncertainties about other important aspects of this application framework.

The prospective application framework of MFN prices that with a high probability can be adopted as certain or highly foreseeable for the next three years would be defined by:

- Medicines subject to MFN prices.
  - The confidential agreements with the 17 companies and the GENEROUS program (Medicaid, non-mandatory and with negotiation of discounts under the IRA) very possibly affect all new medicines that these companies launch onto the market and all Medicaid outpatient medicines. At this date, the main application instrument seems to be that of confidential and bilateral industry/US government agreements.

- The experimental GUARD and GLOBE programs (Medicare, mandatory) include only certain therapeutic groups and only 25% of the Medicare population. Oncology medicines are included in these two programs.

- Countries in the MFN price reference basket.

  - European countries included in the radar of the reference basket for industry/government agreements and GENEROUS: Germany, Denmark, France, Italy, United Kingdom and Switzerland (6 countries). This basket includes 4 of the 5 large European markets (the exception is Spain). Other European countries that escape this radar and that have been adopting the price of some of these countries as IRP are foreseeably going to stop using these countries as a reference.

  - European countries included in the radar of the expanded reference basket of GUARD and GLOBE: Germany, Austria, Belgium, Denmark, Spain, France, Ireland, Italy, Norway, Netherlands, United Kingdom, Czech Republic, Sweden, Switzerland (6 GENEROUS countries plus another 8 countries). This basket includes the 5 large European markets. The market share under MFN includes fewer medicines, but it is also foreseeable that the rest of the countries avoid taking these as a reference in a scenario of global price compression.

- MFN price = second lowest price adjusted for PPP.

  - Industry/government agreements and GENEROUS: MFN price = second lowest net price. The second invoice price index of branded medicines under patent in 2022 corresponds to France, the UK being the lowest (Mulcahy et al., 2024). Net prices must be declared by industry and with the possibility of being subject to audit and sanctions.

  - GUARD and GLOBE programs: second lowest price, which may be the invoice price or the net price. The second invoice price index in 2022 of this group of countries corresponds to non-European countries (Mulcahy et al., 2024).

The main information problems and uncertainties that affect the application of MFN price policies are at this date the following:

- Asymmetric information on the details of bilateral industry/government agreements that may affect all the parameters of an IRP system with

externalities for countries outside the US. Likewise, it is unknown whether other pharmaceutical companies will negotiate similar agreements. The companies that have signed these agreements know with more precision the launch conditions (country and net price) that will allow them to maximize profits.

- Lack of information on the countries that may be willing to negotiate and reach agreements with the US government, similarly to the UK, and on the scope of the application conditions and possible exemptions of MFN prices for national industry, which may have externalities for countries outside the US. The effective legislative capacity to implement tariff threats to specific countries and companies by the US is unknown.

- Uncertainty about the effective capacity of the US to require transparency from pharmaceutical companies on net prices applied in the reference countries, and to verify it, especially when this requirement entails a breach of the legislation of the reference country (conflict of laws).

- Lack of information on the criteria for dynamic updating of the reference price (frequency, exchange rate, GDP PPP adjustment).

- Uncertainty about the political capacity of European governments and the financial capacity of industry to face decisions of non-launch of some new medicines in European countries, or of very restrictive population coverage.

- Uncertainty about the national economic impact in European countries that potential relocation decisions in European pharmaceutical production and R&D may come to have, in addition to tariffs by the US.

5.4.2. Strategies for adjustment to the externalities of MFN prices

The strategic response strategies of European governments and health systems to the prospective application of MFN prices may be based on different combinations of instruments and heterogeneous objectives (health, budgetary, economic and commercial) according to pharmaceutical company and even according to indication or therapeutic group. In simplified form, three main response strategies are identified here based only on decisions about net prices, pharmaceutical expenditure and population coverage of the new pharmacological treatment (conditions of patient access). All of them admit combinations, variants and mixed forms.

- *Adjustment via net prices and pharmaceutical expenditure without affecting patient access.* This strategy entails the acceptance of higher net prices, higher pharmaceutical expenditure also on new medicines, shifting the budget constraint of health systems in order to avoid industry decisions to renounce launch in the country and without increasing the criteria on access restrictions prior to the externalities of MFN prices. This scenario could be described as adaptive or accommodating to the objectives of MFN prices in the US. The choice of this route would be an indication that its marginal benefit (marginal economic benefit in terms of direct, indirect and induced contribution to GDP and employment) could be higher than the marginal cost (opportunity cost in terms of health of the increase in pharmaceutical expenditure). The agreement signed between the UK and US governments is the only one that, for now, is situated in this scenario.

- *Adjustment via net prices and patient access conditions (and willingness to pay per QALY gained), without affecting pharmaceutical expenditure.* In this strategy the country attempts to maintain the budget constraint of health and pharmaceutical expenditure so that the externality in the form of higher net prices is adjusted through access decisions and conditions: restrictions so that only subpopulations with greater added therapeutic benefit and better cost-effectiveness ratio have access, corresponding to higher prices but still compatible with the maximum willingness to pay per QALY gained and, at the extreme, assuming the risk of non-launch of some new medicines in the country. In line with this type of adjustment, 36% of NICE positive recommendations since 2000 have limited patient access by recommending use in populations smaller than those of the marketing authorization. Between 2023 and 2024 these NICE decisions have limited access to 31% of the potential population (Darrow et al., 2025).

- *Delay of any adjustment in prices, expenditure and access (status quo while waiting for better information and less uncertainty) and adoption of evasive measures.* This strategy is based, at least in the short term, on the adoption of measures that hinder the transparency of information on net prices. It is also based on the adoption of forms of financing based on variable prices that turn the average net price into diffuse and difficult-to-measure information in order to avoid the externalities of MFN prices. This scenario, at the extreme, entails betting on the end or the impossibility of applying IRP systems such as MFN prices (Persson and Jönsson, 2016).

One year after the first Executive Order on the adoption of MFN prices in the US, three types of early strategic responses are described below. All of them entail legislative changes, adopted in some European countries and health systems: the

agreement between the UK and US governments; and the imposition of the obligation of confidentiality on national net prices (Germany, Spain, France, Italy), which may be accompanied by the promotion of purchasing policies based on variable prices, without the need for legislative changes (Germany).

5.4.3. Adaptive behavior: United Kingdom (UK)

In 2025, pharmaceutical R&D investment carried out in the UK accounts for 19.4% of investment carried out in Europe, although the sector is equivalent to only slightly more than 7% of European production and employment in the pharmaceutical sector (EFPIA, 2025). Likewise, UK medicine exports account for 4.5% of all European exports (EFPIA, 2025). In Tables 1 and 2 it can be observed that the price index of patented brands in the UK is the lowest of the main European pharmaceutical markets. Likewise, the UK is the European country with greatest experience in applying financing and price criteria for new medicines based on HTA for several decades (comparative efficacy and incremental cost-effectiveness), including the use of maximum thresholds of willingness to pay per QALY gained.

In this context, the UK has been the first country, and the only one at this date, to reach at the end of 2025 an agreement with the US government on price and financing conditions in exchange, mainly, for the guarantee of tariff exemption of imports of medicines and medical technologies into the US from the UK.

Table 7 summarizes the details of the main commitments of the UK government, compliance with which will affect very importantly the decision-making capacity of the Department of Health, the NHS and the independent evaluation agency, NICE. The UK commitments, if fulfilled as established at this date, will have an important upward impact on key indicators of health expenditure such as: the total volume of expenditure on new medicines, the percentage of health expenditure devoted to medicines, the cost-per-QALY threshold and net prices of new medicines. Likewise, the UK commits to adopting restrictive measures on the use of new medicines with lower prices.

The considerations, in addition to tariff exemption by the US, consist of the UK price not being adopted as a reference in programs with MFN prices and an ambiguous commitment, since it contains no measures to force its compliance, that companies will launch new medicines also in the UK. In fact, the UK appears with the lowest price index of branded medicines under patent in the GENEROUS basket of reference countries, so that the reference country adopted, according to the index, would not be the UK either in the case of all individual drugs.

TABLE 7

MAIN COMMITMENTS OF THE ARRANGEMENT BETWEEN THE UNITED STATES AND THE UNITED KINGDOM ON FINANCING AND PRICE OF NEW MEDICINES

COMMITMENTS OF THE GOVERNMENT OF THE UNITED KINGDOM (UK)
1. TOTAL EXPENDITURE ON NEW MEDICINES. Increase expenditure on new medicines from 0.3% of GDP in 2026; 0.35% in 2028; 0.40% in 2030 up to 0.6% in 2036. New medicines are those launched onto the market after this agreement (prospective application).
2. NHS PHARMACEUTICAL EXPENDITURE. Increase the percentage of the budget spent on medicines from 10% in 2026 to 12% in 2036.
3. INCREMENTAL COST-PER-QALY THRESHOLD USED BY NICE. Increase the threshold from £25,000 - £30,000 to £25,000 - £35,000. Adopt EuroQol 5 (EQ-5D) as a measure of health-related quality of life. Establishment of an industry-government working group that will analyze new forms of payment (outcomes-based payments) taking into account industrial policy together with the improvement of the differential of cost-per-QALY thresholds for different medicines.
4. NET PRICE PAID BY NHS FOR NEW MEDICINES. Increase of the net price by 25% from April 2026. The net price is the average price paid by NHS net of discounts, rebates and any other concessions on prices of new medicines (prospective application). Among these, the NHS will avoid increased discounts or rebates, including portfolio-level concessions under the Voluntary Scheme for Branded Medicines Pricing, Access and Growth (VPAG), the Statutory Scheme, or any successor scheme, or price discounts or retrospective payment requests contained in contractual supply agreements such as Managed Access Agreements, Patient Access Schemes and Framework Agreements.
5. CONDITIONS OF ACCESS TO NEW MEDICINES IN THE NHS. In patient access to new medicines with the previous net prices, the NHS will avoid the imposition of increased or excessively burdensome access barriers, or stricter utilization management controls that offset the increase in the net price by reducing the utilization of such medicines.
6. VPAG REFORM. The rebate rate of companies for sales of "newer" branded medicines will be reduced to 15% in 2026 (22.6% in 2025) and may not be subject to increase in subsequent years. The maximum aggregate rebate rate by VPAG and by any other discount program may not be higher than 16%. Establishment of an industry-government working group with the objective of designing a new scheme to replace VPAG (before 30/06/2026), initiating a pilot plan (from 1/09/2026 to 30/06/2028) and applying the new scheme from 1/01/2029.
COMMITMENTS OF THE GOVERNMENT OF THE UNITED STATES (US)
1. TARIFFS. Tariff exemption for patented and non-patented medicines from the UK, as well as medical technologies, from 1/01/2026 to 19/01/2029, on condition that the most important pharmaceutical companies in the UK accept the terms of the bilateral MFN agreements with the US government.
2. MFN PRICE. The Medicare program will not adopt the net price of a new medicine in the UK as reference, even if the price in the UK is the lowest among the reference countries of MFN prices, and other MFN programs in the US (GLOBE and GUARD) "are not designed in a manner that uniquely disadvantages the United Kingdom under its current system of medicine pricing".
3. LAUNCH OF NEW MEDICINES. "US and UK expect to work together so that pharmaceutical companies do not delay the launch of their innovative medicines in the United Kingdom". The agreement does not establish any mechanism to force this forecast to be fulfilled.

Sources: United Kingdom Government. Arrangement between the United States of America and the United Kingdom on pharmaceutical pricing. GOV.UK; 2026 Apr 2.

The estimate of the cost of application in strict terms of this agreement made by the UK government is one billion pounds sterling until 2028/29. Cross et al. (2026) have estimated that the cumulative additional cost will amount to 2.6 billion pounds by the end of 2028 and 44.7 billion pounds by the end of 2036.

Main criticisms that the UK commitments in this agreement have received within the framework of MFN price policies in the US:

- The added therapeutic value (incremental contribution to health) and the cost-effectiveness ratio, which have been the main criteria that have guided coverage and price decisions in the UK since the 1990s with the creation of NICE as an independent HTA agency, run the risk of remaining in the background. Agreements on the level of expenditure and net prices of new medicines independently of evidence-based criteria have the risk of increasing the degree of politicization of the evaluation that should guide coverage and price decisions. Future decisions on expenditure and net price of medicines by future political and health decision makers remain anchored to the quantitative objectives of this agreement, with the loss of political independence and decision-making capacity without any guarantee that expenditure and net price objectives improve NHS efficiency. For NICE this situation may mean a loss of independence and political interference in the orientation based on clinical and economic evidence (Vallejo et al., 2026).

- NICE thresholds have never been based on empirical studies of opportunity cost (marginal productivity of health expenditure, k-thresholds), and in addition this opportunity cost also depends on the budget constraint (Vallejo et al., 2026). The somewhat simplistic simulation of the cost-benefit type with k-thresholds would already be very useful by reasonably informing about the opportunity cost in terms of avoidable deaths, morbidity and QALYs associated with public decisions. The expansion of the upper limit of the threshold lacks economic justification based on opportunity cost. However, something similar could be noted about the use of higher thresholds that NICE has been applying for certain disease groups (oncology, rare diseases, end-of-life treatments, etc.).

- The opportunity cost of increasing the maximum cost-per-QALY threshold in financing decisions for new medicines implies a cost in terms of the difference between the QALYs gained with the new medicines and the QALYs sacrificed by renouncing a more efficient allocation with the same money from NHS services (Paulden, 2026; Vallejo et al., 2026).

Gainsbury and Lomas (2026) estimate the opportunity cost for 2028 at 340,000 cumulative QALYs annually. The excess mortality that could be prevented if resources were not allocated to funding new drugs until 2036, according to estimates by Cross et al. (2026), would reach an excess of 229,000 deaths, a figure higher than the mortality rate during the Covid-19 pandemic. This figure could reach 291,000 deaths if the costs of social services are taken into account.

The agreement signed by the UK government with the US entails, in theory, trade-offs for the UK in terms of industrial and commercial policy. Despite this, at this date no independent estimate of the economic impact is known. In the political scenario of effective application of the agreement, Ruiz and Briggs (2026) in view of the high opportunity cost in terms of health at the expense of other economic objectives, propose the creation of a specific fund for the financing of new medicines separated from the rest of the NHS budget. According to this proposal, this multiannual fund would also include the various specific funds that already exist in the UK for the financing of certain diseases (cancer and others). NICE would continue carrying out its clinical and economic evaluations independently, but using the new threshold. The fund would make transparent the excess cost of the agreement in relation to the previous situation. The volume of the fund would make transparent the cost of industrial and commercial policy objectives transferred to pharmaceutical expenditure and would highlight whether the budget constraint established through the fund is compatible with the new cost-per-QALY thresholds. As the authors of the proposal admit, in this way the opportunity cost does not disappear, but it becomes more transparent for decision makers and taxpayers, and would allow relocating its negative consequences outside health care.

Other European governments could join an agreement with the US government similar to the one signed by the UK, despite the difficulties of legislative concretion that the agreement may pose in the country. Germany could be a candidate given the economic importance of R&D, production and exports of the pharmaceutical sector on the national economy. At date, this agreement has not occurred, although the pressure of US commercial threats may become determinant in the changes adopted in each country.

5.4.4. Confidentiality clauses on net prices

Persson and Jönsson (2018) already predicted the end of the application of IRP systems in pharmaceutical markets due to the restrictions in access to new medicines that result from the lack of transparency of net prices. Confidentiality of net prices, price-volume agreements, risk-sharing agreements, refund

agreements, confidential discounts and other mechanisms contribute to net prices not being known and becoming increasingly diffuse.[16]

Riccaboni et al. (2022) use a simulation model with rational agents to show that transparency of net prices in Europe would not lead to greater price competition but to a reduction in patient access in middle- and low-income countries, moving prices away from the Ramsey rule and from distributive criteria. A similar conclusion is shared by various authors when transparency is combined with IRPs (Shaw and Mestre-Ferrándiz, 2020; Webb et al., 2022; Barrenho and Lopert, 2022).

Despite these initiatives of confidentiality of net prices in Europe, the US government has declared that transparency of net prices in the reference countries will be mandatory in order for companies to be able to market their medicines in the US. The effectiveness of European confidentiality clauses will depend on the result of the conflict of international laws and on the capacity for verification and enforcement of commercial threats by the US.

In France, the prices that result from agreements between the funder and the pharmaceutical industry, which include not only list or official prices but also applicable discounts (dual prices), are confidential for both parties. Variants include, for example, direct discounts (remise a la premiere boite) and price-volume agreements (Stindt, 2024). In 2026 the French government has ruled out the introduction of legislative measures of price transparency in order to protect access to new medicines.

In March 2026 a Spanish legislative proposal justifies the confidentiality of net prices as "a strategic element to preserve the negotiating capacity of the State, guarantee budgetary sustainability and ensure equitable access to therapeutic innovation" (Congreso de los Diputados, 2026). The proposal entails both the guarantee of confidentiality of the SNS towards industry and the prohibition for industry to disclose net prices in Spain to third parties. This measure is based on the threat posed by US MFN prices and the possibility that a judicial ruling may force transparency of net prices (Padilla, 2026).

Germany has introduced the confidentiality option of the AMNOG law according to which manufacturers and GKV-Spitzenverband can now agree confidential net prices to protect German reference prices against international

[16] Persson and Jönsson (2018) argue that international reference prices tend to erode because they create incentives to delay product launches in countries with lower incomes or smaller markets, hinder international price discrimination based on ability to pay, and push manufacturers and payers toward confidential discounts, risk-sharing agreements, and price-volume schemes. As actual net prices are progressively concealed, the information base upon which external price reference systems rely disappears.

price comparison (Global Law Experts, 2026). Previously, a 2024 medical research law already opened the door for the application of a confidential discount on the price negotiated with the GKV-Spitzenverband with the objective of attracting investment and protecting industry from international price referencing (Koyuncu and Aretz, 2024).

Italy is the only one of the 4 main pharmaceutical markets of the European Union that maintains transparency of net prices, although in 2026 a regional judicial ruling has ruled in favor of the confidentiality of the price offered in an auction for a medicine under patent. The ruling allows the company to maintain the confidentiality of discounts and any other factor that may be used for calculating the net price (DLA Piper, 2026).

5.4.5. Financing and purchasing policies based on variable prices

Financing and purchasing agreements for new medicines of the price-volume type, risk-sharing agreements and pay-for-outcomes agreements are already fairly common in Italy, Spain and the United Kingdom. Only list prices were public already before the start of the MFN price policy in the US. Legislative initiatives that introduce a price confidentiality clause include the non-transparency of this type of variable prices.

Denmark has updated in 2026 the procedure of the Danish Medicines Council and Amgros to favor more alternative price agreements, equivalent to risk-sharing agreements, in medicines with high prices and uncertainty. The main novelty is that companies can present proposals for alternative agreements with extension of deadlines in the evaluation process, until week 6 or before the first meeting of the specialized committee, without delaying the planned decision. These agreements may be outcomes-based, for example, payments conditional on effectiveness, or economic, such as discounts linked to volume or use (Medicinrådet, 2026).

The German government has approved the legislative processing of a law that, if it is approved, would entail the application from July 2027 of a dynamic industrial discount: to the mandatory 7% discount would be added an additional dynamic discount that would be adjusted so that pharmaceutical expenditure does not exceed the budget constraint, with selective exemptions from this obligation related to the conduct of clinical trials in the country, job creation and investment. Other regulatory proposals under debate in Germany include price-volume agreements that could even be mandatory and also discounts, and even auctions, for new medicines considered therapeutic equivalents of others under patent (Koyuncu and Aretz, 2026).

Chapter 6

RECOMMENDATIONS FOR A SUSTAINABLE PHARMACEUTICAL FINANCING POLICY IN SPAIN

The implications of medicine price policies called "Most Favored Nation" (MFN) adopted by the United States transcend the scope of pharmaceutical policy and pose relevant challenges for health systems, industrial policy and the economic strategy of European countries. In light of the analysis carried out in the previous chapters on the experience of international reference pricing systems, the price differential between the United States and Europe, the debate on the problem of free riding in the global financing of R&D and the expected impact of MFN measures on prices, access and innovation, this section presents a set of recommendations addressed to Spain.

The proposals are structured in three complementary blocks. The first addresses pharmaceutical policy as an instrument of economic, industrial and commercial policy, paying special attention to the opportunity costs associated with these objectives. The second focuses on decisions of financing and regulation/intervention of prices of new medicines, including aspects related to confidentiality of net prices, therapeutic assessment, efficiency and management of uncertainty. Finally, the third block formulates recommendations on the evaluation of efficacy, effectiveness and efficiency, reinforcing the role of independent evaluation as support for public decision making.

6.1. RECOMMENDATIONS ON PHARMACEUTICAL POLICY AS AN INSTRUMENT OF ECONOMIC POLICY

1. Recognize that pharmaceutical price and expenditure policy has become not only an instrument of health policy but also increasingly an instrument of industrial, commercial and economic geopolitics. It is probable that national policy measures have limited scope, even more when the counterpart is the US. The development of a joint European policy on the matter treated would be recommendable, in which Spain, by market size, by employment and by added value generated by the pharmaceutical industry, should have an important specific weight.

2. Evaluate the Spanish macroeconomic situation in the framework of any negotiation or geopolitical strategy taking into account that the net price indices of new medicines adjusted for PPP and the indicators of

the percentage of pharmaceutical expenditure over health expenditure and of pharmaceutical expenditure over GDP already notably exceed the target values to which the United Kingdom has committed itself for 2036, in exchange for tariff exemption by the United States and the commitment not to use the net price of the United Kingdom as reference for the United States.

3. Adopt measures so that the inclusion of criteria related to objectives of industrial, commercial and economic policy in the negotiation, regulation/intervention of net prices and pharmaceutical expenditure and purchase of new medicines pays special attention to not charging the opportunity cost of these objectives to the health budget.

4. Evaluate the expected economic impact of using the price and purchase policy of new medicines to promote clinical trials carried out in Spain, as well as privately financed R&D, discounting public financing channeled through other fiscal and non-fiscal instruments. Likewise, assess the location in Spain of the production of new medicines, not only for the Spanish market, but also for world markets, as strategic production.

5. Evaluate through economic impact studies the direct, indirect and induced effects on added value, employment and public finances of the specific measures (new medicine/group of medicines/company) of regulation/intervention of prices and purchasing of medicines that wish to provide a price and/or purchase premium based on economic impact criteria and/or also when decisions are taken on net prices valuing productivity gains and changes in the costs of formal and informal care (social perspective).

6. Create a specific fund financed from the General State Budget only in the case that industrial, commercial and economic policy objectives are included in the regulation/intervention and negotiation of net prices of new medicines so that the opportunity cost of these objectives is visible to public decision makers and does not fall on the health budget. There are other industrial/scientific policy mechanisms outside health care and medicine prices whose cost-benefit relationship should be subject to analysis. In the absence of a complementary specific fund, it is recommended to inform decision making through an evaluation of the opportunity cost of the resources devoted to economic objectives in terms of quality-adjusted life years sacrificed.

6.2. RECOMMENDATIONS ON FINANCING AND PRICE REGULATION/INTERVENTION DECISIONS

7. Legislate the obligation to preserve confidentiality before third parties of the net prices of new medicines and of any other purchasing mechanism for new medicines equivalent to variable prices. Establish penalties for the pharmaceutical industry in case of non-compliance, guaranteeing due accountability on the use of public resources. The adoption of a confidentiality clause at European level instead of each country individually could facilitate the requirement of compliance for companies in the face of commercial threats from the United States.

8. Establish prices for new medicines that present reduced or no added therapeutic value with criteria of therapeutic equivalence similar to those of branded medicines under patent that are already on the market. The adoption of tools to measure added therapeutic value at European level, by the EMA, would facilitate the application in Spain of this criterion.

9. Justify in a reasoned manner and preferably supported by evidence the criteria for establishing a premium in the form of incremental prices in relation to the comparator for new medicines in financing and price decisions when the incremental cost-effectiveness ratio is above a certain reference value (threshold or thresholds of cost per additional life year gained).

10. Assess the advantages and disadvantages of creating a virtual budget fund at state level, preferably multiannual, for the financing of new medicines with a favorable financing decision for the whole population or for a subpopulation and with a net price approved from the corresponding budget impact study. This notional fund, compatible with the budget constraint of the health services of the Autonomous Communities, would contribute to the visualization of the budget constraint on which financing and price decisions are made for health payers. Sources of financing for financing and price decisions that exceed this budget constraint should be studied without ruling out that it should be charged to a financial fund from the General State Budget.

11. Adopt financing and price regulation/intervention measures informed from the incremental cost per life year gained of the new treatment, taking into account the rest of the well-established normative criteria (see Royal Decree 415/2025) that must inform these decisions

and negotiations, avoiding the comparison only of the cost of the pharmaceutical component between alternatives, in order to have an integral vision of the impact of new medicines on the health system.

12. Recommend and adopt purchasing policies based on financial risk-sharing agreements and based on health outcomes when uncertainties about effectiveness, budget impact and incremental cost-effectiveness ratio are high, always trying to minimize the transaction costs of monitoring compliance with these agreements by purchasers (support in artificial intelligence).

13. Dynamically review financing and price decisions when there is new relevant information that may modify the measure of added therapeutic value, budget impact and/or additional cost per life year gained, even contemplating improvements (price increases) in the initially established conditions.

6.3. RECOMMENDATIONS ON EVALUATION OF EFFICACY/ EFFECTIVENESS AND EFFICIENCY

14. Separate the evaluation of added therapeutic value and of the incremental cost-effectiveness ratio, carried out transparently and independently, from the assessment or decision making on financing and price.

15. Applications for financing and price of new medicines with a price higher than that of the comparator should mandatorily be accompanied by a budget impact analysis and an economic evaluation (and by the economic impact study when the price premium in whole or in part is based on the economic impact of investment and production). These reports or studies should be presented according to official good-practice guides updated periodically.

16. A body responsible for independent evaluation of added therapeutic value and the incremental cost-effectiveness ratio should review and report on the methodological quality of the studies or reports presented by industry, guarantee that reports with acceptable quality levels are transferred to decision makers and synthesize the technical information, both clinical and economic, from these to be assessed by decision makers.

17. The evaluation should inform decision makers in a clear and structured way of the main sources of uncertainty presented by the clinical, budgetary and economic evidence on the new medicine at the moment of market entry and inform on the type of risk-sharing agreements according to source and magnitude of these uncertainties. A practical harmonization of HTA evaluation criteria and methods between the countries of the European Union could contribute to making access to medicines and health technologies in Europe and in Spain more coherent, rapid and efficient.

BIBLIOGRAPHY

Agency For Healthcare Research And Quality. (2026). *Medical Expenditure Panel Survey (MEPS).* U.S. Department of Health and Human Services. https://meps.ahrq.gov/mepsweb/index.jsp

Ankura Consulting Group. (2025, May 23). *Most-favored-nation, Executive Order 14297: Forward looking perspectives for drug manufacturers, pharmacy benefit managers, health plans, and pharmacies.* https://ankura.com/insights/most-favored-nation-executive-order-14297forward-looking-perspectives-for-drug-manufacturers-pharmacy-benefit-managers-health-plans-and-pharmacies

ASPE. (2024, January 31). *Comparing prescription drugs in the U.S. and other countries: Prices and availability.* U.S. Department of Health and Human Services. https://aspe.hhs.gov/reports/comparing-prescription-drugs

Barrenho, E., & Lopert, R. (2022, September 8). Exploring the consequences of greater price transparency on the dynamics of pharmaceutical markets. *OECD Health Working Papers, No. 146*. OECD Publishing. https://doi.org/10.1787/c9250e17-en

Barros, P. L. O. M. P., Righetti, G., & Sá, L. (2026, March 8). *On the long-run effects of "most favored nation" drug pricing*. SSRN. https://doi.org/10.2139/ssrn.6373278 or https://ssrn.com/abstract=6373278

Berkemeier, F., Whaley, C., & Robinson, J. C. (2019). Increasing divergence in drug prices between the United States and Germany after implementation of comparative effectiveness analysis and collective price negotiations. *Journal of Managed Care & Specialty Pharmacy, 25*(12), 1310-1317. https://doi.org/10.18553/jmcp.2019.25.12.1310. PMID: 31778624; PMCID: PMC10397913.

Berndt, E. R., & Newhouse, J. P. (2012). Pricing and reimbursement in US pharmaceutical markets. In M. V. Pauly, T. G. McGuire, & P. P. Barros (Eds.), *The Oxford handbook of the economics of the biopharmaceutical industry* (pp. 201-265). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199742998.013.0008

Bohnet, I., & Chilazi, S. (2025, February 2). How zero-sum beliefs get in the way of fairness. *Behavioral Scientist*. https://behavioralscientist.org/how-zero-sum-beliefs-get-in-the-way-of-fairness/

Bosch Jou, J., García Villar, J., & Puig-Junoy, J. (2022). El sector farmacéutico en la economía española: Contribución al PIB, al empleo y a los ingresos fiscales. *Working Paper Series, No. 13.* Barcelona School of Management, Universitat Pompeu Fabra.

Brooks, E. (2026, February 12). Conservative leaders come out against codifying Trump's drug policy. *The Hill*. https://nxslink.thehill.com/view/681b62be19d6a439c3062359q9cuc.7oq/4dbce2d4

Cabrales, A., & Jiménez-Martín, S. (2013). The determinants of pricing in pharmaceuticals: Are US prices really so high? *Health Economics, 22*(11), 1377-1397. https://doi.org/10.1002/hec.2887. Epub 2013 Jan 10. PMID: 23303712.

Centers for Medicare & Medicaid Services. (2016, March 11). *Medicare program; Part B drug payment model* (42 C.F.R. § 511). Federal Register. https://www.federalregister.gov/documents/2016/03/11/2016-05459/medicare-program-part-b-drug-payment-model

Centers for Medicare & Medicaid Services. (2026). *Medicaid.gov*. Baltimore (MD): U.S. Department of Health and Human Services. https://www.medicaid.gov/

Chen, L. J. (2025). Alternatives to government-imposed price controls to lower US drug prices. *JAMA Health Forum, 6*(10), e255744. https://doi.org/10.1001/jamahealthforum.2025.5744. PMID: 41129168.

Cohen, J. P. (2026, May 7). Questionable White House math on savings from most favored nation drug prices. *Forbes*. https://www.forbes.com/sites/joshuacohen/2026/05/07/questionable-white-house-math-on-savings-from-most-favored-nation-drug-prices/

Congreso de los Diputados. (2026, 12 marzo). Enmienda núm. 259. *Boletín Oficial de las Cortes Generales*, Serie A, Núm. 64-5. Cortes Generales. https://www.congreso.es/public_oficiales/L15/CONG/BOCG/A/BOCG-15-A-64-5.PDF

Congressional Budget Office. (2021, February). *A comparison of brand-name drug prices among selected federal programs*. Washington (DC): Congressional Budget Office. https://www.cbo.gov/system/files/2021-02/56978-Drug-Prices.pdf

Congressional Budget Office. (2021). *Research and development in the pharmaceutical industry*. Washington (DC): Congressional Budget Office. https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf

Congressional Budget Office. (2022). *Estimated budgetary effects of Public Law 117-169, to provide for reconciliation pursuant to Title II of S. Con. Res. 14*. Washington (DC): Congressional Budget Office. https://www.cbo.gov/publication/58455

Conti, R. M., Frank, R. G., & Cutler, D. M. (2024). The myth of the free market for pharmaceuticals. *New England Journal of Medicine, 390*(16), 1448-1450. https://doi.org/10.1056/NEJMp2313400. Epub 2024 Apr 20. PMID: 38647106.

Cookson, G. (2025, June 2). *Bold politics: What about the economics? An overview of President Trump's "Most Favoured Nation" executive order*. London: Office of Health Economics. https://www.ohe.org/insights/the-free-rider-fallacy-an-overview-of-president-trumps-most-favoured-nation-executive-order/

Cookson, G., Cole, A., & Berdud, M. (2025, June 12). *The Trump administration's US drug pricing proposal: What will happen next?* London: Office of Health Economics. https://www.ohe.org/insights/the-trump-administrations-us-drug-pricing-proposal-what-will-happen-next/

Corzo Santamaría, T., Portela, J., & Schwartz, E. S. (2026, February). Valuation of regulatory risk on pharmaceutical R&D. *NBER Working Paper,* No. 34863. National Bureau of Economic Research. https://www.nber.org/papers/w34863

Council of Economic Advisers. (2018, February). *Reforming biopharmaceutical pricing at home and abroad*. Washington (DC): Executive Office of the President of the United States. https://trumpwhitehouse.archives.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf

Council of Economic Advisers. (2026, May 5). *Savings from most-favored-nation (MFN) drug pricing policy*. Washington (DC): Executive Office of the President. https://www.whitehouse.gov/research/2026/05/savings-from-most-favored-nation-drug-pricing-policy/

Cross, S., Claxton, K., & Hill, A. (2026). Health costs of the UK-US trade deal on pharmaceuticals. *BMJ, 394*, e340588. https://doi.org/10.1136/bmj-2026-340588. PMID: 42386321.

Cutler, D. M., & Klarnet, R. (2026). Has the United States bent the health care cost curve? *NBER Working Paper,* No. 35231. Cambridge (MA): National Bureau of Economic Research.

Danzon, P. M. (2012). Regulation of price and reimbursement for pharmaceuticals. In M. V. Pauly, T. G. McGuire, & P. P. Barros (Eds.), *The Oxford handbook of the economics of the biopharmaceutical industry* (pp. 266-301). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199742998.013.0009

Danzon, P. M. (2018). Differential pricing of pharmaceuticals: Theory, evidence and emerging issues. *PharmacoEconomics, 36*(12), 1395-1405. https://doi.org/10.1007/s40273-018-0696-4. PMID: 30062518.

Danzon, P. M., & Chao, L.-W. (2000). Does regulation drive out competition in pharmaceutical markets? *Journal of Law and Economics, 43*(2), 311-357. https://faculty.wharton.upenn.edu/wp-content/uploads/2014/10/does-regulation-drive-out_7.pdf

Danzon, P., Towse, A., & Mestre-Ferrandiz, J. (2015). Value-based differential pricing: Efficient prices for drugs in a global context. *Health Economics, 24*(3), 294-301. https://doi.org/10.1002/hec.3021. Epub 2013 Dec 11. PMID: 24327269.

Darrow, B., Chowdhury, S., O'Neill, P., & Henderson, N. (2025). *An analysis of NICE's optimised decisions from 2015 to 2024*. London: Office of Health Economics. https://www.ohe.org/publications/an-analysis-of-nices-optimised-decisions-from-2015-to-2024/

Darrow, B., Chowdhury, S., O'Neill, P., & Henderson, N. (2025). *An analysis of NICE's optimised decisions from 2015 to 2024: What is the recommended level of patient access?* London: Office of Health Economics. https://www.ohe.org/wp-content/uploads/2025/04/OHE-NICE-Optimised-Decisions-Report_final_2May.pdf

DLA Piper. (2026, March 24). *Protecting price confidentiality in pharma tenders*. https://www.dlapiper.com/en-es/insights/publications/2026/03/protecting-price-confidentiality-in-pharma-tenders

Dubois, P. (2025). Pharmaceutical regulation and incentives for innovation in an international perspective. *TSE Working Paper,* No. 1674. Toulouse School of Economics. https://www.tse-fr.eu/sites/default/files/TSE/documents/doc/wp/2025/wp_tse_1674.pdf

Dubois, P., Gandhi, A., & Vasserman, S. (2022). Bargaining and international reference pricing in the pharmaceutical industry. *NBER Working Paper,* No. 30053. National Bureau of Economic Research. https://www.nber.org/papers/w30053

Dusetzina, S. B., Castle, G., Han, J., Leech, A. A., & Zhu, J. (2026). Medicare spending implications for semaglutide under voluntary price agreements. *JAMA, 335*(16), 1442-1444. https://doi.org/10.1001/jama.2026.2615

Epstein, D. (2026, junio 17-19). How might the United States Most Favored Nation policy affect prices of branded medicines and research and development? How should European policy makers respond? [Comunicación oral]. *XLV Jornadas de Economía de la Salud.* Asociación de Economía de la Salud. Sevilla, España. https://www.aes.es/jornadas/es/

Espin, J., Schlander, M., Godman, B., Anderson, P., Mestre-Ferrandiz, J., Borget, I., Hutchings, A., Flostrand, S., Parnaby, A., & Jommi, C. (2018). Projecting pharmaceutical expenditure in EU5 to 2021: Adjusting for the impact of discounts and rebates. *Applied Health Economics and Health Policy, 16*(6), 803-817. https://doi.org/10.1007/s40258-018-0419-1. PMID: 30088251; PMCID: PMC6244625.

European Commission. (2024, September 9). *The Draghi report: A competitiveness strategy for Europe*. https://commission.europa.eu/topics/competitiveness/draghi-report_en

European Federation Of Pharmaceutical Industries And Associations. (2025). *The pharmaceutical industry in figures 2025*. Brussels: EFPIA. https://www.efpia.eu/media/uj0popel/the-pharmaceutical-industry-in-figures-2025.pdf

Fein, A. J. (2025, March 31). The top pharmacy benefit managers of 2024: Market share and key industry developments. *Drug Channels*. https://www.drugchannels.net/2025/03/the-top-pharmacy-benefit-managers-of.html

Filson, D., Van Nuys, K., Lakdawalla, D., & Goldman, D. (2025, February 18). *The elasticity of pharmaceutical innovation: How much does revenue drive new drug development?* Los Ángeles (CA): USC Schaeffer Center for Health Policy & Economics. https://schaeffer.usc.edu/research/the-elasticity-of-pharmaceutical-innovation-how-much-does-revenue-drive-new-drug-development/

Fontrier, A. M., Gill, J., & Kanavos, P. (2019). International impact of external reference pricing: Should national policy-makers care? *European Journal of Health Economics, 20*(8), 1147-1164. https://doi.org/10.1007/s10198-019-01083-w. Epub 2019 Jul 9. PMID: 31289948.

Frank, R. G., Conti, R. M., & Gruber, J. (2022). International reference pricing in the context of US drug policy. *Journal of Health Politics, Policy and Law, 47*(6), 779-796. https://doi.org/10.1215/03616878-10041177

Frech, H. E., Iii, Pauly, M. V., Comanor, W. S., & Martinez, J. R. (2026). Pharmaceutical pricing and R&D as a global public good. *Health Economics*. Advance online publication. https://doi.org/10.1002/hec.70105. PMID: 41944252.

Gainsbury, S., & Lomas, J. (2026). The UK government must publish a detailed impact assessment of the costs and benefits of the US-UK medicines partnership. *BMJ, 393*, s733. https://doi.org/10.1136/bmj.s733. PMID: 41997610.

Gamba, S., Pertile, P., & Righetti, G. (2022). Spillovers of pharmaceutical price regulations: Evidence from the AMNOG reform in Germany. *HEDG Working Paper*, 22/20. York: University of York, Health Econometrics and Data Group. https://www.york.ac.uk/media/economics/documents/hedg/workingpapers/2022/2220.pdf

Gandjour, A. (2025). Trump's drug pricing order and the domestic economic trade-off. *Applied Health Economics and Health Policy, 23*(5), 755-758. https://doi.org/10.1007/s40258-025-00986-5. PMID: 40533642; PMCID: PMC12364957.

Gill, J., Fontrier, A. M., Kyriopoulos, D., & Kanavos, P. (2019). Variations in external reference pricing implementation: Does it matter for public policy? *European Journal of Health Economics,* 20, 1375-1397. https://doi.org/10.1007/s10198-019-01100-y

Global Law Experts. (2026). *Germany's 2026 drug pricing & reimbursement reforms: What pharma, medtech and digital-health companies must do*. https://globallawexperts.com/germany-drug-pricing-reimbursement-2026/

Gondi, S., Papanicolas, I., & Rome, B. N. (2025). Lowering drug prices in the US: Look within, not abroad. *JAMA, 334*(9), 765-766. https://doi.org/10.1001/jama.2025.12324. PMID: 40720233.

Gonzalez Lopez-Valcarcel, B. (2026). Drug policy in the Trump era: Expected and observed consequences for the United States and Europe. *Journal of Healthcare Quality Research, 41*(3), 101206. https://doi.org/10.1016/j.jhqr.2026.101206. Epub 2026 Mar 18. PMID: 41855700.

Government Accountability Office (GAO). (2020, December 15). Prescription drugs: Department of Veterans Affairs paid about half as much as Medicare Part D for selected drugs in 2017 (GAO-21-111). Washington (DC): U.S. Government Accountability Office. https://www.gao.gov/products/gao-21-111

Grueger, J., Martin, K., & Sullivan, S. D. (2025). Referencing drug prices of other countries may not sustainably lower prices in the United States: Lessons from Europe. *Value in Health, 28*(9), 1305-1308. https://doi.org/10.1016/j.jval.2025.06.010. Epub 2025 Jul 1. PMID: 40609636.

Gurung, S. (2026, March 25). The most favored nation policy: Early insights into Europe's response. *Pharmaceutical Technology*. https://www.pharmaceutical-technology.com/analyst-comment/most-favored-nation-policy-early-insights-into-europe-response/

Hiltzik, M. (2017, June 11). How pharmacy benefit managers are driving up drug costs. *Los Angeles Times*. https://www.latimes.com/business/hiltzik/la-fi-hiltzik-pbm-drugs-20170611-story.html

Ho, K., & Pakes, A. (2025). Policy options for the drug pricing conundrum. *Proceedings of the National Academy of Sciences, 122*(9), e2418540122. https://doi.org/10.1073/pnas.2418540122. PMID: 39999179; PMCID: PMC11892685.

Hwang, T. J., Clemans-Cope, L., & Kesselheim, A. S. (2026). Reforming payment for clinician-administered drugs: Most-favored-nation pricing in Medicare Part B. *New England Journal of Medicine, 394*(18), 1774-1777. https://doi.org/10.1056/NEJMp2600417. Epub 2026 May 2. PMID: 42080625.

Iqvia Institute For Human Data Science. (2023, January 18). *The global use of medicines 2023: Outlook to 2027*. IQVIA Institute. https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/the-global-use-of-medicines-2023

Jeon, Y. K., Hansen, R. N., Gabriel, N., Martin, K., & Sullivan, S. D. (2026). Spending impact of the first 10 drugs selected for Medicare drug price negotiation in the United States. *Value in Health, 29(7), 1228–1234*. https://doi.org/10.1016/j.jval.2026.03.010. Epub ahead of print. PMID: 41912106.

Juneja, M., Mai, L., & Albu, N. (2024). *The economic impact of the global pharmaceutical industry: Measurement of the economic impact relating to the pharmaceutical industry's global economic and R&D activities*. Darmstadt (DE): WifOR Institute; 2024. Commissioned by: International Federation of Pharmaceutical Manufacturers & Associations (IFPMA).

Kakani, P., Khullar, D., McGinty, E. E., Barry, C. L., Bond, A. M. (2026). Experts Mixed On How Most-Favored-Nation Drug Pricing Would Affect Prices, Access, And Innovation. *Health Affairs Forefront*. 2026 Feb 4. doi:10.1377/forefront.20260203.317549.

Kanavos, P., Fontrier, A. M., Gill, J., & Efthymiadou, O. (2020). Does external reference pricing deliver what it promises? Evidence on its impact at national level. *European Journal of Health Economics, 21*(1), 129-151. https://doi.org/10.1007/s10198-019-01116-4. Epub 2019 Oct 3. PMID: 31583483; PMCID: PMC7058621.

Katebi, C. (2025, March 21). *Put Americans first by ending global freeloading*. America First Policy Institute. https://www.americafirstpolicy.com/issues/put-americans-first-by-ending-global-freeloading

Kearney, A., Montalvo, J., Iii, Kirzinger, A., & Hamel, L. (2026, March 31). *Public opinion on prescription drugs and their prices*. KFF. https://www.kff.org/health-costs/public-opinion-on-prescription-drugs-and-their-prices/

Kelkar, A. H., & Cliff, E. R. S. (2025). Reducing drug prices: The most favored nation policy vs price negotiation. *JAMA, 334*(9), 761-762. https://doi.org/10.1001/jama.2025.11614. PMID: 40720104.

Kesselheim, A. S., Avorn, J., & Sarpatwari, A. (2016). The high cost of prescription drugs in the United States: Origins and prospects for reform. *JAMA, 316*(8), 858-871. https://doi.org/10.1001/jama.2016.11237. PMID: 27552619.

Kirschenbaum, A. M. (2020, September 15). Trump embraces international reference pricing in executive order. *FDA Law Blog*. https://www.thefdalawblog.com/2020/09/trump-embraces-international-reference-pricing-in-executive-order/

Kirson, N. Y., Dooley, J. M., Ge, Z., & Chandra, A. (2026). Taking stock of most-favored-nation deals: How have markets reacted? *Health Affairs Scholar*. Published online July 9, 2026. Accepted manuscript. https://doi.org/10.1093/haschl/qxag176

Koh, J., & Shah, K. (2026). What costs and benefits should be counted in health technology assessments and guidelines? The NICE perspective. *Value in Health, 29*(2), 175-178. https://doi.org/10.1016/j.jval.2025.09.003. Epub 2025 Sep 19. PMID: 40976341.

Kolchinsky, P. (2020). *The great American drug deal: A new prescription for innovative and affordable medicines*. Boston (MA): Broad Institute. ISBN-13: 978-1-7349760-0-4.

Kolchinsky, P., & Xie, R. (2025, May 24). No more freeriding on the great American drug deal: Making wealthy countries pay their fair share for novel medicines without sacrificing America's current bargain. *RApport*. https://rapport.racap.com/all-stories/no-more-freeriding-great-american-drug-deal

Koyuncu, A. D., & Aretz, M. (2026, April 30). Germany plans significant cuts in drug pricing and reimbursement: How would the GKV-Beitragssatzstabilisierungsgesetz impact pharmaceutical companies? *Global Policy Watch*. https://www.globalpolicywatch.com/2026/04/germany-plans-significant-cuts-in-drug-pricing-and-reimbursement-how-would-the-gkv-beitragssatzstabilisierungsgesetz-impact-pharmaceutical-companies/

Kumar, G., Radu, P., Cubi-Molla, P., Garau, M., Bell, E., Pan, J., Gilardino, R., Van Bavel, J., Brandtmüller, A., Nelson, K., & Goodall, M. (2025). Navigating change: A comparative analysis of health technology assessment reforms across agencies, processes, drivers, and interdependencies. *International Journal of Technology Assessment in Health Care, 41*(1), Article e21. https://doi.org/10.1017/S0266462325000133 PMID: 40083319; PMCID: PMC12018853.

Kyle, M. K. (2025). Lessons for the United States from pharmaceutical regulation abroad. *Journal of Economic Perspectives, 39*(2), 53-78. https://doi.org/10.1257/jep.20241418

Lakdawalla, D., MacEwan, J. P., Dubois, R., Westrich, K., Berdud, M., & Towse, A. (2017). What do pharmaceuticals really cost in the long run? *The American Journal of Managed Care, 23*(8), 488-493. PMID: 29087143.

Lerner, A. P. (1934). The concept of monopoly and the measurement of monopoly power. *Review of Economic Studies, 1*(3), 157-175. https://doi.org/10.2307/2967480

Li, K. H., Cousin, E. M., Gabriel, N., & Sullivan, S. D. (2026). Integrating price benchmarks and comparative clinical effectiveness to predict initial price offers for Medicare drug price negotiation (Initial Price Applicability Year 2027). *Value in Health, 29*(1), 64-72. https://doi.org/10.1016/j.jval.2025.09.3054 Epub 2025 Oct 1. PMID: 41043560.

Maini, L., & Pammolli, F. (2023). Reference pricing as a deterrent to entry: Evidence from the European pharmaceutical market. *American Economic Journal: Microeconomics, 15*(2), 345-383. https://doi.org/10.1257/mic.20210053.

Maini, L., Sachs, R. E., Kyle, M. A., & Kakani, P. (2026). Medicaid's generous most-favored-nation pricing model: Promise and limitations. *New England Journal of Medicine, 394*(18), 1772-1774. https://doi.org/10.1056/NEJMp2518292. Epub 2026 May 2. PMID: 42080661.

Medicinrådet. (2026, June 3). *Medicinrådet og Amgros giver lægemiddelvirksomheder mere tid til at foreslå alternative prisaftaler*. København: Medicinrådet. https://medicinraadet.dk/nyheder/2026/medicinradet-og-amgros-giver-laegemiddelvirksomheder-mere-tid-til-at-foresla-alternative-prisaftaler

Megerlin, F. (2026). Most favored nation policies and value-based drug pricing: A European view. *Health Affairs, 45*(4), 361-364. https://doi.org/10.1377/hlthaff.2026.00115. PMID: 41941684.

Moreno, S. G., & Epstein, D. (2019). The price of innovation: The role of drug pricing in financing pharmaceutical innovation. A conceptual framework. *Journal of Market Access & Health Policy, 7*(1), Article 1583536. https://doi.org/10.1080/20016689.2019.1583536. PMID: 30956782; PMCID: PMC6442120.

Morgan Lewis. (2025, May). *Bipartisan drug pricing reform: The FPDP Act and revival of most-favored-nation pricing*. https://www.morganlewis.com/blogs/asprescribed/2025/05/bipartisan-drug-pricing-reform-the-fpdp-act-and-revival-of-most-favored-nation-pricing

Mulcahy, A. W. (2024b). *Comparing new prescription drug availability and launch timing in the United States and other OECD countries* (Research Report RR-A788-4). Santa Monica (CA): RAND Corporation. https://www.rand.org/pubs/research_reports/RRA788-4.html

Mulcahy, A. W. (2026). Most favored nation drug pricing: An idea to what end? *Health Affairs, 45*(4), 356-360. https://doi.org/10.1377/hlthaff.2026.00184. PMID: 41941681.

Mulcahy, A. W., Schwam, D., & Lovejoy, S. L. (2024a, February 1). *International prescription drug price comparisons: Estimates using 2022 data*. Santa Monica (CA): RAND Corporation. https://www.rand.org/pubs/research_reports/RRA788-3.html

Mulcahy, A. W., Whaley, C. M., Gizaw, M., Schwam, D., Edenfield, N., & Becerra-Ornelas, A. U. (2021, January 28). *International prescription drug price comparisons: Current empirical estimates and comparisons with previous studies*. Santa Monica (CA): RAND Corporation. https://www.rand.org/pubs/research_reports/RR2956.html

Mulligan, C. B. (2022, July). The value of pharmacy benefit management. *NBER Working Paper*, No. 30231. Cambridge (MA): National Bureau of Economic Research. https://doi.org/10.3386/w30231

Murphy, S. (2026, June). *Measuring the pull-side innovation burden for pharmaceutical drugs by OECD country*. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. https://aspe.hhs.gov/sites/default/files/documents/46a124755270588091b21a491026ffef/Innovation_Burden_Issue_Brief_06102026.pdf

Naci, H., Murphy, P., Woods, B., Lomas, J., Wei, J., & Papanicolas, I. (2025). Population-health impact of new drugs recommended by the National Institute for Health and Care Excellence in England during 2000-20: A retrospective analysis. *The Lancet, 405*(10472), 50-60. https://doi.org/10.1016/S0140-6736(24)02352-3. Epub 2024 Dec 12. Erratum in: Lancet. 2025 Feb 1;405(10476): 382. https://doi.org/10.1016/S0140-6736(25)00159-X. PMID: 39675371.

Nash, J. F., JR. (1950). The bargaining problem. *Econometrica, 18*(2), 155-162. https://www.haverford.edu/sites/default/files/Nash1950.pdf

No Patient Left Behind. (2024, April 29). *Foreign countries rely on flawed and outdated HTA or "value assessment" methods to justify low prices for medicines*. https://www.nopatientleftbehind.org/resource-materials/ex-us-report

Oliva, J., Rodríguez-Sánchez, B., Peña-Longobardo, L. M., Aranda-Reneo, I., López-Bastida, J., Hidalgo-Vega, Á., Et Al. (2020). *Deliverable D4.2: How relevant is the societal perspective in economic evaluations? Evidence from five case studies*. IMPACT HTA. https://29fc9734-3e90-46b6-9e22-9a9705501c78.filesusr.com/ugd/e1a359_320d547725804e218692c40245605d50.pdf

Organisation for Economic Co-Operation and Development. (2013). *Value in pharmaceutical pricing*. OECD Publishing. https://www.oecd.org/content/dam/oecd/en/publications/reports/2013/07/value-in-pharmaceutical-pricing_g17a2332/5k43jc9v6knx-en.pdf

Oxera. (2008). *Parallel trade in pharmaceuticals*. Oxera. https://www.oxera.com/wp-content/uploads/2018/03/Parallel-trade-in-pharmaceuticals.pdf

Padilla, J. (2025, September 22). Medicamentos: acceso y transparencia en tiempos de trumpismo. *A gran escala (Substack).* https://agranescala.substack.com/p/medicamentos-acceso-y-transparencia

Patented Medicine Prices Review Board. (2007). *Annual report 2006*. Ottawa (ON): Government of Canada. https://www.pmprb-cepmb.gc.ca/view.asp?ccid=905

Patented Medicine Prices Review Board. (2012). *Annual report 2011*. Ottawa (ON): Government of Canada. https://www.pmprb-cepmb.gc.ca/view.asp?ccid=905

Patented Medicine Prices Review Board. (2017). *Annual report 2016*. Ottawa (ON): Government of Canada. https://www.pmprb-cepmb.gc.ca/view.asp?ccid=1334

Patented Medicine Prices Review Board. (2022). *Annual report 2021*. Ottawa (ON): Government of Canada. https://www.canada.ca/en/patented-medicine-prices-review/services/annual-reports/annual-report-2021.html

Paulden, M. (2026). Economic consequences of increasing the NICE cost-effectiveness threshold. *PharmacoEconomics, 44*(1), 5-8. https://doi.org/10.1007/s40273-025-01579-9. Epub 2025 Dec 15. PMID: 41396544.

Persson, U., & Jönsson, B. (2016). The end of the international reference pricing system? *Applied Health Economics and Health Policy, 14*(1), 1-8. https://doi.org/10.1007/s40258-015-0182-5. PMID: 26112982.

Pines, J. (2026, April 27). TrumpRx has signed deals with nearly every major drugmaker. Are prices actually falling? *Forbes*. https://www.forbes.com/sites/jessepines/2026/04/27/trumprx-has-signed-deals-with-nearly-every-major-drugmaker-are-prices-actually-falling/

Puig-Junoy, J. (2010). Impact of European pharmaceutical price regulation on generic price competition: A review. *PharmacoEconomics, 28*(8), 649-663.

Puig-Junoy, J. (2026, February 28). "Umbrales" costes-efectividad: Una guía demasiado controvertida para la toma de decisiones que requiere humildad analítica. *Gestión Clínica y Sanitaria*. https://gestionclinicaysanitaria.es/umbrales-costes-efectividad-una-guia-demasiado-controvertida-para-la-toma-de-decisiones-que-requiere-humildad-analitica/

Radu, P., Biurrun, C., Boysen, M., Whittington, M., & Skedgel, C. (2026, March 3). *The case for adopting a broader perspective on value in health technology assessment*. London: Office of Health Economics. https://www.ohe.org/publications/the-case-for-adopting-a-broader-perspective-on-value-in-health-technology-assessment/

Ramagopalan, S. V., & Ryan, M. L. (2026). Most-favored-nation pricing meets joint clinical assessment: Early evidence of compounding pressure on European drug launches. *Journal of Comparative Effectiveness Research, 15*(7), e260110. https://doi.org/10.57264/cer-2026-0110. Epub 2026 Jun 19. PMID: 42319363; PMCID: PMC13329871.

Ramsey, F. P. (1927). A contribution to the theory of taxation. *The Economic Journal, 37*(145), 47-61.

Rand, L. Z., & Kesselheim, A. S. (2021). International reference pricing for prescription drugs in the United States: Administrative limitations and collateral effects. *Value in Health, 24*(4), 473-476. https://doi.org/10.1016/j.jval.2020.11.009. Epub 2020 Dec 31. PMID: 33840424.

Rebitzer, J. B. (2024, December 19). What are pharmacy benefit managers? A health economist explains how lack of competition drives up drug prices for everyone. *The Conversation*. https://doi.org/10.64628/AAI.e59rvkk4v

Rebitzer, J. B., & Rebitzer, R. S. (2023). *Why not better and cheaper? Healthcare and innovation*. Oxford University Press. https://doi.org/10.1093/oso/9780197603109.001.0001

Rémuzat, C., Urbinati, D., Mzoughi, O., El Hammi, E., Belgaied, W., & Toumi, M. (2015). Overview of external reference pricing systems in Europe. *Journal of Market Access & Health Policy,* 3, 27675. https://doi.org/10.3402/jmahp.v3.27675 PMID: 27123181; PMCID: PMC4802694.

Riccaboni, M., Swoboda, T., & Van Dyck, W. (2022). Pharmaceutical net price transparency across European markets: Insights from a multi-agent simulation model. *Health Policy, 126*(6), 534-540. https://doi.org/10.1016/j.healthpol.2022.03.013. Epub 2022 Mar 31. PMID: 35459584.

Robbins, R. (2024, January 17). Why the US pays so much more for drugs. *The New York Times*. https://www.nytimes.com/2024/01/17/health/us-drug-prices.html

Robbins, R. (2026, March 18). Trump promised the 'world's lowest' drug prices. We checked the numbers. *The New York Times*. https://www.nytimes.com/2026/03/18/world/europe/trumprx-drug-prices-really-cheapest-world-comparison.html

Robinson, J. (2025a, May 23). On US and foreign drug prices, 'most favored nation' policy is an unreasonable answer to a reasonable question. *Health Affairs Forefront*. https://doi.org/10.1377/forefront.20250520.477038

Robinson, J. (2025b). In (faint) praise of pharmaceutical import tariffs. *JAMA, 334*(10), 851-852. https://doi.org/10.1001/jama.2025.12207. PMID: 40788629.

Robinson, J. C. (2026). Most favored nation drug pricing is an idea whose time has come. *Health Affairs, 45*(4), 350-355. https://doi.org/10.1377/hlthaff.2025.01127. PMID: 41941673.

Rodwin, M. A., & Gerke, S. (2022). German pharmaceutical pricing: Lessons for the United States. *International Journal of Health Services, 52*(1), 146-158. https://doi.org/10.1177/00207314211040948. Epub 2021 Oct 20. PMID: 34668806.

Rodwin, V. G. (2020). Average international market pricing for US pharmaceuticals: Lessons from Europe. *Health Affairs Forefront*. https://www.healthaffairs.org/content/forefront/average-international-market-pricing-us-pharmaceuticals-lessons-europe

Roehrig, C. (2018, April). *The impact of prescription drug rebates on health plans and consumers*. Altarum. https://f.hubspotusercontent00.net/hubfs/8011857/Admere_August2020/Pdf/Altarum-Prescription-Drug-Rebate-Report_April-2018.pdf

Ruiz, F., & Briggs, A. (2026). A budget apart: The case for ringfencing medicines in the UK. *BMJ,* 393, s755. https://doi.org/10.1136/bmj.s755. PMID: 42014127.

Sampson, C., & Ollendorf, D. (2024, June 11). Around the world in HTAs: United States, making HTA great again. *OHE Insights*. https://www.ohe.org/insights/around-the-world-in-htas-united-states-making-hta-great-again/

Schmidt, F., Egler, M., & Geursen, R. G. (2001). Ramsey pricing as an explanation and justification for price differences in the European pharmaceutical market. *Drugs Made in Germany, 44*(3), 61-66.

Schuhmacher, A., Gassmann, O., Kwisda, S., Kremer, M., Hinder, M., & Hartl, D. (2025). The R&D productivity challenge: Transforming the pharmaceutical ecosystem. *Drug Discovery Today, 30*(11), 104494. https://doi.org/10.1016/j.drudis.2025.104494. Epub 2025 Oct 9. PMID: 41067368.

Shafrin, J., Kim, J., Cohen, J. T., Garrison, L. P., Goldman, D. A., Doshi, J. A., Krieger, J., Lakdawalla, D. N., Neumann, P. J., Phelps, C. E., Whittington, M. D., & Willke, R. (2024). Valuing the societal impact of medicines and other health technologies: A user guide to current best practices. *Forum for Health Economics & Policy, 27*(1), 29-116. https://doi.org/10.1515/fhep-2024-0014. PMID: 39512185; PMCID: PMC11567015.

Shaikh, M., Del Giudice, P., & Kourouklis, D. (2021). Revisiting the relationship between price regulation and pharmaceutical R&D investment. *Applied Health Economics and Health Policy, 19*(2), 217-229. https://doi.org/10.1007/s40258-020-00601-9. PMID: 32666383; PMCID: PMC7902591.

Shaw, B., & Mestre-Ferrandiz, J. (2020). Talkin' about a resolution: Issues in the push for greater transparency of medicine prices. *PharmacoEconomics, 38*(2), 125-134. https://doi.org/10.1007/s40273-019-00877-3. PMID: 31956967.

Skinner, B. J. (2026, February 5). Does Canada pay its fair share of the global cost of pharmaceutical innovation? *Canadian Health Policy*. https://canadianhealthpolicy.com/does-canada-pay-its-fair-share-of-the-global-cost-of-pharmaceutical-innovation/

Stindt, J. (2024). *2024 EU-5 pricing strategies: Confidential net prices and list price erosion*. Justin Stindt Consultants. https://jstindt.com/2024-new-eu5-pricing-strategies

Sullivan, S. D. (2023). Medicare drug price negotiation in the United States: Implications and unanswered questions. *Value in Health, 26*(3), 394-399. https://doi.org/10.1016/j.jval.2022.11.015. Epub 2022 Dec 9. PMID: 36503034.

Sullivan, S. D., Dayer, V., Kasle, A., Nourhussein, I., & Hansen, R. N. (2026). Reestimation of Medicare spending for semaglutide after most favored nation and Medicare drug price negotiation announcements. *Value Health, 29*(7):1151-1154. 2026 Jul. https://doi.org/10.1016/j.jval.2026.01.016. PMID: 41651376.

Sullivan, S. D., Sullivan, K. D., Dabbous, O., & Garrison, L. P. (2022). International reference pricing of pharmaceuticals in the United States: Implications for potentially curative treatments. *Journal of Managed Care & Specialty Pharmacy, 28*(5), 566-572. https://doi.org/10.18553/jmcp.2022.28.5.566. PMID: 35471069; PMCID: PMC10373031.

United Kingdom Government. (2026, April 2). *Arrangement between the United States of America and the United Kingdom on pharmaceutical pricing*. GOV.UK. https://www.gov.uk/government/publications/uk-us-arrangement-on-pharmaceutical-trade-and-pricing/arrangement-between-the-united-states-of-america-and-the-united-kingdom-on-pharmaceutical-pricing-html

University of Kansas Institute for Policy & Social Research. (2025). Medicare enrollment by state, 2022–2024. En *Kansas Statistical Abstract 2024*. Lawrence (KS): University of Kansas. https://ksdata.ku.edu/ksdata/ksah/vital/3health12.pdf

Vallejo-Torres, L., Edney, L. C., Espinosa, O., Karnon, J., Longo, F., Paulden, M., Howdon, D., & Vanness, D. J. (2026). Politicised changes to the NICE threshold risk making cost-effectiveness analysis performative, not informative. *Applied Health Economics and Health Policy*.

Webb, E., Richardson, E., Vogler, S., et al. (2022). *What are the implications of policies increasing transparency of prices paid for pharmaceuticals? A primer for understanding the policy perspective in light of the empirical evidence* (Policy Brief No. 45). Copenhagen (Denmark): European Observatory on Health Systems and Policies. https://www.ncbi.nlm.nih.gov/books/NBK589241/

Woods, B. (2025). The TrumpRx website won't slash drug prices, but this will. *Nature, 646*(8086), 777. https://doi.org/10.1038/d41586-025-03397-7. PMID: 41120794.

Wouters, O. J., Sullivan, S. D., Cousin, E. M., Gabriel, N., Papanicolas, I., & Hernandez, I. (2025). Drug prices negotiated by Medicare vs US net prices and prices in other countries. *JAMA, 333*(1), 85-87. https://doi.org/10.1001/jama.2024.22582. PMID: 39621331; PMCID: PMC11612909.

ANNEX I

SUMMARY OF THE 17 CONFIDENTIAL BILATERAL AGREEMENTS US GOVERNMENT / PHARMACEUTICAL COMPANIES (as of 31/05/2026)

Company	*Date*	*Description*
ABBVIE	January 2026	AbbVie has stated that it has reached a three-year agreement with the administration of United States President Donald Trump to reduce medicine prices through Medicaid and has promised 100 billion dollars over the next decade for research and development in the country. The medicine manufacturer said that the investment will include manufacturing and will expand direct-to-patient offers through TrumpRx for widely used medicines such as Alphagan, Combigan, Humira and Synthroid. This three-year agreement provides AbbVie with an exemption from tariffs and future price mandates, the company said, adding that other terms of the agreement remain confidential.
AMGEN	December 2025	Amgen has stated that it will add the cholesterol medicine Repatha at a monthly price of 239 dollars, the migraine medicine Aimovig and the arthritis treatment Amjevita at 299 dollars per month to its direct-to-patient program, which represents between a 60% and 80% discount on the list price. Amgen will reduce the price of its cholesterol-lowering medicine Repatha from 573 dollars to 239 dollars for patients who buy it directly through TrumpRx.
ASTRAZENECA	October 2025	AstraZeneca agreed in October to reduce prescription medicine prices for US patients, including discounts of up to 80% through TrumpRx.gov.
BOEHRINGER INGELHEIM	December 2025	Boehringer Ingelheim stated in December that it would make its medicines available through TrumpRx.gov at reduced prices. Boehringer Ingelheim will reduce the price of its type 2 diabetes medicine, Jentadeuto, from 525 dollars to 55 dollars for patients who buy it directly through TrumpRx.
BRISTOL MYERS SQUIBB	December 2025	Bristol Myers Squibb stated in December that it will provide its flagship anticoagulant Eliquis to Medicaid free of charge as part of its agreement with the Trump administration. It also agreed to donate more than seven tons of active pharmaceutical ingredient for Eliquis. Bristol Myers Squibb will reduce the price of its HIV medicine, Reyataz, from 1,449 dollars to 217 dollars for patients who buy it directly through TrumpRx.
ELI LILLY	November 2025	Eli Lilly agreed in November to offer Medicare beneficiaries its obesity medicines Zepbound and orforglipron, with the brand Foundayo, for no more than 50 dollars per month, with additional discounts for patients who pay directly through LillyDirect. Zepbound's multidose pen will be available for 299 dollars per month at the lowest dose, with additional doses priced up to 449 dollars, while Foundayo will be available from 149 dollars per month at its lowest dose through LillyDirect. Lilly will also offer Emgality, a migraine treatment, for 299 dollars per pen, and Trulicity, a diabetes medicine, for 389 dollars per month through TrumpRx.
EMD SERONO	October 2025	Trump and Merck KGaA's EMD Serono unit (MRCG.DE) stated in October that the German company would sell its fertility treatments, including Gonalf, Ovidrel and Cetrotide, directly to consumers with a combined discount of 84% on the list price if three of them were used in IVF. It would offer all new medicines launched in the United States at the prices it charges in other developed countries.

ANNEX I (CONTINUED)

SUMMARY OF THE 17 CONFIDENTIAL BILATERAL AGREEMENTS US GOVERNMENT / PHARMACEUTICAL COMPANIES (as of 31/05/2026)

Company	*Date*	*Description*
GILEAD SCIENCES	December 2025	Gilead Sciences stated in December that it will provide certain medicines to treat HIV, hepatitis C, hepatitis B and COVID19 at a reduced price for Medicaid beneficiaries. It agreed to set prices for future medicines in parity with other key developed nations and to make its hepatitis C treatment, Epclusa, available at a reduced cash price through TrumpRx and its own direct-to-patient program. Gilead Sciences will reduce the price of its Hepatitis C medicine, Epclusa, from 24,920 dollars to 2,425 dollars for patients who buy it directly through TrumpRx.
GSK	December 2025	GSK agreed in December to make most of its inhaled respiratory medicines and other medicines available to patients on a direct-to-patient platform with savings of up to 66%. It also agreed to reduce the price of certain medicines in Medicaid and launch new medicines with a "more balanced pricing approach" among developed nations. GSK will reduce the prices of its inhaler portfolio. Prices for the popular asthma inhaler Advair Diskus 500/50 will fall from 265 dollars to 89 dollars for patients who buy it directly through TrumpRx.
JOHNSON & JOHNSON	January 2026	The medicine manufacturer J&J agreed in January to reduce medicine prices for US patients, including through the TrumpRx.gov platform. The specific terms of the agreement were not disclosed, including details on revised medicine prices or which medicines are covered.
MERCK	December 2025	The US manufacturer Merck stated in December that it would sell its diabetes medicines Januvia, Janumet and Janumet XR —which will face generic competition in 2026— directly to consumers in the United States with a discount of approximately 70% on list prices. If approved, its experimental cholesterol medicine enlicitide will also be offered through direct-to-consumer channels, including TrumpRx. Merck will reduce the price of its diabetes medicine, Januvia, from 330 dollars to 100 dollars for patients who buy it directly through TrumpRx.
NOVARTIS	December 2025	Novartis stated in December that it would launch new medicines in the United States at prices comparable to those of other developed countries. It also agreed to make the multiple sclerosis medicine Mayzent, as well as the cancer medicines Rydapt and Tabrecta, available through its direct-to-patient platform and TrumpRx.gov. Novartis will reduce the price of its Multiple Sclerosis medicine, Mayzent, from 9,987 dollars to 1,137 dollars for patients who buy it directly through TrumpRx.
NOVO NORDISK	November 2025	The weight-loss medicine manufacturer Novo Nordisk agreed in November to reduce the prices of its semaglutide medicines, including Wegovy and Ozempic, for US patients through Medicare, Medicaid and a direct-to-patient payment channel. Prices of Ozempic and Wegovy will fall from 1,000 and 1,350 dollars per month, respectively, to 350 dollars when purchased through TrumpRx. Novo Nordisk will also provide widely used insulin products, including NovoLog and Tresiba, for 35 dollars per month through TrumpRx.
PFIZER	September 2025	The company agreed in September to reduce prescription medicine prices for US patients, including discounts of up to 85% through TrumpRx.gov. Pfizer said that most of its primary care treatments and some selected brands, such as the rheumatoid arthritis medicine Xeljanz, the dermatitis medicine Eucrisa and the postmenopausal osteoporosis medicine Duavee, will be offered with average savings of 50% that can reach up to 85%.

ANNEX I (CONTINUED)

SUMMARY OF THE 17 CONFIDENTIAL BILATERAL AGREEMENTS US GOVERNMENT / PHARMACEUTICAL COMPANIES (as of 31/05/2026)

Company	*Date*	*Description*
REGENERON	April 2026	The agreement will provide all state Medicaid programs in the country with access to MFN prices for medicines of Regeneron products, resulting in hundreds of millions in savings and continuing President Trump's historic efforts to strengthen the program for the most vulnerable Americans. The agreement guarantees that foreign nations can no longer use price controls to benefit freely from American innovation by guaranteeing MFN prices on all new innovative medicines that Regeneron brings to market. The agreement requires Regeneron to repatriate the additional foreign revenues from existing products that it obtains as a result of the President's strong "America First" US trade policies, for the benefit of US patients. Regeneron also announces that it will invest 27 billion dollars in research, development and manufacturing in the United States by 2029. In this commitment, the company will move to US territory more than double its manufacturing capacity for the production of its biological pharmaceutical medicines that are distributed in the United States. This announcement raises pharmaceutical investments in the United States under President Trump to a total of 448 billion dollars in only 15 months. The President also announced that Regeneron's new gene therapy for a rare type of genetic deafness, called Otarmeni, will be delivered to US patients at no cost as part of this agreement.
ROCHE	December 2025	Roche, the Genentech unit, stated in December that it would reduce the prices of many of its medicines under Medicaid to levels comparable to those available in other rich countries. It also agreed to make its influenza medicines available through TrumpRx.gov and its own direct-to-patient program. Genentech will reduce the price of its influenza medicine, Xofluza, from 168 dollars to 50 dollars for patients who buy it directly through TrumpRx.
SANOFI	December 2025	Sanofi stated in December that it will offer lower-cost medicines through TrumpRx and other direct-to-patient platforms, with average savings of around 70% in treatments for infectious diseases, heart disease and diabetes. It also agreed to align the Medicaid price of several medicines with those of other high-income countries. Sanofi will reduce the price of its prescription anticoagulant, Plavix, from 756 dollars to 16 dollars for patients who buy it directly through TrumpRx and Sanofi will price its insulin products on TrumpRx at 35 dollars per monthly supply.

Sources: www.reuters.com; www.whitehouse.gov

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