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SEPTEMBER 2025
KEY FINDINGS

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ACRONYMS

AGCM	Italian Competition Authority
AIFA	Agencia Italiana del Farmaco (Italian Medicines Agency)
ALBVG	Act to Combat Drug Shortages and Improve Supply (Germany)
AMR	Antimicrobial Resistance
API	Active Pharmaceutical Ingredients
COG	Cost of Goods
EMA	European Medicines Agency
ERP	External Reference Pricing
ESG	Environmental, Social and Governance
EU	European Union
FAMHP	Federal Agency for Medicines and Health Products (Belgium)
INN	International Non-proprietary Name
IRP	Internal Reference Pricing
MAH	Marketing Authorization Holder
MEAT	Most Economically Advantageous Tender
NHS	National Health Service
OHE	Office of Health Economics
PPI	Producer Price Index
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
SEK	Swedish Krona
UK	United Kingdom
VPAS	Voluntary Pricing and Access Scheme
WHO	World Health Organization

I. INTRODUCTION

This study examines the impact of macro-economic indicators in the economic viability and availability of off-patent antibiotics in Europe, using them as a case study for other off-patent medicines¹. Antibiotics, an essential class of medicines for public health, are becoming increasingly vulnerable to economic and policy pressures. The study also proposes policy recommendations to improve access.

1. Why do off-patent medicines matter?

In several disease areas with the highest public health impact, **off-patent medicines** are typically the **first treatment option**. As a result, the effectiveness of public health initiatives in enhancing population health relies heavily on ensuring access to and proper use of these more affordable medicines[1]. Antibiotics were selected as a case-study because they are at the cornerstone of modern medicine, essential for treating bacterial infections and preventing complications in various medical procedures. However, **Europe has been grappling with recurring shortages of these and other vital medicines**, particularly off-patent medicines, jeopardizing patient care and public health.

When first-choice antibiotics are not available, and patients are instead provided with a suboptimal antibiotic with a different therapeutic spectrum, this can lead to poorer patient outcomes, an increased risk of adverse effects and a rise in antimicrobial resistance (AMR)[2,3].

“Antibiotic resistance is one of the most urgent threats to public health. The development of antibiotic resistance can be reduced using narrow-spectrum antibiotics that target specific bacteria, meaning that fewer non-harmful bacteria are killed and other harmful bacteria are not exposed to selection pressure.”[4]

Price pressures on off-patent medicines force manufacturers to prioritize efficient production to remain viable. The continued price pressure **contributes to market consolidation and reduced medicine availability**, creating a vicious cycle. While price pressures have allowed health systems to reduce their expenditure on pharmaceutical

¹ Off-patent medicines correspond to the mature medicines, branded, generic and biosimilar ones. They are medicines which launch happened several years ago (at least 10 years ago). In this report we will also use the term essential medicines due to the importance of off-patent antibiotics for populations and public health.

products, it has resulted in less diversified and consequently more fragile supply chains, that are lean to the point of vulnerability[3].

Amoxicillin is an example, where availability has fluctuated, and shortages occurred frequently in recent years, due to price pressures and, consequently, concentration of manufacturers of active substance worldwide[3]. Some European Governments, worried about antibiotic shortages, have tried to find ways to incentivize greater production in Europe with the aim to strengthen the long-term future of integrated antibiotics manufacturing[5,6].

Most medicines that are permanently withdrawn from a particular market are products with low or negative margins, for which the Market Authorization Holder (MAH) decides that the revenue from the product doesn't support the costs of maintaining the product on the market. This might happen because market conditions no longer enable a sufficient profit margin on the product[3].

The sustainability of off-patent critical medicines must thus be treated as a strategic issue comparable to energy or food security, as the EU and several countries are starting to consider. As costs have kept rising in the last years, **Europe must recalibrate its pharmaceutical policies to protect essential off-patent medicines.**

2. Key questions and methodology

The study covers 16 European countries and is based on a mix of literature review (scientific and grey) and a quantitative analysis for off-patent antibiotics.

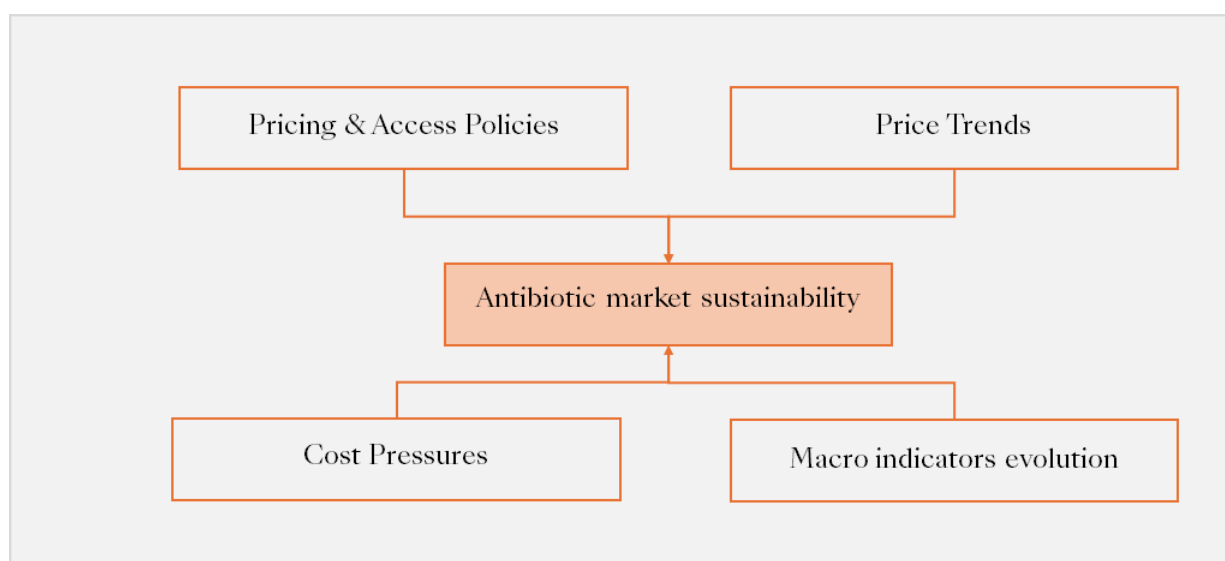
Table 1: Scope of countries included in the study

Austria	Belgium	Croatia	Estonia	Finland	Germany
Hungary	Ireland	Italy	Norway	Poland	Portugal
Spain	Sweden	Switzerland	UK		

We developed a conceptual framework that explores the main issues currently affecting off-patent antibiotics, and medicines in general, with two main questions to be answered:

What is the evolution of off-patent antibiotic prices and its relationship with the evolution of costs and economic indicators? Which policy solutions can be proposed to enhance access?

Figure 1: Conceptual Framework



A mixed methods approach was used:

- A quantitative method to explore antibiotic price trends for the period 2020 to 2024 for a basket of the top 10 antibiotics (chosen by sales value in 2024)² for each country, costs and economic indicators exploring the relationships between them.
- A qualitative method with a scoping review of literature on policies and issues related to pricing mechanisms and shortages and interviews with local professionals for four selected countries (Italy, Portugal, Sweden and United Kingdom).

The integrated evidence provided both numerical insights and contextual understanding of policy dynamics.

² IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024 extracted 31st May 2025. Counting units is the smallest unit of measure defined by IQVIA for a product form. It represents the number of individual tablets, millilitres of liquid, grams of ointment, and so on for each product purchased. Similar product or pack dosage forms can be compared, and the effect of different pack sizes eliminated.

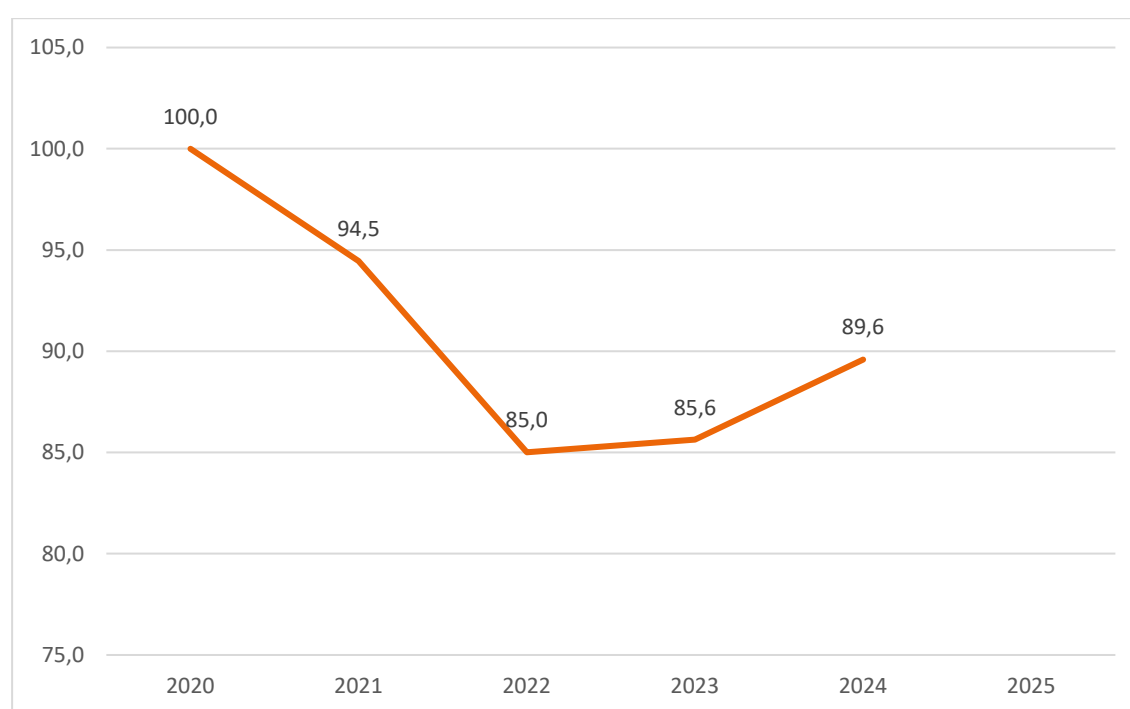
II. MAIN FINDINGS

1. Price evolution for off-patent antibiotics and their availability

We have analysed the price evolution of a basket composed of the top 10 antibiotic INNs for each country, selected based on the ex-factory retail revenue as of 2024. Thirty INNs were considered in total³.

Our analysis shows that **for the top 10 most used INNs** in these 16 countries, **prices in 2024 are lower than they were in 2020, by 10,4%.**

Figure 2: Top 10 INN for each country - price index



Source: IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. 2020 index=100. New Angle analysis.

On average, prices decreased by 15% from 2020 to 2022, followed by an increase from 2022 to 2024 as certain measures began to be implemented in some countries. Overall, **the net decline in prices was 10,4%**. Extremely low prices have raised concerns about the economic viability and availability of certain molecules. Amoxicillin, Amoxicillin with Clavulanic Acid, and

³ Amoxicillin, Amoxicillin Clavulanic Acid, Azithromycin, Aztreonam, Cefaclor, Cefadroxil, Cefalexin, Cefditoren Pivoxil, Cefixime, Cefpodoxime Proxetil, Cefprozil, Ceftriaxone, Cefuroxime Axetil, Ciprofloxacin, Clarithromycin, Clindamycin, Colistin, Dicloxacillin, Doxycycline, Erythromycin, Flucloxacillin, Levofloxacin, Lyme cycline, Moxifloxacin, Penicillin V, Pivmecillinam, Sulfamethoxazole Trimethoprim, Sultamicillin, Tobramycin, Trimethoprim.

Azithromycin, which together accounted for 52% of total sales revenue in 2024, experienced price drops of 18,9%, 5,9%, and 7,9%, respectively. Dicloxacillin, Trimethoprim (only commercialized in Norway), and the combination of Sulfamethoxazole and Trimethoprim (only commercialized in Poland), had the largest price increases, but represented only 0,3% of total sales revenue. Overall, price increases were observed in medicines accounting for 19,6% of total sales revenue, while price decreases affected medicines representing 80,4% of total sales revenue.

Table 2: Price index evolution for the top 10 INNs (All countries), 2020-2024

INN	INDEX					TREND
	2020	2021	2022	2023	2024	
DICLOXACILLIN	100,00	110,54	112,79	126,89	173,91	
TRIMETHOPRIM	100,00	102,66	111,92	129,72	149,14	
SULFAMETHOXAZOLE/TRIMETHOPRIM	100,00	81,23	83,63	116,20	141,33	
ERYTHROMYCIN	100,00	110,01	100,10	105,25	118,38	
CEFACLOR	100,00	111,41	94,05	88,89	115,83	
PIVMECILLINAM	100,00	99,96	93,80	99,13	113,84	
CEFUROXIME AXETIL	100,00	114,75	97,30	85,35	109,52	
CLARITHROMYCIN	100,00	93,36	87,14	107,01	102,19	
CLINDAMYCIN	100,00	98,07	102,13	105,12	102,18	
CEFDITOREN PIVOXIL	100,00	100,47	99,85	100,33	101,65	
CEFPROZIL	100,00	91,61	98,72	93,93	101,53	
CEFPODOXIME PROXETIL	100,00	86,50	89,50	75,55	99,83	
CIPROFLOXACIN	100,00	98,68	98,95	100,63	99,35	
PENICILLIN V	100,00	94,92	68,51	92,48	98,97	
LEVOFLOXACIN	100,00	96,83	99,08	101,39	98,43	
SULTAMICILLIN	100,00	96,77	88,14	88,94	98,28	
TOBRAMYCIN	100,00	95,41	91,18	98,63	97,71	
AZTREONAM	100,00	99,89	100,03	99,09	97,16	
MOXIFLOXACIN	100,00	96,82	95,83	95,80	95,55	
AMOXICILLIN/CLAVULANIC ACID	100,00	97,48	90,46	90,54	94,11	
CEFTRIAZONE	100,00	100,76	99,70	96,06	93,52	
CEFADROXIL	100,00	71,77	63,73	50,53	93,39	
COLISTIN	100,00	100,62	106,92	99,19	92,38	
AZITHROMYCIN	100,00	93,34	93,77	92,03	92,11	
CEFALEXIN	100,00	94,93	79,60	91,26	90,66	
FLUCLOXACILLIN	100,00	88,97	77,74	92,35	85,98	
DOXYCYCLINE	100,00	86,08	70,42	73,10	85,95	
CEFIXIME	100,00	90,57	86,08	77,18	85,59	
AMOXICILLIN	100,00	90,60	82,54	84,83	81,11	
LYMECYCLINE	100,00	111,31	89,45	84,15	78,53	

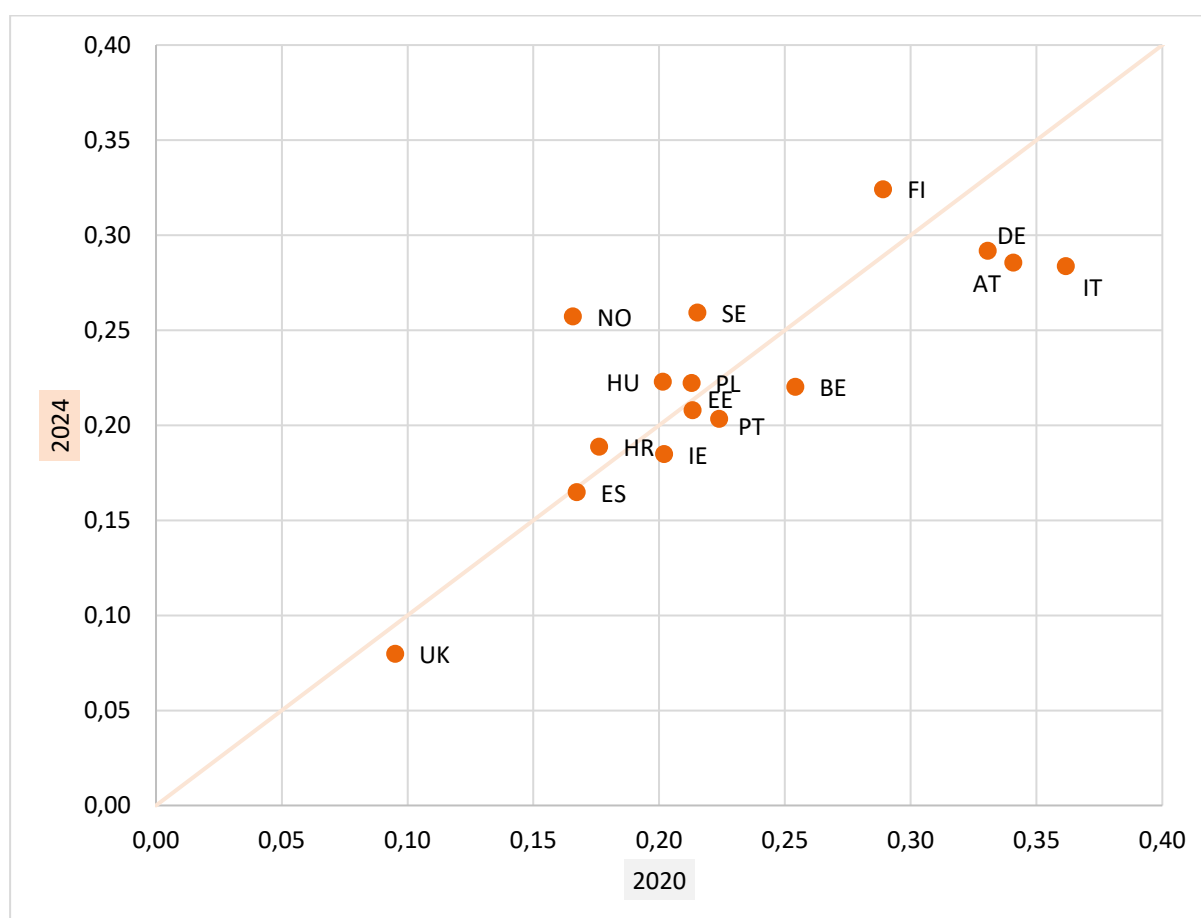
Source: IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. New Angle analysis.

In general, most countries had price decreases to their top 10 INNs in the period from 2020 to 2024.

Although some countries had price increases over the period, notably Norway, Sweden and Finland, most of them had price decreases, the highest being Switzerland and Italy, with -26,5% and -21,6% respectively. Most countries had price decreases from 2020 to 2022-2023, with some increases thereafter, as countries started to implement some initiatives to minimize the unsustainable prices.

The graph below shows the countries for which prices have increased and those for which prices have decreased in the period from 2020 to 2024. All countries below the 45° line, have had price decreases for their top 10 INN during the period. Switzerland is an outlier as prices have dropped 26,5% in the period (not shown in the graph due to scale), the highest change in the countries analysed.

Figure 3: Price changes per country, 2020-2024



Source: IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. Price per counting unit. New Angle analysis.

In the last four years, several products have been withdrawn from the market, including molecules that belong to the Union list of critical medicines[7]. In some countries for some molecules, the number of suppliers and products in the market is very low, creating a greater risk of shortages and access to medicines. In total, 240 products for the top 10 INN in the 16 countries were withdrawn from the market. Only 7 INN out of 20 didn't have any product withdrawal in the period, highlighting the potential vulnerabilities in the market.

Table 3: Medicines withdrawals from 2020-2024

INN	# OF PRODUCTS	PRODUCT WITHDRAWALS	% WITHDRAWALS	# OF SHORTAGES	CRITICAL MEDICINE
AMOXICILLIN	125	27	21,6%	29	YES
AMOXICILLIN&CLAVULANIC ACID	185	46	24,9%	60	YES
AZITHROMYCIN	182	31	17,0%	32	YES
AZTREONAM	2	0	0,0%	1	YES
CEFACTOR	8	0	0,0%	6	
CEFADROXIL	1	0	0,0%	2	
CEFALEXIN	19	4	21,1%	2	
CEFDITOREN PIVOXIL	4	0	0,0%		
CEFIXIME	19	3	15,8%	6	YES
CEFPODOXIME PROXETIL	20	1	5,0%	5	
CEFPROZIL	1	0	0,0%		
CEFTRIAZONE	42	6	14,3%	16	YES
CEFUROXIME AXETIL	60	16	26,7%	4	YES
CIPROFLOXACIN	137	24	17,5%	50	YES
CLARITHROMYCIN	124	28	22,6%	48	YES

INN	# OF PRODUCTS	PRODUCT WITHDRAWALS	% WITHDRAWALS	# OF SHORTAGES	CRITICAL MEDICINE
CLINDAMYCIN	53	4	7,5%	11	YES
COLISTIN	22	0	0,0%	1	
DICLOXACILLIN	4	2	50,0%		
DOXYCYCLINE	39	7	17,9%	21	YES
ERYTHROMYCIN	14	4	28,6%		YES
FLUCLOXACILLIN	23	6	26,1%	7	YES
LEVOFLOXACIN	90	11	12,2%	27	YES
LYMECYCLINE	14	1	7,1%	3	
MOXIFLOXACIN	5	1	20,0%	19	
PENICILLIN V	35	4	11,4%	14	YES
PIVMECILLINAM	12	2	16,7%		
SULFAMETHOXAZOLE& TRIMETHOPRIM	14	7	50,0%	5	
SULTAMICILLIN	10	2	20,0%		
TOBRAMYCIN	23	3	13,0%	16	YES
TRIMETHOPRIM	2	0	0,0%		YES
TOTAL	1.289	240	18,6%	385	

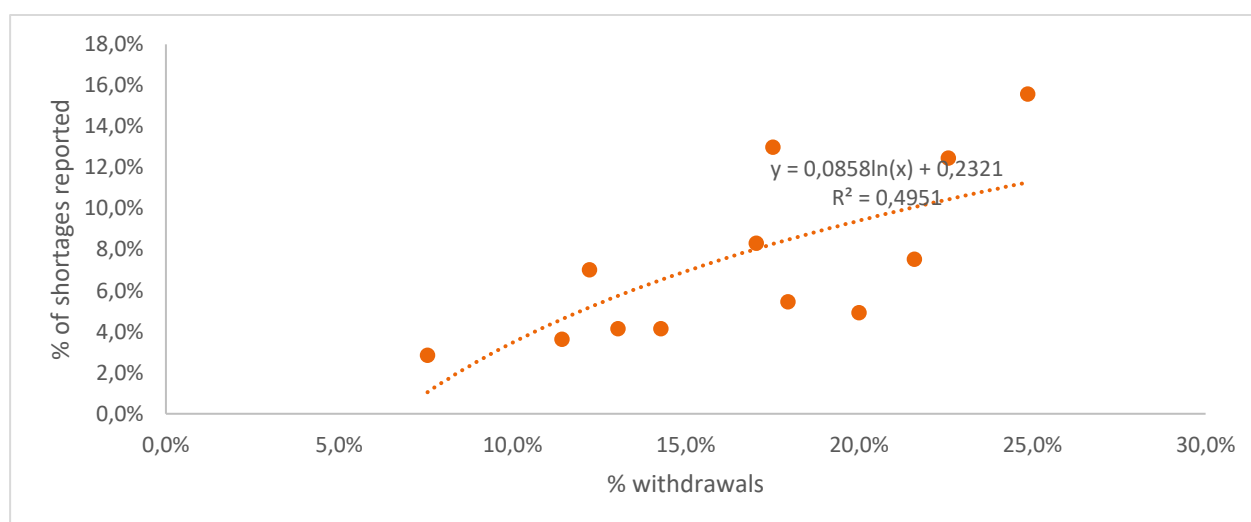
Source: IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. Shortages were obtained from the national medicines' agencies in each country during the period from 23rd June to 7th July and they reflect shortages at a point in time. Information not available for Estonia. New Angle analysis.

A significant proportion of INNs (~77%) had shortages reported between 23rd June and 7 July 2025. Shortages were usually higher for molecules with withdrawals. About 74% of the shortages are in INNs that had more than 15% of their products withdrawn from the market.

That is the case for Amoxicillin, Amoxicillin and Clavulanic Acid, Azithromycin, Ciprofloxacin and Clarithromycin, which each had more than 25 shortages on those days.

The following graph highlights that INNs with a higher percentage of withdrawals have a positive trend with greatest percentage of shortages reported (for all shortages that represent more than 2% of the shortages).

Figure 4: Shortages vs withdrawals



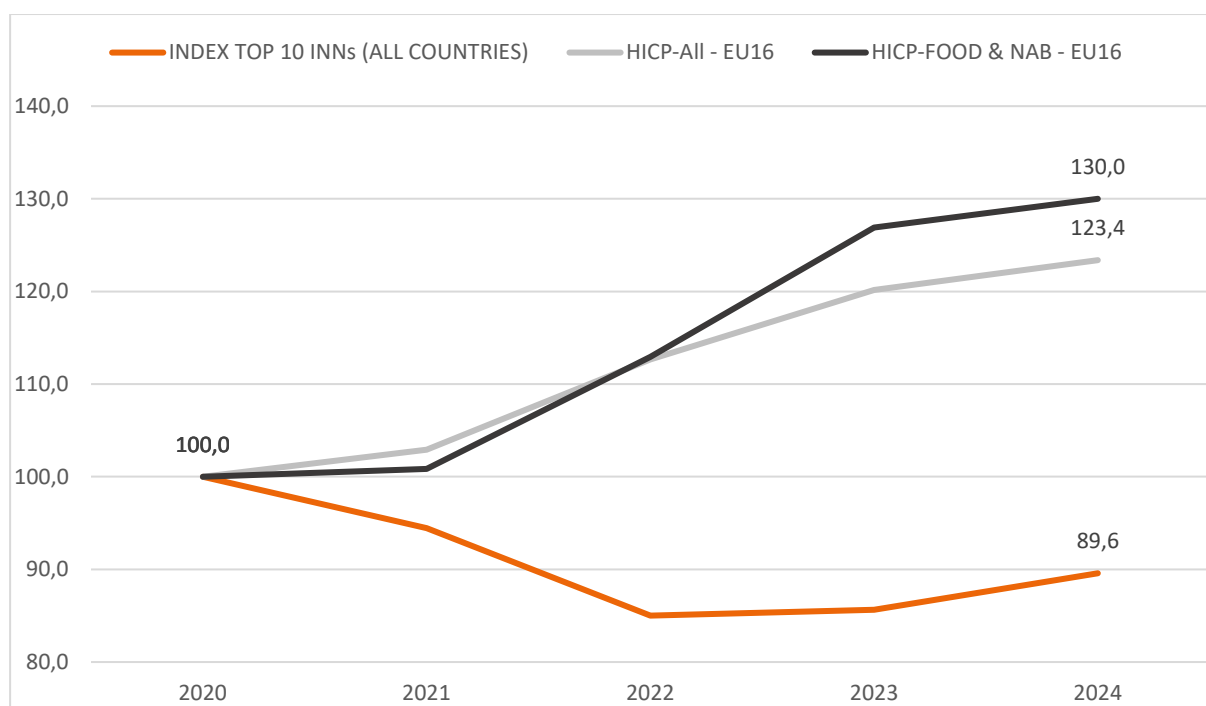
Source: IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. Shortages were obtained from the national medicines' agencies in each country during the period from 23rd June to 7th July and they reflect shortages at a point in time. Information not available for Estonia. New Angle analysis.

2. Compared analysis with Cost of Goods (COGs) and economic indicators

While off-patent medicines prices have decreased from 2020 to 2024, most of the cost of goods used in production and inflation have gone up substantially, generating a gap that risks viability and availability. In several countries, policies have been drafted to solve some of the problems that are surging due to low off-patent antibiotics prices, as we will discuss further in this study.

From 2020 to 2024 inflation grew by 30% and 23,4% for food and non-alcoholic beverages and general inflation, respectively, while off-patent antibiotic prices for the top 10 INNs, decreased by 10,4%.

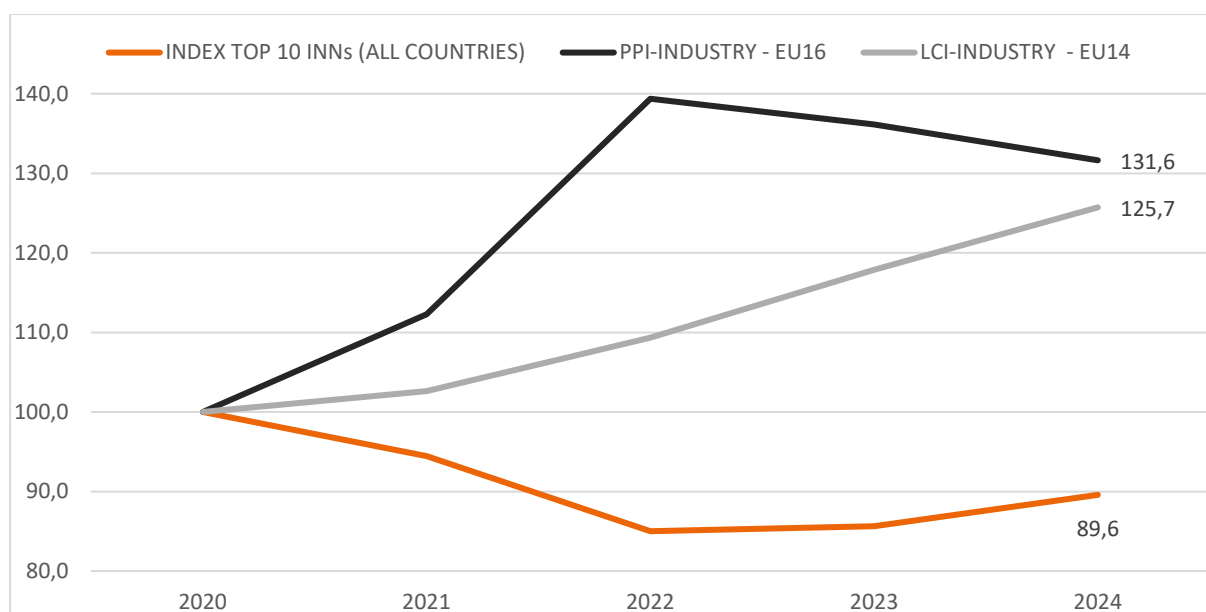
Figure 5: INN average price index with HICP and HICP – Food and NAB indexes comparison



Source: (1) IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. (2) Eurostat and Office for National Statistics (UK). 2020 index=100. New Angle Analysis.

COGs with impact on medicine production costs have also increased substantially to a level that risks creating vulnerabilities in the supply chain, as companies find ways to optimize costs to be able to maintain their products in the market. As information about companies' production costs is not available, we have used the production price index for industry as a proxy, which increased 31,6% in the period. Labor costs, which are significant production costs for medicines, increased 25,7%, while prices dropped 10,4%, creating a significant pressure for off-patent antibiotics included in the basket.

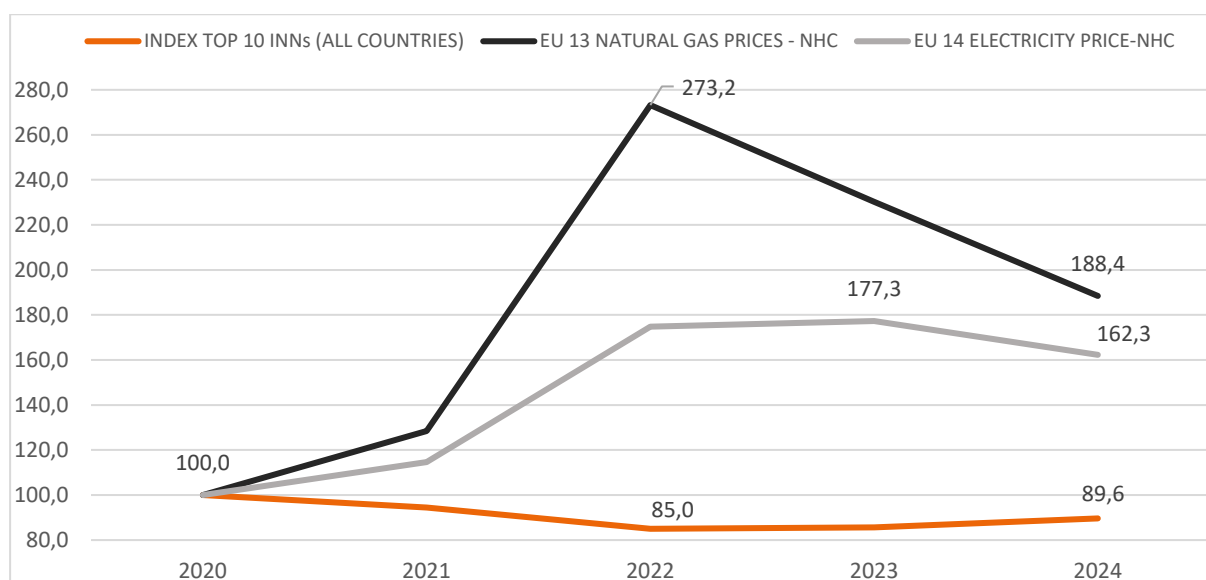
Figure 6: INN average price index with PPI industry and LCI industry indexes comparison



Source: (1) IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May, 2025. (2) Eurostat and Office for National Statistics from each country (for industry PPI). 2020 index=100. Labor costs not available for Switzerland and Sweden. New Angle analysis.

Energy prices, electricity and gas, had huge increases during the period 2020 to 2024, mainly gas in 2022, which increased by 173,2%. Although prices have since stabilized somewhat, the increase in 2024 was still 88,4% and 62,3% for natural gas and electricity respectively.

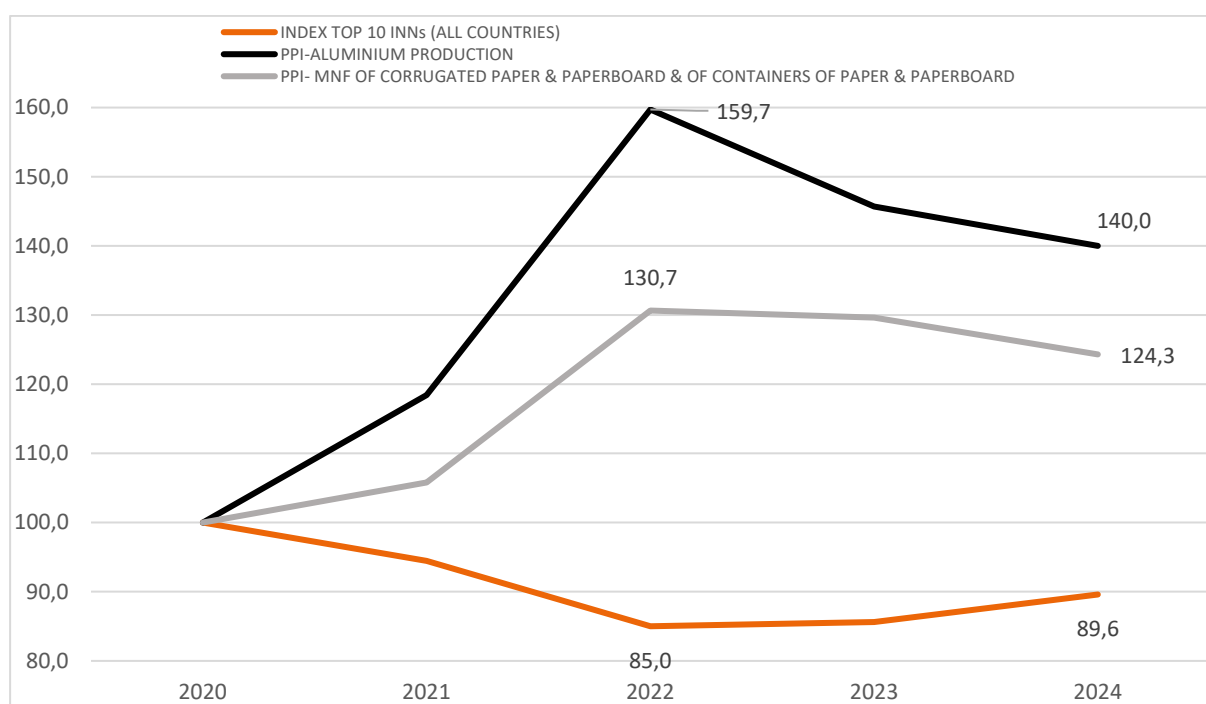
Figure 7: INN average price index with Electricity and Natural Gas prices for non-household consumers



Source: (1) IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. (2) Eurostat. Natural gas prices for non-household consumers not available for Norway, Switzerland and United Kingdom. Electricity prices for non-household consumers not available for Switzerland and United Kingdom. 2020 index=100. Analysis prepared by New Angle.

The following graph highlights the increase in prices for aluminium production and for corrugated paper and paperboard, which are also part of the costs to produce medicines. PPI for aluminium reached 159,7 index value in 2022 falling to 140 in 2024, representing a 40% increase from 2020. PPI for corrugated paper and paperboard, also increased by 24,7% by 2024.

Figure 8: INN average price index with PPI aluminium production and PPI of corrugated paper and paperboard



Source: (1) IQVIA Midas Data, Ex-Factory Price in EUR (LEU MNF) & Counting Units, FY 2020-2024, extracted on 31st May 2025. (2) Eurostat. PPI aluminium production and PPI-MNF of corrugated paper & paperboard & containers of paper & paperboard are presented for EU 27. 2020 index=100. New Angle analysis.

The significant increase in input costs has pressured the margins of medicines, particularly of off-patent medicines as they are already operating on the low margin side, to make them affordable and competitive to treat many diseases.

In the following chapter we will highlight some of the problems and issues felt in some of the countries, along with some interventions that have been tested or implemented with the aim of improving off-patent antibiotics sustainability.

III. MAIN POLICIES PRESSURING OFF-PATENT MEDICINES PRICES

In several parts of Europe, countries regulate medicine prices, except for the UK and Denmark which apply free pricing. Germany and the Netherlands adopt a mixed approach, combining elements of free pricing with measures such as tendering, mandatory discounts, preferential policies, and reference pricing. **Pricing mechanisms and budget controls** such as clawbacks, paybacks, rebates, and statutory price cuts are widely used across Europe to contain pharmaceutical expenditure.

External reference pricing (ERP) involves comparing medicine prices across countries to establish a benchmark for setting or negotiating prices domestically. **Internal reference pricing (IRP)**⁴ is widely used in Europe to regulate the off-patent medicines market by setting a financing threshold usually applied for groups of interchangeable medicines. In most countries, IRP targets reimbursable medicines totally or partially funded by national health systems or insurers[8,9].

External Reference Pricing (ERP) and Internal Reference Pricing (IRP) are central to European pharmaceutical pricing. ERP can amplify price erosion when one low-price country drags down the reference basket. Current expert consensus views ERP as unsuitable for off-patent medicines markets as the market is already open to competition. IRP, often linked to mandatory discounts upon generic entry, rapidly compresses margins. IRP tends to have greater impact in the short term, but latter flatten price not promoting ongoing competitive pricing. For off-patent medicines, **these policies often drive prices to unsustainable low levels**[8,10].

Clawback (or payback or extraordinary contribution) policies require pharmaceutical manufacturers, wholesalers, or pharmacies to refund a fixed percentage of sales or excess revenues when public pharmaceutical spending exceeds predefined thresholds. While intended to contain costs, they **disproportionately impact low-margin off-patent medicines**. Clawbacks compound the effects of reference pricing and mandatory price cuts, driving down net revenues close to or below production cost – especially for injectable or small-volume

⁴ Some countries use the acronym IRP to refer to International Reference Price. In our study we use ERP – External Reference Price.

medicines. Clawbacks jeopardize supply continuity of mature medicines when applied without product-specific exemptions[8].

Clawbacks/paybacks and statutory price cuts in countries such as Spain, Portugal, and Italy impose additional financial burdens[8]. In **Germany**, **statutory rebates** reduce manufacturer prices by up to 12%[11], while **Portugal** levies **extraordinary contributions** exceeding 10% on many medicines[12]. **Spain's 7,5% clawback** across both retail and hospital channels erodes margins for essential antibiotics like paediatric amoxicillin[8,13]. **Evidence links these measures to repeated shortages**, particularly of injectables and paediatric formulations, as manufacturers withdraw from unprofitable markets[8].

In summary, some countries choose to implement payback/clawback policies aiming to recover financial resources from medicines, while other countries do not implement such mechanism on all medicines.

- **Countries with industry-level payback/clawback** mechanisms, such as Belgium, Hungary, Italy, Poland, Portugal and Spain, lead to reduced profitability and increased exit risk from the market[9].
- **Countries without payback/clawbacks or where these are product-level and include only innovative medicines and/or some off-patent medicines**, such as, Austria, Croatia, Estonia, Finland, Germany, Ireland, Norway, Switzerland, Sweden and UK (for patent medicines and branded generics), provide a less punitive environment—although low prices remain a challenge[9].

Price freezes (also known as a price moratorium) refers to regulatory restrictions that prevent manufacturers from raising the list or reimbursement price of certain medicines for a defined period. This policy is commonly applied to older, off-patent medicines not subject to regular internal reference pricing. The freeze maintains prices at historical levels, often without periodic adjustment for inflation or cost increases – effectively locking them in. **Off-patent antibiotics**, as other off-patent medicines, already subject to aggressive cost-containment measures, are often too low-priced to absorb inflation or manufacturing cost increases under a price freeze, contributing to profit margins shrink, discouraging manufacturers from maintaining supply[8].

OHE, EU, and academic studies consistently link drug shortages—particularly off-patent antibiotics—to cumulative pricing pressures from rebates, freezes, and blanket cuts. In the past, multiple EU countries report decreasing supplier diversity – with around one-third of generic antibiotic molecules having disappeared in a 10-year period[14]. In our study, **we found that almost 20% of antibiotics had been withdrawn from the market from 2021 to 2024** in the 16 countries analysed, **many of them belonging to the Union list of critical medicines**.

Tendering is among the most widely applied procurement tools for medicines, mostly for hospitals, often focused on achieving lowest-cost supply. **Single-winner tenders**, common in Italy and Sweden, reduce supplier diversity and heighten risks of disruption when the winning supplier cannot maintain production. Short contract cycles discourage investment in manufacturing resilience, while race-to-the-bottom pricing leaves little incentive for continued supply. **Multi-winner or value-based tenders**, less common but present in Norway, Belgium or Germany, demonstrate more balanced outcomes, promoting redundancy and supplier diversity. Nevertheless, overall tendering practices across Europe have concentrated supply chains and increased vulnerabilities in essential off-patent medicines markets[2,8,15].

Environmental, social, governance (ESG) compliance, logistics, and regulatory requirements significantly raise production costs for medicines, especially low-margin off-patent medicines. **Rising energy, freight, and material prices**, along with supply chain disruptions, increase input costs that companies cannot easily pass on[16]. Environmental measures, such as Extended Producer Responsibility and EU regulations like Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), add substantial direct and indirect costs, with compliance sometimes consuming up to 10% of chemical firms' capital budgets, escalating production costs[17]. For MAH, these burdens can push up to a quarter of product lines below break-even[18]. According to the *Critical Medicines Alliance strategic report*, the full cost of producing generics in Europe can be 2,5–5 times higher than in India or China; margins are eroded heavily by supply-chain and regulatory burdens. Off-patent products are typically low-volume and face **downward reimbursement pressure** (ERP/IRP) in Europe, making it **difficult to absorb rising upstream costs**[19].

The **cumulative effect** pricing and tendering policies (e.g., IRP/ERP, mandatory rebates, clawbacks) leads to:

- **Margin squeeze:** Some off-patent medicines, particularly low volume ones, become commercially unattractive.
- **Disincentivized production:** Manufacturers may divert capacity to more profitable markets or products (e.g., oncology).
- **Market exits:** Either due to unsustainable retail prices or withdrawals from tenders due to unsustainable pricing.
- **Supply disruptions:** Over-reliance on a **single winner** can backfire if that supplier faces API shortages, manufacturing quality issues, or recalls.

Together, pricing policies and tendering rules create downward spirals that disincentivize manufacturers from maintaining critical off-patent medicines in the market.

1. Country case studies

We present a few case studies from some European countries that have taken or are designing some initiatives to improve access to off-patent medicines, with some specific cases for antibiotics.

Belgium Case

Aggressive austerity-driven price cuts combined with ERP, IRP and tendering in hospital procurement have led to supplier exits and shortages.

In 2024, Belgium launched an unprecedented initiative inviting companies to request price increases for at-risk antibiotics. As of October 2025, around 105 antibiotic packs will see price increases⁵.

Belgium played a central role in establishing the Critical Medicines Alliance in April 2024 during its Presidency of the EU Council, advocating reforms that prioritize resilience over lowest-cost criteria. The Alliance brings together policymakers, industry, healthcare stakeholders, and EU Member States to identify supply chain bottlenecks and recommend sustainable solutions to medicine shortages, including those caused by tendering mechanisms. The EU Critical Medicines Act aims to improve procurement frameworks to enhance supply

⁵ As per negotiations at country level.

security beyond lowest-price tendering, ensuring decisions prioritize long-term supply security, environmental sustainability and geographic diversification with a preference for EU suppliers, over price alone.[19–21].

Complementing proposed measures, Belgium’s FAMHP operates the PharmaStatus platform, an official tool for monitoring medicine shortages and stock levels, which supports early detection and proactive management of supply disruptions[22].

Belgium’s new government (2025) has unveiled a wide-ranging health reform agenda including pharmaceutical measures aimed at securing medicine supply and accelerating innovation. The Roadmap Medicines initiative focuses on modernizing reimbursement and procurement procedures to improve efficiency and access, indirectly supporting sustainable supply[23].

Germany Case

Germany applies IRP extensively, grouping off-patent antibiotics into reimbursement clusters and enforcing low ceilings, applying also mandatory manufacturer discounts (e.g., 7% rebate) which further compress margins. Tendering and rebate contracts favour the lowest-price suppliers in the drug market, leading to a limited number of suppliers. These policies have led to **supply shortages**, especially for off-patent antibiotics such as amoxicillin, penicillin V, mainly for paediatric formulations[11,24].

The **Act to Combat Drug Shortages and Improve Supply** (ALBVVG) enacted in July 2023, introduced exemptions for critical antibiotics and paediatric medicines and mandated multi-winner tenders prioritizing EU-based manufacturers[11,25]. In 2025, Germany removed ERP from negotiations on new medicines and allowed confidential discounts, mitigating spillover effects from low-priced countries.

Germany’s evolving approach highlights the shift from pure cost-containment to balancing affordability with supply security.

Italy Case

Italy’s procurement system relies heavily on CONSIP tenders, often single-winner and lowest-price. Recent years have seen a decline in the number of offers submitted, an increase in unfilled tender lots, and failures to fulfil awarded contracts, especially for off-patent medicines. This has led to supplier concentration, market exits, and irregular supply, contributing to

medicine shortages and regional disparities in access. Regional tender pressure has contributed to irregular supply and regional disparities in access to off-patent medicines. The number of unavailable drugs more than doubled between 2018 and 2024, partly due to tendering-driven supplier exits and production challenges[26–28].

Reform efforts include improved tendering procedures, with better splitting of lots, multi supplier award for off-patent biologics, regional pilots to address disparities caused by central procurement, and active monitoring by AIFA and AGCM. Italy also supports the EU Critical Medicines Act to prioritize supply chain resilience[29,30].

Italy is subject to several price regulations, including reference pricing, paybacks and clawbacks. Italy applies a Reference Price (“prezzo di riferimento”) and Transparency List, grouping medicines with the same active ingredient, formulation, dosage, and pack size. For reimbursed Class A off-patent medicines, including most community antibiotics, the National Health Service (SSN) reimburses only up to the lowest-priced option, with patients paying the difference for higher-priced brands, creating strong downward price pressure[31,32].

A 2025 law introduced incentives for innovative antibiotics under patent or data protection that are listed as WHO reserve or priority antibiotics. These benefit from[33,34]:

- A dedicated fund of up to €100 million per year.
- Exemption from the payback mechanism, expected to increase annual revenues by around 15%.

Although not focused on off-patent antibiotics, it opens discussions for key critical off-patent medicines. Off-patent antibiotics and critical medicines remain vulnerable under Italy’s rigid reference pricing and procurement rules, unless specific incentives are introduced.

Portugal Case

Portugal applies several cost containment policies such as ERP, IRP, clawbacks and paybacks, creating a harsh environment for off-patent medicines[9]. In response to rising pharmaceutical expenditures, Portugal adopted a series of cost-containment measures to ensure both fiscal sustainability and continued access to essential medicines. During Troika intervention, an extraordinary contribution (a type of clawback) was implemented, which

further increased the pressure on prices and margins, specially for low cost off-patent medicines[12].

Infarmed has also responded with operational measures such as mandatory stock requirements and export bans during shortages, but these do not address the underlying financial disincentives as they increase costs and complexity for MAH[35,36].

Portugal has more recently introduced limitation in annual price revisions (a discretionary measure for the year), allowing low-price medicines (below €16) to align with inflation and limiting annual ERP-driven cuts, providing some relief[37]. Nevertheless, structural sustainability challenges remain for off-patent medicines subject to multiple overlapping controls.

Spain Case

Since the financial crisis of 2010–2012, **Spain has implemented a series of cost-containment measures in response to rising public pharmaceutical expenditures**. Among these, **IRP has led to very low prices** that in many cases don't allow to recover from increasing costs. In Spain more than 50% of generics volume is sold below the reference price threshold (established at € 1,6). These measures were part of broader austerity reforms and were codified through successive Royal Decrees, such as RD 4/2010, RD 8/2010, and RD 9/2011, which mandated price reductions and tightened reimbursement systems for a wide range of pharmaceutical products—namely off-patent medicines[13,38–42].

Spain's IRP's aggressive price cuts and fixed discounts have undermined antibiotic supply, particularly paediatric amoxicillin. Mandatory rebates and internal reference pricing pressure compressed margins further to levels that prompted repeated shortages and supplier exits.

Spain is advancing pharmaceutical pricing reforms to support sustainability and innovation. In 2023, paediatric antibiotics received an exceptional 40% price increase. In July 2024, a legal amendment introduced recognition of Incremental Innovation (Value-Added Medicines), allowing exceptions to reference pricing and price increases for products that demonstrate added patient value, new combinations or indications, as well as for strategic medicines and paediatric formulations[43,44].

Sweden Case

Sweden faced significant challenges with access to critical antibiotics, that resulted not only from a small market but also from pricing policies for off-patent medicines such as antibiotics, which contributed to shortages. These challenges stemmed from the financial disincentives created by such mechanisms, where pharmaceutical companies had to return revenues or faced reduced income due to price cuts and clawbacks, making it economically unsustainable to keep older, off-patent medicines on the market[4,45].

Sweden has piloted one of the most innovative reimbursement models to address antibiotic shortages: revenue guarantees for critical products, **still with patents but that weren't entering** the Swedish market and has also planned similar measures for off-patent critical antibiotics[45,46]. For on patent antibiotics, by guaranteeing SEK 4 million per product annually, Sweden ensured suppliers-maintained availability despite low volumes[46]. Swedish government is considering expanding this “subscription-style” model to include more off-patent antibiotics, with stockpiling requirements and rapid delivery commitments, guaranteeing SEK 400 thousand per product annually, to be kept in the market[45].

UK Case

The UK's recurring shortages of mature off-patent medicines arise from structural weaknesses—very low margins, rigid low-cost procurement, concentrated globalised supply, and limited incentives for building resilience. These vulnerabilities mean demand surges or production disruptions can rapidly trigger shortages, for which some recent measures are being proposed[47]. While the UK recognises free market principles and uses price concessions to raise reimbursement temporarily during shortages, this reactive approach cannot secure long-term stability. The NHS introduces price concessions to temporarily increase reimbursement during shortages, but this reactive mechanism cannot ensure long-term stability[48–50].

More positively, the UK pioneered the “Netflix model” subscription payment for two antibiotics, paying fixed annual fees regardless of sales. While targeted at novel agents, this model demonstrates recognition of the flaws in volume-linked pricing and has inspired similar pilots abroad[51,52].

Nordic Collaboration

The Nordic collaboration is a joint initiative among Denmark, Finland, Iceland, Norway, and Sweden designed to secure sustainable access and supply of essential antibiotics, particularly older, off-patent and narrow-spectrum ones. These countries face shared challenges: small and fragmented markets, low consumption levels, and limited profitability for manufacturers, which makes many critical antibiotics at risk of withdrawal. In response, Nordic policymakers launched coordinated studies and pilots to identify solutions, recognizing that EU-level efforts often focus more on innovation than on maintaining access to existing medicines[2,53].

A key element has been the development of a policy roadmap. Based on research by Uppsala University, six priority measures were identified: enhanced shortage monitoring, harmonized packaging and electronic leaflets, mutual recognition of market approvals, better purchasing practices, revenue-guaranteed reimbursement models, and mapping of regional production capacity[53].

Harmonizing essential medicine lists and aligning approved dosage forms reduces fragmentation and increases predictability for manufacturers. These efforts are complemented by innovative reimbursement models with income guarantees, making it financially viable for suppliers to maintain or re-enter the market despite low sales volumes. Regulatory efficiency is addressed through mutual recognition of approvals, minimizing administrative duplication and speeding access to medicines across countries. Strategic stockpiling and coordinated antimicrobial stewardship and resistance surveillance further reinforce supply security and rational use[53].

Sweden, as previously highlighted, piloted a partial de-linked reimbursement system from 2020–2022, guaranteeing minimum revenue and buffer stock incentives for certain antibiotics, which was later expanded to include low-volume off-patent medicines such as paediatric and TB treatments[45,46].

With political commitment and shared resources, the Nordic countries are creating a model of collective action to safeguard the availability of essential antibiotics in small and vulnerable markets.

IV. POLICIES RECOMMENDATIONS

The main findings section demonstrates several examples where tight, eroded prices lead to fragility in the market for off-patent medicines, namely antibiotics. EU policy now treats a subset of medicines – including many antibiotics – as “critical,” with a Union list, a European Medicines Agency Coordination Mandate, and a new Critical Medicines Alliance to craft structural fixes that include market-shaping and procurement/pricing approaches[54].

In crafting the policies recommendations, we have considered some policy goals that can be achieved, summarized as:

- a. Ensure minimum viable economics model for reliable and stable supply of off-patent medicines.
- b. Preserve competition (≥ 3 suppliers per INN) and supply diversity rather than price races to the bottom.
- c. Stay budget-sustainable, to maintain the sustainability of health budgets, while guaranteeing access to patients. And,
- d. Align with stewardship (e.g., no incentives to overuse antibiotics). For the case of antibiotics, it should be noted that the policy options must be in alignment with the EU Council AMR Recommendation (2023)[55] that imposes a target of reducing antibiotic consumption by 20% by 2030.

Policy options to secure off-patent medicines focus on four areas: (1) **pricing systems** to keep medicines viable, (2) **administrative and regulatory simplification** to reduce burdens and avoid unnecessary withdrawals, (3) **supply chain resilience** through mapping, stockpiling, and stronger manufacturing and international partnerships, and (4) **strategic purchasing** with multi-supplier tenders, joint procurement, and revenue-guaranteeing contracts.

It is possible to reconcile the goal of cost efficiency for health systems with the need for suppliers to sustain the availability of off-patent medicines at accessible prices. Most of the off-patent medicines have seen their prices pushed to low levels, ongoing efforts to monitor and control further price reductions may no longer be necessary, nor relevant. Instead, a more forward-looking model that reflects the importance of ensuring long-term access to these

medicines may be more appropriate[56]. Prolonged periods of low financial returns have led many antibiotic manufacturers to exit the market, leaving behind a limited number of suppliers who lack motivation to enhance the production and availability of older, off-patent medicines.

Pricing Interventions

Key pricing interventions that are viable and deserve discussion on the above mentioned four goals can be (not limited to):

a. Minimum price and automatic indexation to input-cost proxies

Automatic indexation approach allows for **periodic, formula-based price adjustments** for a defined list of off-patent critical medicines tied to objective indices (e.g., inflation, API/producer price indices, energy, wages). With this approach, it is possible to prevent real-price erosion that triggers market exits and to reduce need for emergency hikes. Some policy design elements can include annual/biannual caps that apply only to the Critical Medicines subset to protect national budgets. An approach may be starting with annual adjustments using a transparent basket (e.g., EU industrial energy index, API PPI proxy, wage index), with caps/floors and no retroactivity. **Defining minimum prices at sustainable price levels can also be considered**[57].

b. Tiered pricing linked to market structure

A tiered pricing approach offers a dynamic mechanism for safeguarding supply sustainability. This model establishes reference **price bands that adjust according to the level of market competition**, expanding when supplier numbers fall below a critical threshold (e.g., fewer than three active suppliers), and contracting as competition intensifies. While traditionally employed to exert downward price pressure, tiered pricing can serve as a pragmatic alternative to rigid price caps, particularly in markets vulnerable to supplier exit[8,57].

c. Exemption (or attenuation) of ERP/IRP for critical off-patent medicines

ERP is often regarded as ill-suited to off-patent markets and can distort competition. **Removing or softening ERP linkages (e.g., wider corridors, excluding outliers, adopting longer update cycles) could be an effective tool to reduce cross-country downward spirals.**

Establishing clear criteria to designate certain medicines as “critical,” based on factors such as unmet clinical needs, vulnerability to shortages, and importance for public health would be a critical first step. Collaborative assessments involving EMA, national authorities, and expert panels to maintain and update the list of critical off-patent medicines could be employed.

d. **Volume-delinked reimbursement approach and revenue guarantees**

Revenue guarantees can provide a predictable baseline revenue to sustain supply of clinically essential, low-volume/low-margin medicines while preserving stewardship (no volume-linked bonuses). As described in detail in section 3A, Sweden has piloted the revenue guarantee model for a select set of antibiotics and is now working to expand the tested model to include some selected off-patent antibiotics. Volume de-linked revenue guarantees as a policy option have been in the agenda of Nordic Collaboration[53] along with being under consideration by the EC, as proposal on EU-coordinated subscription payment mechanisms encouraging wide member state participation, for both new and existing antimicrobials. Pilot implementations can be designed for very small volume of existing off-patent medicines, with guaranteed annual revenue.

e. **Targeted, time-limited price uplifts for shortage mitigation**

A temporary, narrowly scoped reimbursement/ex-factory price increase when there is a risk of shortage due to too few suppliers. These increases should remain in place until healthy market competition is restored, at which point prices will self-regulate through competitive dynamics. The uplift can be in the form of a **capped percentage uplift**, such as “up to X% above last regulated price for the affected INN/presentation during the activation window” as in Germany case or a **cost indexed reopener**. Eligibility can be limited to off-patent medicines **on the EU Union List of Critical Medicines** (or a national subset of it) and to specific **presentations** (e.g., paediatric suspensions, IV injectables) with recurrent vulnerability. Periodic uplift reviews based on market recovery and supply stabilization indicators can be made[2]. A **hard sunset** (e.g., max 12 months) and an **automatic rollback** to baseline pricing once security of supply returns to normal can be introduced. It should be noted that production planning timelines are long, and even extraordinary incentives should give companies mid-term predictability.

f. De-linkage from originator's price for generics

In many countries, generic medicine prices are tied to the originator's price by a set percentage, which can trigger a “race to the bottom” and make some medicines unviable. Two alternatives could be: (1) a partial de-linkage, where the originator's price is fixed once as a reference; or (2) a competition maturity de-linkage, where the link remains until sufficient market competition is established[8,57]. The discount over the reference price should consider the complexity of the generics entering the market, its production costs and its importance for public health.

g. Limit paybacks, clawbacks and extraordinary price measures for off-patent medicines

A policy could be implemented where off-patent medicines in general, or below a certain price and/or belonging to a critical medicines list, could be exempt from any type of payback, clawback or other cost cutting related measures, as Italy has recently approved and the UK does for generic medicines.

Administrative and Regulatory Burdens

Administrative and regulatory burdens become especially significant when the market volumes are low, which is the case in several European countries.

a. Removing disproportionate financial disincentives to marketing off-patent medicines

Lowering barriers to market entry and re-entry could help restore and sustain off-patent supply. Current practices – such as imposing penalties for shortages and fees for re-registration, add financial risk and discourage manufacturers from participating. To improve market resilience, policy adjustments could include:

- proportional penalty frameworks.
- removal of re-filing fees, reducing or waiving annual maintenance fees and adapting sunset clause requirements, as Norway has been implementing and Sweden is preparing to implement, for key off-patent antibiotics.
- expedited approval for new manufacturers (especially those with diverse API sources).

b. Informed decision making for the impact of environmental regulations

Regulatory transitions should be guided by thorough impact assessments that consider market segments, price sensitivity, and public health, ensuring that rules do not impose disproportionate costs on low-priced essential off-patent medicines. Proportionate or exception-based fees can help prevent product withdrawals, while continuous stakeholder dialogue between industry, environmental experts, and health authorities is key to developing balanced standards. A risk-based approach, focusing first on substances or processes with the highest environmental impact, can ease financial pressure and support a smoother transition.

c. Easier Transition for Environmental Liabilities

Manufacturers are required to comply with a set of environmental regulations, which has financial impact on the manufacturer. Some measures could help limit the negative financial impact on the companies:

- **Flexible Regulatory Timelines and Transitional Support**, through phased approaches or transitional periods for compliance implement with new environmental requirements. This reduces immediate cost shock and gives companies time to adapt production processes or reformulate products without abrupt market exits.
- **Subsidies or Financial Incentives for Green Transition**: Offering targeted subsidies, tax breaks, or grants specifically for switching to eco-friendlier substances or cleaner production technologies.
- **Procurement reforms**: Rewarding companies for investments in reducing their impact on the environment, proving a level playing field with companies that are competing on cost bases only.

d. Introduction of Core Pack Size

Different countries have different package size requirements often driven by national treatment guidelines, reimbursement rules and other clinical rules, such as antimicrobial stewardship policies. This results in a fragmented market where pharma companies must manufacture and stock multiple pack sizes for the same product across countries. Some initiative towards harmonization of the packaging could be:

- **Enabling core pack size**, facilitating it through creating a core pack-size table cross-referenced to national guidelines.
- **Fee-light variations** for MAHs adding those core pack sizes to off-patent medicines (esp. those on the Union list of critical medicines) could be defined.

Procurement Related Interventions

Strategic procurement frameworks, by considering other factors but price, can play a pivotal role in incentivising manufacturers to sustain supply and invest in buffer production capacity. By adjusting contract conditions, governments can actively shape supply chain behaviour and promote long-term resilience. Some procurement-related policy approaches can include:

a. Replacing single winner modality with a multi-winner award modality

A widely recognised strategy for fostering sustainable competition in the off-patent medicines market is the allocation of tender contracts to **multiple suppliers**, with each successful tenderer securing a sufficiently large market share to ensure financial viability and supply continuity. This approach mitigates the risk of supply disruptions by avoiding overreliance on a single provider across individual or aggregated markets[56]. It also enables a more equitable distribution of market share, thereby incentivising broader supplier participation and enhancing long-term market stability. To further reinforce supply resilience, a more advanced measure involves the **diversification of active pharmaceutical ingredient (API) sources**. By reducing dependence on any single manufacturer, this strategy provides a critical safeguard against upstream supply chain vulnerabilities, including geopolitical disruptions, quality failures, or production bottlenecks.

b. Better forecasting for tender volume

Incorporating realistic volume forecasts into tender specifications—accompanied by minimum purchase guarantees and a lead time of at least six months between contract award and initial delivery, can significantly enhance supplier responsiveness. These measures reduce uncertainty and financial exposure for manufacturers, enabling more accurate production planning and risk mitigation. As a result, suppliers are better positioned to submit more competitive and sustainable bids, thereby strengthening the overall resilience and efficiency of the procurement process[58].

c. Contract lengths

Contract lengths play a key role in management of the risk and financials. A contract duration of 24–48 months with annual re-openers (mini-competition confined to incumbents/new entrants) would serve to keep the competitive tension while making sure the supply is not destabilized[59].

d. Changing the award criteria (shifting to MEAT)

Awarding tenders solely on price can erode profit margins, prompting manufacturers to exit the off-patent market and increasing the risk of supply disruptions and de facto monopolies. To safeguard long-term value and supply resilience, procurement models should adopt broader evaluation criteria. The **Most Economically Advantageous Tender (MEAT)** framework allows for consideration of qualitative, technical, and sustainability factors, such as recommending two distinct API sources in registration dossiers and incorporating security-of-supply into bid assessments. This shift supports more competitive, stable, and strategically aligned procurement outcomes.

e. Rejection of “abnormally low” offers

Applying Article 69 logic from 2014/24/EU which implies that contracting authorities must request explanations from bidders if a tender appears abnormally low in relation to the works, supplies, or services; if an offer implies non-compliance (e.g., unrealistic cost base), it should be rejected. This could prevent low bids that damage the market and public in the medium-long run more than the profit from the lowest price.

f. Indexation for pricing clauses

Automatic indexation approach that was mentioned in pricing section can be reflected on procurement processes where input-cost proxies could be used for indexation. To prevent supply exits when costs spike, indexation to objective indicators (e.g., inflation, electricity/natural gas indices; API/solvent benchmarks) and reopener triggers (such as changes in input basket; regulatory fees) could be used as effective tools.

V. CONCLUSIONS

This study has highlighted that the **viability** of off-patent antibiotics, as a case study for off-patent medicines, **is critical but many times undervalued** putting them under a significant strain in Europe. Historical price reductions, while delivering important savings to health systems, have progressively eroded the economic viability of many critical molecules. Our analysis shows that between 2020 and 2024, **prices for the most widely used off-patent antibiotics in 16 countries fell on average by more than 10%, while production costs, labour costs, and energy prices rose substantially**. This divergence between declining prices and increasing costs has placed off-patent antibiotics that already have a thin margin, at the brink of commercial unsustainability. The result has been widespread market withdrawals, recurrent shortages, and a dangerous reliance on a small number of suppliers. The results observed for antibiotics, are believed to be similar for other off-patent medicines, because the unsustainability root causes are the same.

The policy mechanisms traditionally employed in Europe, such as external and internal reference pricing, tendering, and clawback/payback schemes—have achieved Governments' cost-containment objectives but at the expense of long-term supply resilience. Also, these policies might create dependency risks on one or very few suppliers. Evidence across multiple country case studies confirms that these measures, when applied indiscriminately, create perverse incentives for manufacturers, discourage investment in European production, and ultimately threaten patient access. At the same time, broader cost drivers, including regulatory complexity, environmental compliance, and rising logistical expenses, disproportionately affect low-margin off-patent medicines, intensifying their vulnerability.

The European policy debate has increasingly recognised that critical off-patent medicines, particularly antibiotics, cannot be solely subject to cost minimisation. Rather, they constitute strategic public health assets whose availability is essential to preserving the effectiveness of health systems and, in the case of antibiotics, preventing the further spread of antimicrobial resistance. **Innovative policy responses, such as revenue guarantees, volume-delinked reimbursement models, multi-winner tenders, tiered pricing and exemption of critical off-patent medicines from rigid reference pricing**, offer promising avenues to reconcile cost efficiency with supply sustainability. Some countries, notably Sweden and the

United Kingdom, have pioneered revenue guarantees, and their early results underscore the feasibility of balancing financial incentives with stewardship objectives.

Ensuring the long-term sustainability of off-patent medicines requires a shift from short-term cost containment towards a resilience-oriented approach at both national and European levels. This entails integrating pricing reforms, strategic procurement frameworks, and regulatory adaptations into a coherent policy mix that safeguards both affordability and availability. Moreover, the development of EU-wide mechanisms, such as the Critical Medicines Act and coordinated procurement strategies, may provide the necessary legal and institutional framework to align national actions with shared European objectives.

In conclusion, **the sustainability crisis facing off-patent medicines is neither accidental nor inevitable.** It is the outcome of accumulated structural imbalances between policy goals and market realities. **By adopting forward-looking, evidence-based interventions that support viable economics for manufacturers, preserve supplier diversity, and strengthen supply security, Europe can protect access to essential off-patent medicines and ensure that these critical treatments remain available for future generations.** The lessons from this study extend beyond antibiotics and can be applied to other off-patent medicines which are critical for public health in Europe.

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About New Angle

New Angle was founded by specialists across health, finance, automotive, public sector and industry, bringing many years of consulting expertise to highly complex and demanding environments, operating out of Portugal and Angola. Our interdisciplinary team combines deep domain knowledge with strategic insight to deliver creative, integrated, and high-impact solutions. New Angle's Health Unit is a center of excellence in strategy, market access, and research. We support health stakeholders across Portugal, Angola, Central Asia, and other African regions, driving meaningful impact through region-adapted, evidence-based approaches.

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