

Inflation, competitive dynamics, and economic sustainability in the Spanish pharmaceutical sector

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Abstract

Objective: Spain's pharmaceutical industry has faced inflation within a closely regulated pricing system. The objective of this study was to quantify the resulting economic pressure at sector level and for three medicines that exemplify different market situations.

Methods: Covering a 10-year period analysis, the study followed a four-stage framework. First, a narrative review described how inflation, competition, and regulation shape pharmaceutical pricing. Second, three medicines—ustekinumab, nivolumab, and daratumumab—were used to reflect the additional economic impact of distinct competitive mechanisms, including biosimilar entry, therapeutic competition within patented markets, and multi-indication repricing. Third, macro-economic series (consumer-price indexes, wages, electricity, and fuel indices), industry accounts, and price-volume data were consolidated with national tender records. Finally, cost-turnover indices and unit-level price models quantified resulting economic impacts.

Key findings: Cumulative excess sector costs attributable to inflation totalled €6.5 billion. Purchases of goods and services and staff each accounted for €3.1 billion, while energy added €0.3 billion. At medicine level, the combined economic impact of unadjusted list prices, inflation-driven production costs, and reimbursed-price reductions amounted to €494 million for ustekinumab, reflecting approaching biosimilar competition; €498 million for nivolumab, associated with successive indication-based repricing within a value-alignment framework; and €580 million for daratumumab, in the context of intense competition.

Conclusions: Inflation, regulated pricing mechanisms, and competitive repricing coincided with a measurable divergence between cost evolution and revenues. Transparent and publicly available metrics would provide a reliable baseline for monitoring Spain's pharmaceutical adaptability within an evolving macro-economic conditions landscape.

Keywords health policy, pharmaceutical industry, economics

Introduction

The pharmaceutical sector faces notable economic pressures driven by several interrelated factors. Key factors include inflation, rising market competition, and regulatory measures linked to authorizing new therapeutic uses for existing medicines—all of which directly affect pricing [1].

Inflation—the sustained rise in general prices—affects every part of the economy. In Spain, average annual consumer price index (CPI) turned from −0.5% in 2015 to 8.4% in 2022, the highest increase in nearly four decades. Overall, consumer prices are about 17% higher than a decade ago, driving up the cost of raw

materials, energy, and logistics that are the basis of medicine manufacture [2–4]. This rise in CPI reflects a combination of factors, including pandemic-related supply disruptions, energy price spikes, global logistics bottlenecks, and, more recently, the war in Ukraine.

Because medicine prices are tightly regulated by the healthcare system, pharmaceutical companies have limited scope to transfer higher development and production costs onto their sales [5]. Most of the additional expense, therefore, remains on their balance sheets, generating accounting pressure within firms operating under regulated pricing conditions. This may influence the

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financial context in which the sector operates when addressing new health challenges [2].

Further market dynamics also influence both the supply of and demand for medicines. A prime example is the arrival of generic versions, which provide lower-cost alternatives once the originator's period of market exclusivity—comprising patent protection and regulatory data exclusivity—expires [6]. Because clinical development and regulatory review can last more than a decade, the effective period of market exclusivity often falls below ten years. When this period ends, the entry of generics changes the competitive environment, leading originator companies to lower prices and adjust their commercial approaches [7, 8].

Similarly, when regulators approve new therapeutic indications for an established medicine—producing what is known as a multi-indication product—the price is often revised downwards. Alongside growing competition between manufacturers, this keeps prices under constant downward pressure, while production costs are rising due to inflation [9, 10].

Importantly, these repricing mechanisms are not arbitrary adjustments but deliberate policy instruments. Multi-indication repricing frameworks are formally intended to align reimbursement levels with the therapeutic value demonstrated in different patient populations. In practice, however, price revisions following indication expansion often reflect a combination of value reassessment and budget-impact considerations, particularly in systems such as Spain, where indication-specific pricing is not systematically implemented. Similarly, generic and biosimilar entry mechanisms—and competitive dynamics among patented therapeutic alternatives—are intended to generate savings and expand access once exclusivity ends. The interaction between these value-oriented policies and macroeconomic inflation constitutes the focus of the present analysis.

In this context, the study pursues two goals. First, it provides an estimate of the impact of inflation on the operating costs of Spain's pharmaceutical industry from 2015 to 2024. Second, it examines how inflation, the lack of price pass-through, and price changes from multi-indication approvals, generic entry, and mature-market competition have jointly affected three illustrative medicines over a ten-year period in Spain. These examples are ustekinumab (an anti-IL-12/23 monoclonal antibody approved for psoriasis, psoriatic arthritis, and Crohn's disease or ulcerative colitis in adults [11]), nivolumab (an anti-PD-1 checkpoint inhibitor with 14 reimbursed oncological indications [12]), and daratumumab (an anti-CD38 antibody indicated for multiple myeloma [13] and light chain amyloidosis [14]).

These three medicines are not intended to constitute a statistically representative cross-section of the Spanish pharmaceutical market. Rather, they function as structured analytical archetypes reflecting three distinct pricing pathways within the national reimbursement framework. The study, therefore, adopts a mechanism-focused approach: it examines how macro-inflation interacts with specific regulatory triggers that are recurrent in Spain's hospital pharmaceutical sector, rather than estimating a mean sector-wide product effect.

Materials and methods

The study followed a two-part methodology. It contains a narrative literature review, together with an empirical analysis based on data from Spain's pharmaceutical sector. Four stages were applied

for: (i) reviewing relevant literature to outline the influence of inflation and other economic factors; (ii) selecting three medicines that typify distinct market dynamics situations; (iii) gathering key information on macro-economic indicators, industry metrics, and medicine prices; and (iv) estimating the economic impact on the sector as a whole and on the chosen products.

Literature review

We conducted a narrative review to understand the effects of inflation and to assess how generic entry, mature-market competition, and new indications influence medicine prices. Academic databases (PubMed, Google Scholar) and grey sources were searched for Spanish- and English-language material published between 2010 and 2024. Macroeconomic analyses of inflation's impact on operating costs, studies on generic competition and multi-indication pricing, and papers on regulatory-economic interactions were all considered. Data sets from the Spanish National Institute of Statistics (INE), the official Spanish medicines information system maintained by the General Council of Spanish Pharmacists' Colleges (Botplus), and IQVIA, together with institutional reports, supplied Spain-specific context.

Selection of medicines analysed

Three medicines were selected as structured case studies on the basis of explicit, pre-defined criteria intended to maximize analytical contrast rather than statistical representativeness.

The three medicines were selected according to four pre-defined criteria: regulatory archetype differentiation (ustekinumab representing biosimilar entry following loss of exclusivity, nivolumab illustrating indication-based repricing under centralized negotiation, and daratumumab exemplifying competitive pressure in a mature biologics market); economic materiality, ensuring each product accounted for a non-negligible share of total pharmaceutical turnover ([Supplementary Material 3](#)); hospital-market relevance, as all three are predominantly hospital-dispensed with systematically recorded procurement adjustments; and temporal comparability, with each product having a sufficient market history to allow longitudinal modelling across both stable periods and the 2021–2 inflation spike.

Importantly, the objective was not to construct a representative sample of the Spanish pharmaceutical market, nor to estimate an average product-level effect. Rather, the case-study design intentionally captures three structurally distinct pricing-competition mechanisms embedded in Spain's regulatory system, which together account for a substantial proportion of price revisions observed in hospital medicines over the past decade. The analytical strategy therefore follows a mechanism-based comparative design in which inference is directed at regulatory pathways—biosimilar competition, multi-indication repricing, and mature-market rivalry—rather than at individual molecules per se.

Data collection

All quantitative inputs were compiled from publicly available national statistics, institutional pricing records, and syndicated hospital market data, covering three analytical dimensions: inflation effects on industry operating costs; revenue shortfalls

Table 1 Core data domains underpinning the economic-impact model.

Model block	Type of information included	Temporal scope	Primary data sources
Sector-level cost structure	Annual financial magnitudes and index construction for turnover and operating cost components (purchase of goods and services, staff costs, energy consumption)	2014–24	National Institute of Statistics—INE (2015 [15], 2018 [16], 2022 [17], 2024 [18])
Macroeconomic inflation series	General and pharmaceutical-specific CPI series used for price indexation and cost adjustments	2014–24	National Institute of Statistics—INE (2015 [15], 2018 [16], 2022 [17], 2024 [18])
Product-level pricing data	Official notified price and observed reimbursed-price adjustments linked to competition and indication expansion	Launch year onward	- The official Spanish medicines information system—Botplus (2024 [19]). - Price reductions for Nivolumab [10, 20–22]. - Other price reductions, public tender records; CIPM documentation (Supplementary Material 1)
Product-level market dynamics	Annual sales volumes and relative market shares within the hospital pharmaceutical market	2014–25 ^a	IQVIA hospital database (2024 [23])
Derived impact components	Inflation non-pass-through, turnover-adjusted cost exposure, and revenue effects of competitive price reductions	2014–25 ^a	Author calculations (Supplementary Material 3)

Notes: ^aWhere applicable. For nivolumab, the analysis incorporates the indication-based price adjustments observed in France, using the figures reported by Michaeli (2022) [10] for the second, third and fourth indications. **Definitions:** *Turnover*: net sales of goods and services (excluding product taxes), as defined in INE's 'Key variables by activity sector'. *Purchases of goods and services, excluding energy*: outlays on materials and services directly linked to production, excluding energy. *Staff costs*: gross remuneration (wages, salaries and employer social-security contributions) paid to employees. *Energy consumption*: expenditure on electricity, natural gas and fuels (diesel and petrol) used in production. *Notified price*: retail price to the public including VAT, set by the Inter-ministerial Committee on Medicine Prices. **Sources:** as listed in the table itself.

from the absence of inflation pass-through to regulated prices; and revenue effects of reimbursed-price reductions linked to biosimilar entry, multi-indication repricing, and mature-market competition. As summarized in Table 1, the dataset comprises five core domains, which together allow construction of turnover-adjusted cost indices and annual decompositions of inflation exposure and competitive price effects. Complete year-by-year inputs, index constructions, and intermediate calculations are reported in Supplementary Material 3.

For nivolumab, indication-based price adjustments were inferred from publicly available French data, as Spanish reimbursement decisions publish notified list prices but do not disclose indication-specific price differentials. This approach is justified by the structural comparability between the two systems: both operate centralized reimbursement frameworks in which national authorities negotiate prices after European marketing authorization and may revise them following additional indication approvals. The extrapolation nonetheless acknowledges potential quantitative divergence arising from differences in transparency, assessment criteria, and the role of confidential discounts.

Impact estimation

Sector-wide impact of inflation

The effect of inflation on the operating costs of Spain's pharmaceutical industry was quantified for three cost categories—purchases of goods and services (excluding energy), staff expenses,

and energy consumption—after correcting each series for the evolution of total turnover between 2015 and 2024. The procedure comprised four steps:

We first constructed base indices for each cost heading—purchases of goods and services (excluding energy), staff expenses, and energy consumption—by dividing the value in year t by the 2014 baseline and multiplying by 100:

$$I_t = \frac{x_t}{x_{2014}} \times 100 \quad (1)$$

where I_t is the index in year t , and x each type of cost.

Secondly, we built turnover-adjusted variations by subtracting the index of total industry turnover I_t^{TO} from each cost index, which isolated the portion attributable solely to inflation:

$$\Delta_t = I_t - I_t^{TO} \quad (2)$$

Thirdly, we converted these percentage variations into euros, applying each Δt to the corresponding year's value:

$$\text{Impact}_t^{\text{€}} = \Delta_t \times x_t \quad (3)$$

Finally, we summed up the three cost headings impacts in euro (k) to obtain the total annual burden of inflation on the

sector:

$$\text{Total impact}_t^{\epsilon} = \sum_k \text{Impact}_{t,k}^{\epsilon} \quad (4)$$

To distinguish structural inflation from episodic shocks, cumulative excess costs were decomposed into three phases—pre-shock (2015–9), shock-affected (2020–2), and normalization (2023–4)—and the contribution of the peak years 2021–2 was calculated as a proportion of total cumulative impact.

Medicine-level impacts

For each of the three study medicines the model calculated, year by year over a ten-year horizon, the combined effects of (i) not passing inflation through to price, (ii) inflation-driven production-cost increases and (iii) reimbursed-price reductions arising from multi-indication pricing, biosimilar or generic entry and competition in mature markets.

Inflation not passed through to price

A counter-factual, inflation-adjusted price P_t^{infl} was calculated by taking the launch-notified retail price [including Value Added Tax (VAT)] (P_t) and scaling it by the cumulative pharmaceutical CPI up to year t . The revenue shortfall is:

$$\text{Shortfall}_t = (P_t^{\text{infl}} - P_t) Q_t \quad (5)$$

where P_t is the notified price and Q_t the units sold in year t .

Inflationary rise in production costs

The medicine's sales share in total industry turnover (s_t) was multiplied by the excess cost calculated for each cost component j :

$$\text{Cost impact}_t = s_t \sum_j \frac{\Delta_j}{100} C_{2014}^j \quad (6)$$

where C_{2014}^j is the 2014 baseline value for component j .

Reimbursed-price reductions

When tenders or negotiations imposed a lower reimbursed price P_t^{new} , the loss of revenue was:

$$\text{Price cut impact}_t = (P_t - P_t^{\text{new}}) Q_t \quad (7)$$

Total medicine impact

For each year:

$$\begin{aligned} \text{Total medicine impact}_t &= \text{Shortfall}_t + \text{Cost impact}_t \\ &+ \text{Price cut impact}_t \end{aligned} \quad (8)$$

The full set of numerical inputs feeding these formulae is listed in [Supplementary Material 3](#).

Complete year-by-year calculations underlying all sector-level and product-level estimates—including annual indices, turnover-adjusted cost components, counterfactual prices, and price reduction effects—are reported in [Supplementary Material 3](#).

Nature of the analytical framework

The analytical framework is descriptive and accounting-based: it quantifies observed divergences between input-cost evolution and regulated pricing trajectories under real-world volume dynamics, without attempting causal inference or counterfactual modelling. The objective is to measure cumulative economic exposure associated with inflation and regulated price adjustments under observed market conditions.

Sensitivity and robustness analysis

A deterministic sensitivity analysis was conducted, varying key inputs across three dimensions: pharmaceutical CPI ($\pm 10\%$), total industry turnover ($\pm 10\%$), and product-level sales shares ($\pm 5\%$). For nivolumab, alternative structural scaling scenarios (75% and 50% of observed French price adjustments) were applied to assess sensitivity to cross-country extrapolation. Sector-level robustness was further tested using alternative baseline years (2015–8), evaluated through average annual excess cost estimates. Full methodology and results are reported in [Supplementary Material 2](#).

Results

To facilitate interpretation of the empirical findings, [Fig. 1](#) presents a consolidated timeline aligning inflation dynamics, major macroeconomic shocks, and key regulatory or competitive pricing events affecting the three case-study medicines. This visual synthesis situates the subsequent quantitative estimates within their broader temporal and institutional context.

Sector-wide impact of inflation

Over the decade 2015–24 cumulative inflation added an estimated €6.5 billion to the operating costs of the Spanish pharmaceutical industry. The burden was not uniformly distributed across years: it rose sharply in 2021 (€1.4 billion) and peaked in 2022 (€2.2 billion) due to energy and logistics costs from the global supply-chain crisis ([Fig. 2](#)).

The total is made up of three cost streams. Purchases of goods and services (excluding energy) accounted for €3.06 billion, with the heaviest single-year increases again in 2021 and 2022, whereas seven of the 10 years under review (2016–20 and 2023–4) showed modest relief. Staff costs constituted the largest component—€3.10 billion in aggregate—driven by strong rises in 2023 (€808 million) and 2024 (€1.4 billion) that outweighed the compensatory reductions registered in 2021–2. Energy expenditure contributed a comparatively smaller €348 million, almost entirely concentrated in 2022 when wholesale electricity and gas prices spiked.

When decomposed temporally, €988 million (15.2%) of cumulative excess costs accrued during the pre-pandemic structural phase (2015–9). The shock-affected phase (2020–2) accounted for €3.67 billion (56.4%), of which €3.59 billion (55.2% of the total cumulative burden) was concentrated in 2021–2 alone. Excess costs were also observed beyond the acute shock period: €1.85 billion (28.5%) accumulated during 2023–4, including €1.19 billion in 2024, exceeding any single pre-pandemic year.

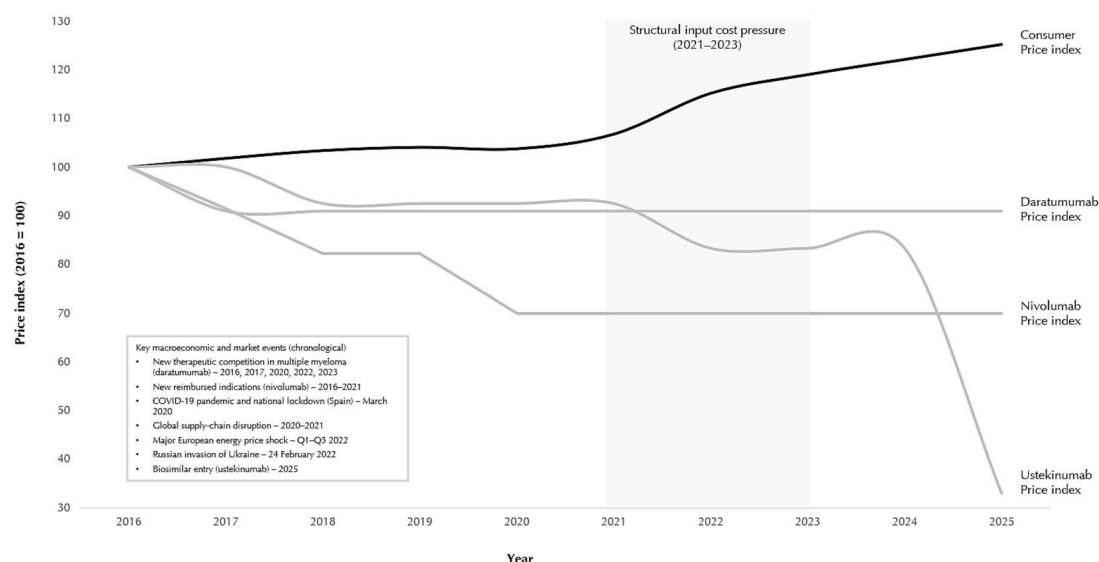


Figure 1 Temporal alignment of inflation shocks and regulated medicine price dynamics in Spain (2016–2025). Note: Price indices are normalized to 2016 = 100. The shaded area denotes the structural input cost pressure period (2021–3).

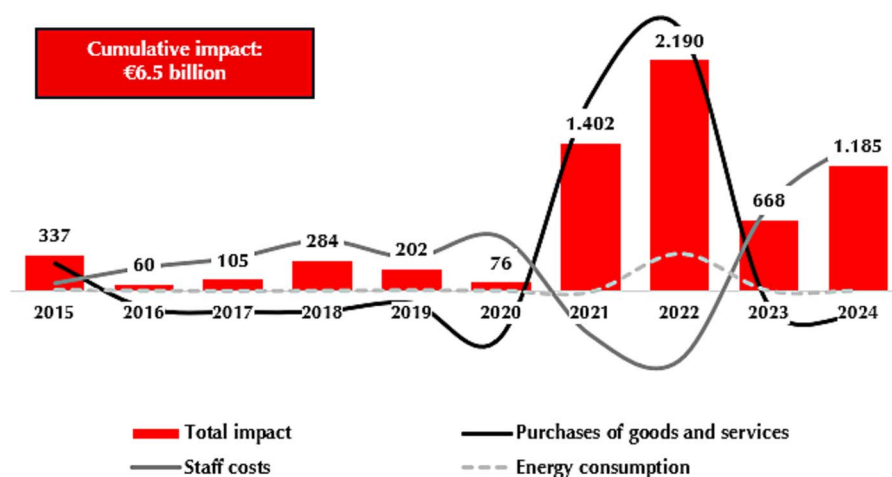


Figure 2 Inflation-driven cost increases in the Spanish pharmaceutical industry, 2015–24 (million €).

Medicine-level impacts

Ustekinumab—illustrative case of biosimilar entry

Ustekinumab entered the Spanish market in 2009. Market exclusivity ended in early 2024, triggering rapid sequential approvals of biosimilar versions (Stada, Samsung Bioepis, Amgen, Celltrion, Fresenius Kabi, and, in early 2025, Accord). Although just a small number of competitive tenders had been adjudicated by March 2025, the expectation of wider biosimilar uptake began to weigh on reimbursed prices: the award-price index, stable at about 92 until 2021, dropped to 83 in 2022–4 and fell further to 33 once biosimilar supply was firmly established, in 2025.

The resulting economic effects fall into three components. First, foregoing inflation pass-through reduced cumulative revenues by €39.4 million, with the largest shortfalls concentrated in 2023–4. Secondly, higher production costs attributable to general inflation added €112.6 million to expenditure, again peaking during the recent inflationary spike. Thirdly, price reductions following biosimilar entry were associated with a far larger cumulative loss of €342.4 million; the sharpest single-year declines occurred in 2023 and 2024 as notified prices adjusted in anticipation of full

competition. Taken together, these three channels generated a total negative impact of €494.3 million over the study horizon, illustrating the quantitative interaction between loss of exclusivity, competitive price adjustments, and contemporaneous inflationary cost growth (Fig. 3).

Nivolumab—illustrative case of multi-indication pricing

Nivolumab, first reimbursed in Spain in 2016, has since gained successive approvals for a broadening list of tumour types. Following successive indication approvals, notified prices were revised downward, and the index of award prices fell from 100 in 2016 to about 70 by 2023. The steepest decline occurred between 2018 and 2020, coinciding with the largest waves of indication expansion; prices have remained stable, but at this lower level, since 2020.

Over 2016–23 three mechanisms shaped the medicine's economics. The absence of inflation adjustment in notified prices was associated with a cumulative revenue shortfall by €40.4 million, with the largest shortfalls in 2022–3. Inflation-driven

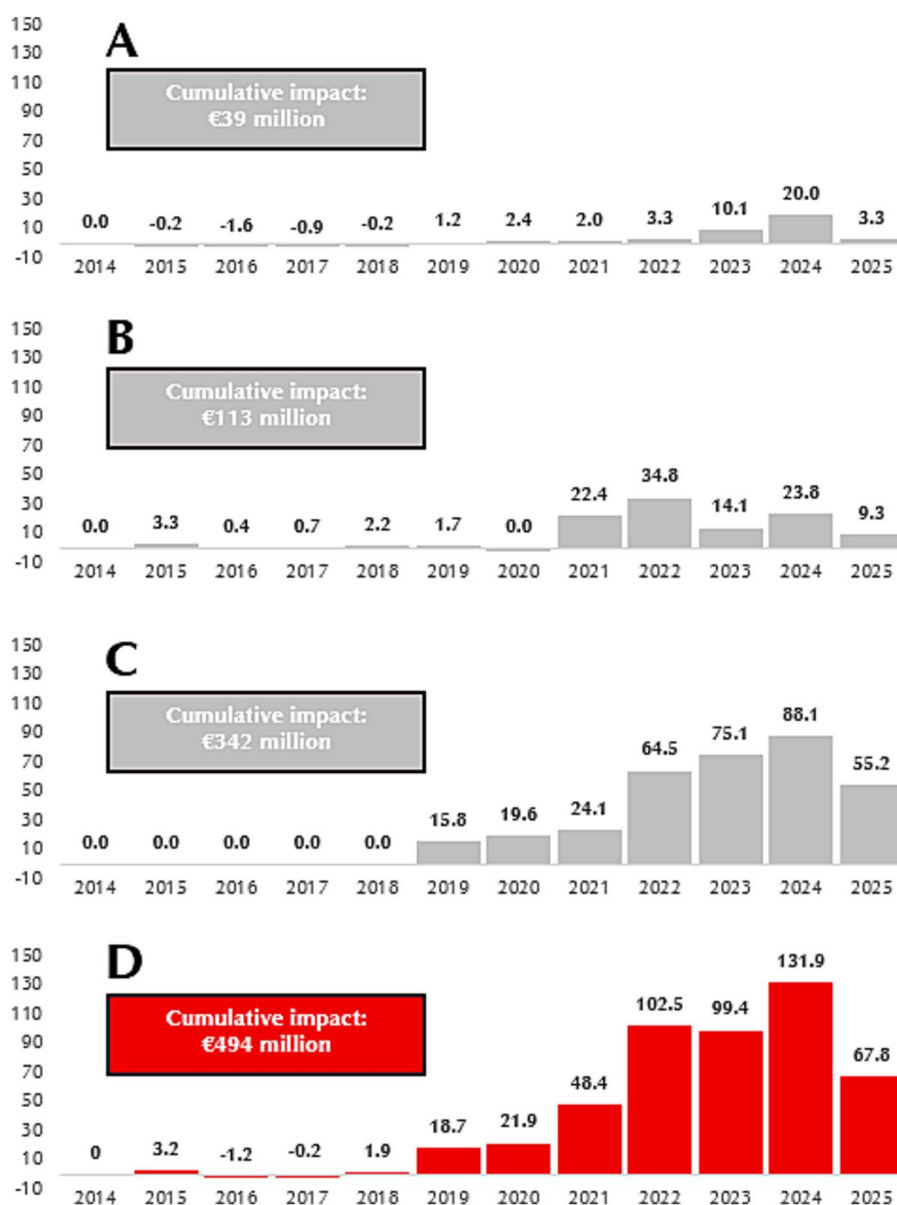


Figure 3 Estimated economic impact of ustekinumab, 2014–March 2025. Legend: A. Total impact of not passing inflation through to price (million EUR). B. Total impact of inflation-driven cost increases (million EUR). C. Total impact of price reductions (million EUR). D. Combined impact of all three factors (million EUR).

risks in production inputs added €37.5 million to costs, peaking in 2021–2 during the wider inflation surge. The largest component of the observed impact was the cumulative effect of stepwise reimbursed-price reductions associated with indication expansion, amounting to €420 million over the study period. Taken together, the three components yielded a total estimated economic adjustment of €498 million (Fig. 4).

Daratumumab—illustrative case of competition in a mature market

Daratumumab reached Spanish reimbursement in 2016, entering a multiple-myeloma field that has since become increasingly crowded. New entities such as elotuzumab, carfilzomib, and isatuximab expanded biological options, while the arrival of chimeric

antigen receptor T-cell (CAR-T) and bispecific antibodies from 2022 onwards further intensified competition. Despite 112 hospital tenders, nearly all negotiated under single-supplier contracts with multi-year extensions, award prices have remained remarkably steady: the index slipped from 100 in 2016 to 91 in 2017 and has hovered around that level ever since.

From 2016 to March 2025, three economic forces shaped the medicine's performance. First, keeping notified prices flat while general prices rose removed €43.8 million in potential revenue, most of it during the high-inflation year 2024. Secondly, observed increases in macroeconomic input indices were reflected in higher estimated production costs, adding €183.9 million in extra costs, a burden that grows noticeably from 2021 onwards. Thirdly, cumulative reductions in the reimbursed price led to a revenue loss of €352.6 million, with 2024 alone accounting for more than

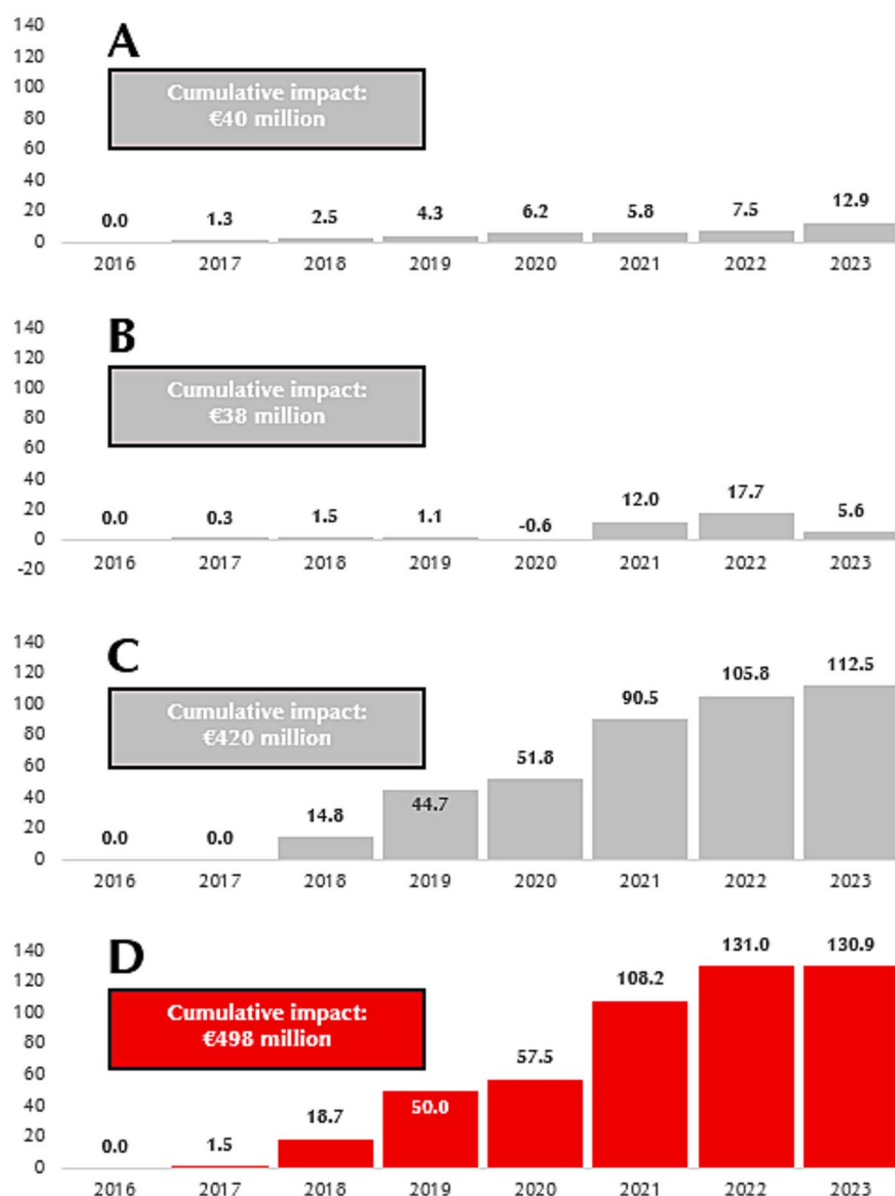


Figure 4 Estimated economic impact of nivolumab, 2016–23. Legend: A. Total impact of not passing inflation through to price (million EUR). B. Total impact of inflation-driven cost increases (million EUR). C. Total impact of price reductions (million EUR). D. Combined impact of all three factors (million EUR).

€100 million. Combined, these channels produced a total negative impact of €580.4 million (Fig. 5).

Sensitivity and robustness analysis

Sensitivity analyses confirmed the structural robustness of the model. Sector-level estimates were invariant to $\pm 10\%$ turnover variation. Pharmaceutical CPI variation ($\pm 10\%$) altered product-level cumulative impacts by less than 1%, while sales-share variation ($\pm 5\%$) produced deviations of up to 1.6%. For nivolumab, applying 75% and 50% of the French indication-based adjustments yielded total impacts of €401 million and €299 million, respectively, versus €498 million at baseline. Alternative sector-level baseline years (2015–8) confirmed stability of average annual estimates. Across all scenarios, the direction, order of magnitude, and relative ranking of results remained unchanged. Full results are reported in [Supplementary Material 2](#).

Discussion

The present analysis examines how macroeconomic inflation, regulated pricing mechanisms, and competitive repricing interacted within Spain's pharmaceutical reimbursement system over the past decade. At sector level, cumulative turnover-adjusted excess costs reached €6.5 billion between 2015 and 2024, illustrating the materiality of recent macroeconomic shocks within a regulated pricing environment [24–26].

The timing aligns closely with the national inflation cycle, with costs accelerating during the energy-price spike that drove inflation to 10.8% in July 2022, consistent with external evidence of 10-fold rises in electricity bills and double-digit raw-material cost growth across European manufacturers [27, 28].

Although over half of cumulative excess costs concentrate in 2021–2, the divergence between cost evolution and regulated prices predates the pandemic and persists beyond it: the

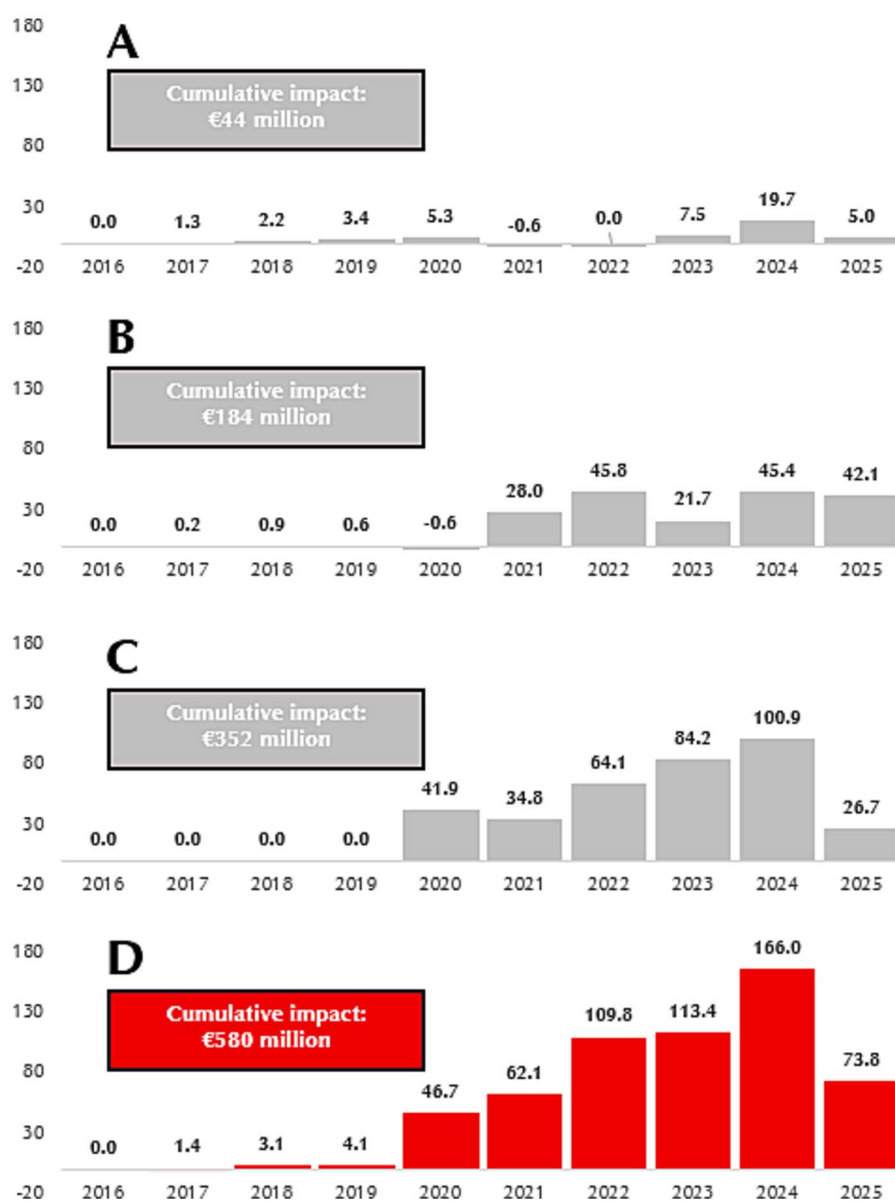


Figure 5 Estimated economic impact of daratumumab, 2016–March 2025. Legend: A. Total impact of not passing inflation through to price (million EUR). B. Total impact of inflation-driven cost increases (million EUR). C. Total impact of price reductions (million EUR). D. Combined impact of all three factors (million EUR).

€988 million accumulated during 2015–9 and the continued €1.85 billion during 2023–4 indicate that the pressure cannot be attributed exclusively to temporary macroeconomic shocks.

When mapped onto individual products, impacts vary by competitive trajectory. Ustekinumab illustrates loss-of-exclusivity dynamics, with price adjustments from the low nineties to the low thirties amplifying inflation-related costs. Nivolumab shows how successive indication approvals drove a price index decline from 100 to 70 between 2016 and 2023. Daratumumab, in a mature yet innovation-intensive market, exhibited relative price stability but still yielded a high total impact through sustained competitive dynamics and inflation-driven production costs.

These figures should be interpreted within the policy logic of regulated systems. Indication-based repricing, biosimilar competition, and tender procurement are designed to improve

allocative efficiency and generate system savings. The €498 million adjustment for nivolumab reflects the mechanical financial consequence of regulated repricing under concurrent inflation, not a deviation from intended policy design.

The total burden is substantial relative to each product's own turnover: ustekinumab's €494 million shortfall equates to ~18% of cumulative sales; nivolumab's €498 million impact represents roughly 37%; and daratumumab's €580 million gap corresponds to ~26%—demonstrating that significant cost–price divergence can arise even in markets with relative price stability.

From a system perspective, revenue compression must be interpreted alongside the corresponding affordability and access gains generated by these mechanisms. The present analysis does not evaluate whether these trade-offs are optimal; it quantifies financial exposure under existing policy structures when input costs evolve more rapidly than regulated prices.

The analysis reveals two structural themes. First, input costs are set in global markets while statutory medicine prices move only when a formal regulatory trigger materializes, creating systematic cost–price divergence during macroeconomic shocks. Second, the temporal pattern shows that macroeconomic effects are delayed: energy-related costs peaked in 2022, but the largest revenue shortfalls were recorded in 2023–4, reflecting the annual cadence of national tenders and the lead time for revising reimbursement terms.

The three case studies also illustrate how competitive mechanisms interact differently with inflation. Biosimilar entry delivers abrupt price corrections but only after regulatory steps complete, allowing costs to accumulate beforehand. Multi-indication pricing yields concessions spread over years—nivolumab's effect is equivalent in scale to a large patent expiry. Mature-market competition, as in daratumumab, compounds these effects through steady incremental price concessions alongside next-generation competition, collectively generating sustained cost–price divergence even where headline prices appear stable.

The comparative interpretation is analytical rather than statistical. The selected medicines exemplify three recurring regulatory mechanisms within Spain's pricing architecture, and while absolute magnitudes are product-specific, the underlying interaction between inflation, regulated price rigidity, and competitive repricing reflects structural system features rather than product-level anomalies.

Several methodological strengths underpin the analysis: a transparent four-step sectoral cost index and three-component product model consistent with the 2023 Farmaindustria report; exclusive reliance on publicly available national statistics; a ten-year horizon covering both stable years and the inflation spike; and structured sensitivity analyses confirming stability of direction, magnitude, and ranking across plausible parameter variations.

Several limitations should temper interpretation. Alternative baseline-year specifications (2015–8) were tested and confirm directional stability, though cumulative magnitudes vary mechanically due to index re-anchoring. The study period also overlaps with COVID-19 supply-chain shocks whose effects are embedded within CPI components but not separately identified.

The temporal decomposition distinguishes concentration of excess costs across phases but does not fully separate structural inflation from extraordinary energy or supply-chain effects within CPI components. Results should therefore be interpreted as identifying temporal patterns rather than attributing causality to specific macroeconomic drivers.

For nivolumab, indication-based price reductions were inferred from French public data, so absolute values may diverge from Spanish actuals. Sensitivity testing yields a total impact range of €299–€401 million under conservative scaling (50%–75% of the French adjustment), versus €498 million at baseline, a deviation of 19%–40%, while preserving indication-driven repricing as the principal economic factor.

The analysis relies exclusively on publicly available list prices and documented tender outcomes; confidential rebates, claw-backs, and managed-entry agreements could not be incorporated. Effective net prices are therefore likely lower than those used, which may affect absolute product-level magnitudes without altering the structural direction of the cost–price divergence identified.

The model does not control for clinical uptake, therapeutic substitution, or evolving standards of care; results represent accounting-based estimates under observed market evolution rather than causal effects attributable to inflation or pricing regulation alone.

Because the product-level analysis covers three purposively selected cases representing distinct regulatory archetypes, reported euro magnitudes are specific to these medicines and should not be interpreted as sector-wide averages or statistically generalizable estimates.

Sensitivity analyses varying pharmaceutical CPI ($\pm 10\%$), industry turnover ($\pm 10\%$), and product-level sales shares ($\pm 5\%$) did not materially alter the magnitude or direction of estimated impacts, suggesting findings reflect stable structural relationships. Nevertheless, access to confidential cost-of-goods data and negotiated net prices would allow further refinement.

Policy implications

The findings illustrate the structural tension that may emerge when input costs evolve more rapidly than statutory prices in regulated pharmaceutical systems. The results do not imply that current mechanisms are inappropriate but highlight areas where design adjustments could reduce volatility.

One potential tool is structured indexation: inflation-adjustment clauses—automatic or trigger-based—could allow limited, transparent price updates when macroeconomic indicators exceed pre-defined thresholds, balancing payer predictability with supplier sustainability while avoiding pro-cyclical expenditure growth.

A second option is dynamic tendering design, incorporating conditional review points linked to major cost shocks into multi-year hospital procurement contracts, or risk-sharing components that distribute unexpected macroeconomic burdens between suppliers and purchasing authorities.

Third, enhanced transparency in multi-indication repricing frameworks—particularly regarding how macroeconomic context is considered during renegotiations—could improve predictability for both regulators and manufacturers when successive indication approvals coincide with inflationary conditions.

These options involve trade-offs between expenditure predictability, financial sustainability, access, innovation incentives, and supply resilience. The appropriate balance depends on broader policy objectives that extend beyond this analysis.

This analysis remains descriptive and does not advocate specific reforms. Its purpose is to document where structural cost–price divergences arise and to inform evidence-based policy dialogue; normative judgments on indexation, tender flexibility, or repricing design lie beyond the scope of the present accounting-based model.

Conclusions

Over 2015–24, macroeconomic inflation was associated with an estimated €6.5 billion increase in turnover-adjusted operating costs in Spain's pharmaceutical sector, with excess costs concentrated but not exclusive to the 2021–2 energy and supply-chain shock. Product-level modelling shows that the magnitude and composition of cost–price divergence vary by regulatory pathway, with biosimilar entry, multi-indication repricing, and mature-market competition each producing distinct impact patterns. Together, these findings illustrate how inflation, limited price

indexation, and structured competitive repricing interact within Spain's regulated reimbursement system—quantifying their combined economic effects without evaluating the normative desirability of the mechanisms involved. The transparent and reproducible accounting framework provided offers a reference point for monitoring how future macroeconomic cycles and regulatory events shape cost–price dynamics in the Spanish pharmaceutical market.

Conflicts of interest

R.P., D.B., N.R., and T.D. are employees of Johnson & Johnson Innovative Medicine, two of whose medicines are included as case studies in this analysis: ustekinumab (Stelara), marketed by Johnson & Johnson Innovative Medicine until loss of exclusivity in August 2024, and daratumumab (Darzalex), which remains under patent. F.A., J.V., and Á.H.-V. are employees of Weber España, which received funding from Johnson & Johnson Innovative Medicine for this study. Notwithstanding these affiliations, the authors declare no conflict of interest. The analysis is based exclusively on publicly available data, applies a symmetric and pre-specified analytical framework to all three case-study medicines, and does not advocate for any specific pricing or reimbursement outcome. The findings and conclusions are those of the authors and do not represent the position of Johnson & Johnson Innovative Medicine.

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Data availability

The macroeconomic and sector-level data underlying this analysis are publicly available from the Spanish National Institute of Statistics (INE) at <https://www.ine.es>. Official medicine pricing data were obtained from the Spanish medicines information system BotPlus (<https://botplusweb.farmaceuticos.com>) and from publicly available records of the Interministerial Pricing Commission (CIPM). French indication-based pricing data used for the nivolumab extrapolation were obtained from publicly accessible sources as cited in the reference list. Hospital market sales and volume data were obtained from the IQVIA hospital database (EMH), a proprietary syndicated data source available under subscription from IQVIA; these data are not publicly available and cannot be shared by the authors. No primary data were collected for this study. All intermediate calculations, index constructions, and year-by-year numerical inputs required to reproduce the reported estimates are documented in [Supplementary Material 3](#).

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