White Paper

Beneath the Surface: Unravelling the True Value of Generic Medicines

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Executive summary

Today, generic medicines are an integral part of the healthcare system and demand for these products continues to rise. However, while increased usage of generic medicines has led to unprecedented savings for healthcare systems, perspectives often remain focused solely on their cost-saving potential. This can underplay the societal value of generic medicines in Europe and underestimate their contributions, compounding the challenges that healthcare systems are facing today.

This report explores the broad spectrum of contributions from generic medicines to European health systems, through an examination of their savings potential but also their role in supporting financial sustainability, increasing patient access, supply chain resilience, and better outcomes for patients.

Although 70% of all medicines sold in Europe (by volume) are generics, the added societal value of these medicines beyond their cost-saving benefits has not often been discussed. This study aims to quantify generic medicines' past contributions and future role, highlighting implications for all stakeholders in a time of increased demand and constraints on healthcare systems.

While the results show the benefits that a sustainable generic sector can provide to country healthcare systems through savings, it also focuses on areas for improvement. Opportunities to improve patient access remain, new therapeutic options are expected to provide a level of innovation that will improve health outcomes, and as Europe's priorities change, the role in supporting supply chain resilience and continued investments by generic manufacturers show systems cannot be viewed in isolation.

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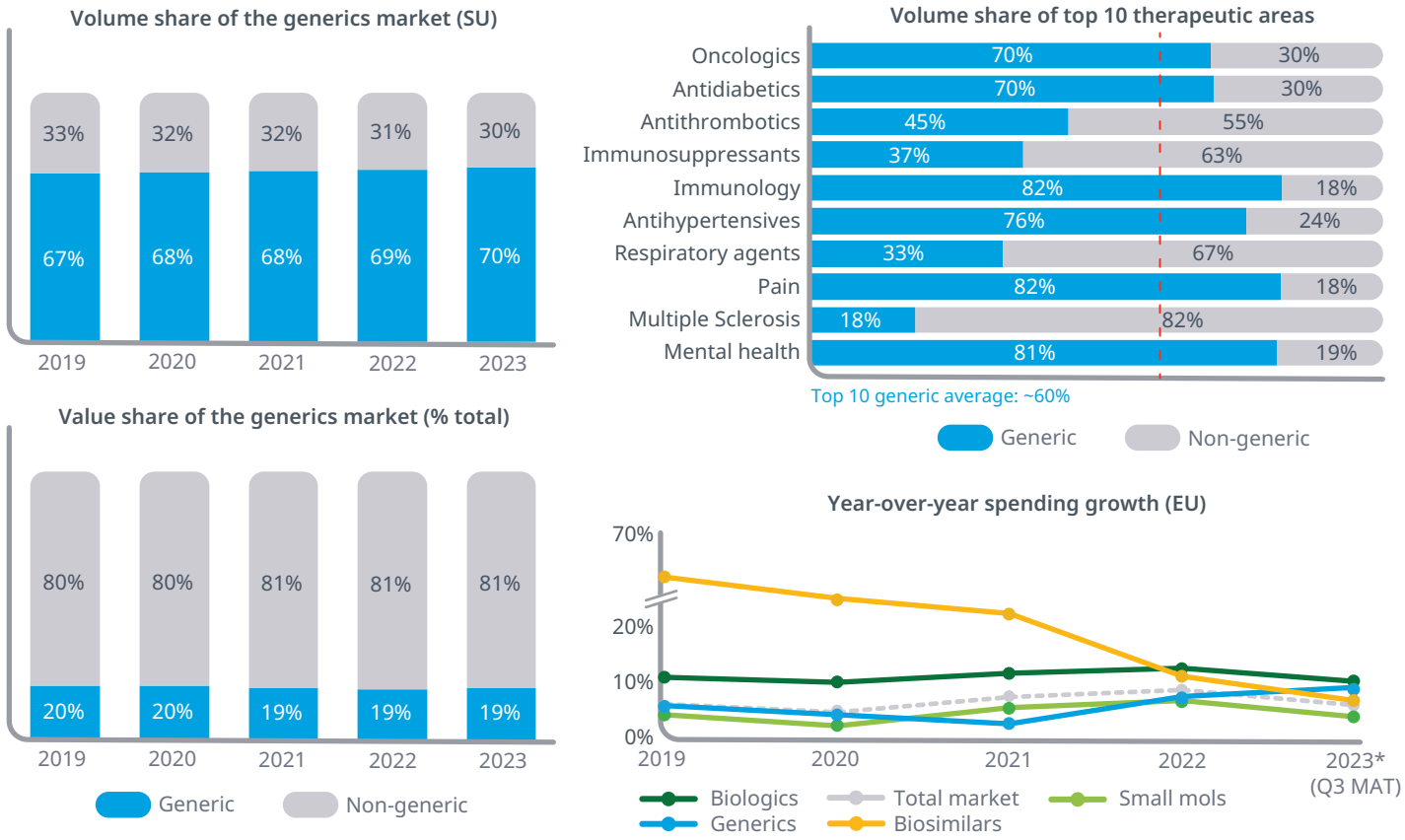
Introduction

Generic medicines represent the majority of treatments in Europe, accounting for 70% of treatment volume and 19% of the market value in 2023 (Exhibit 1). Generic molecules are increasingly available for complex chronic conditions, reflecting the profile of originator molecules losing protection, and represent 60% of the top 10 therapeutic areas in Europe.

At list prices (excluding confidential discounts and rebates), the generic medicine spending growth rate has recovered since dropping to its lowest levels in almost a decade in 2021 (2%), reflecting European markets' policies focused on savings. This recent shift comes after a series of challenging years, and although the market appears to be benefiting from growth in the short-term, the benefits of generic medicines to European healthcare systems longer-term are not a foregone conclusion.

The role of the generic industry has undergone an evolution in the past decades. Since the industry's inception in the 1980s, the US was seen as the most attractive location for generic manufacturers, due to progressive regulatory frameworks and the need for mitigating high brand prices. By contrast, market fragmentation, comparably lower brand prices, complex intellectual property (IP) and regulatory systems limited the European market. Between the 1980s and the early 2000s, slow growth rates combined with limited government incentives shaped the view of these medicines as 'opportunists', eroding the market share of incumbent manufacturers of branded products.[1] As a result, generic market growth in Europe lagged behind the US, creating few opportunities for savings.

Exhibit 1: European generic market overview



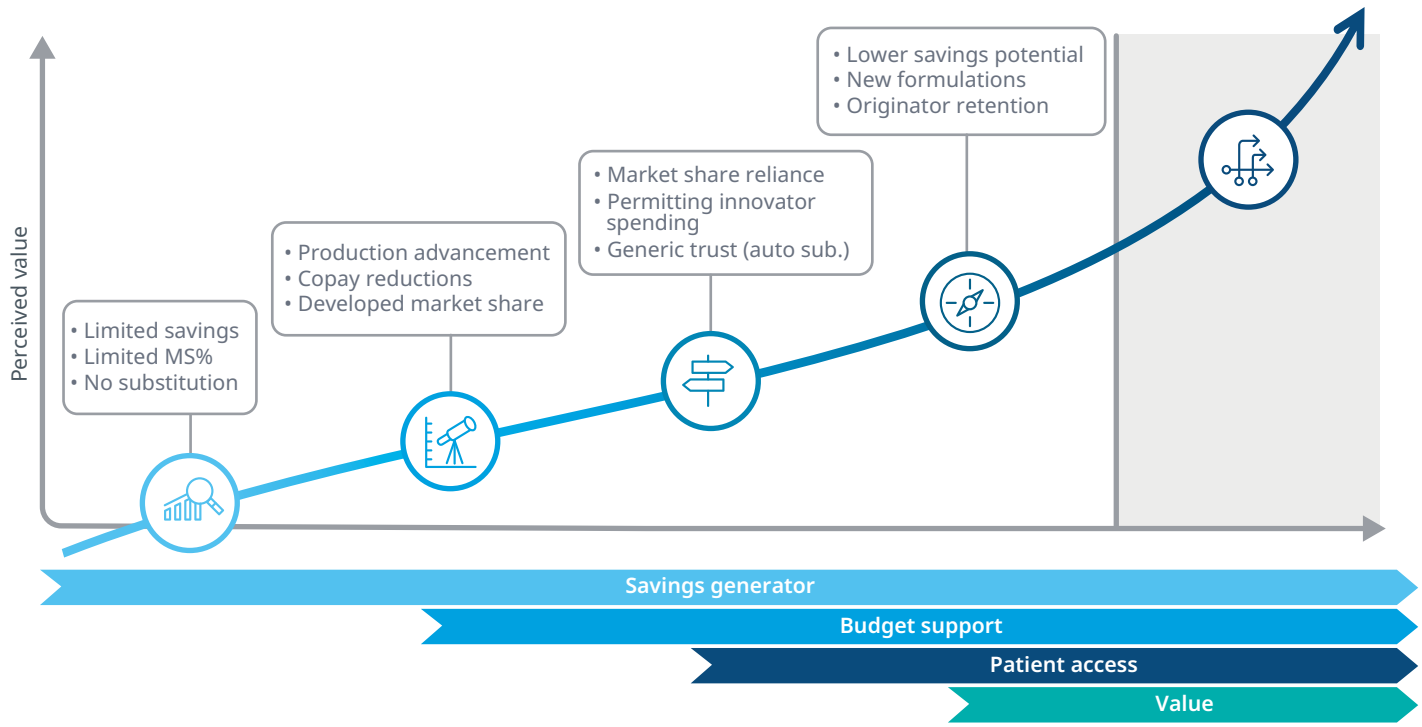
Source: IQVIA MIDAS Q3 MAT 2023. Chart notes: INN insights (excl. vaccines, Inn insights not assigned, hospital solutions, diagnostics and ATC V products). Volume=standard units. Data is in LC€ (inflation adjusted) and includes hospital and retail panels. Rx only; Total biologic growth includes biosimilars. European geographic scope (includes Norway, UK, and Switzerland). Top 10 therapeutic area ordered by value (LCEUR).

IIn the following decade, extensive reforms in EU Member States and the large volume of products facing loss of exclusivity, including several blockbuster products, changed the role of generic medicines. Until 2005, Member States operated different periods of data protection, creating uncertainty for generic manufacturers. Exclusivity rules changed in 2005 when the EU pharmaceutical legislation harmonized regulatory protection for all Member States, paving the way for increased generic penetration in Europe. A report published by the European Commission in 2009 shows that although Member States accrued their benefits differently, between 2000 and 2007 average prices in Europe fell by 20% one year after loss of exclusivity (LoE) and 40% after two years[2], a relatively modest figure compared to recent times (~60%[iii]). Notably, these figures do not account for confidential discounts and rebates, meaning that the actual prices were likely to be even lower. Regardless, before the financial crisis, generic medicines were seen as key sources of cost savings, contributing to significantly higher access for patients.

Following the financial crisis (2007-2009), many European countries introduced new austerity programs that included expanding the use of generic drugs as a way to keep budgets under control. During this time, generic medicines were often viewed as 'commodities' to describe a market with large numbers of buyers and sellers, and with prices approximating the cost of production and distribution. Commoditization, combined with policy reforms in both regulated and unregulated markets, further increased generic usage, and thus savings, in Europe. Estimates suggest that spending on medicines in 2014 was €100 billion less than it would have been if prices had not been lowered with the introduction of generics.[3]

Today, the value of generic medicines continues to be centred on affordability and access. However, while the generic medicine industry has long played a critical role in keeping budgets under control, it is important to recognise that the nature and extent of that role is now evolving (Exhibit 2). As highlighted above, generic medicines are now used to treat the majority of complex chronic diseases and their role in bolstering pharmaceutical supply chain is increasingly recognized by all stakeholders.

Exhibit 2: Evolution of perspectives around generic medicines consumption in Europe

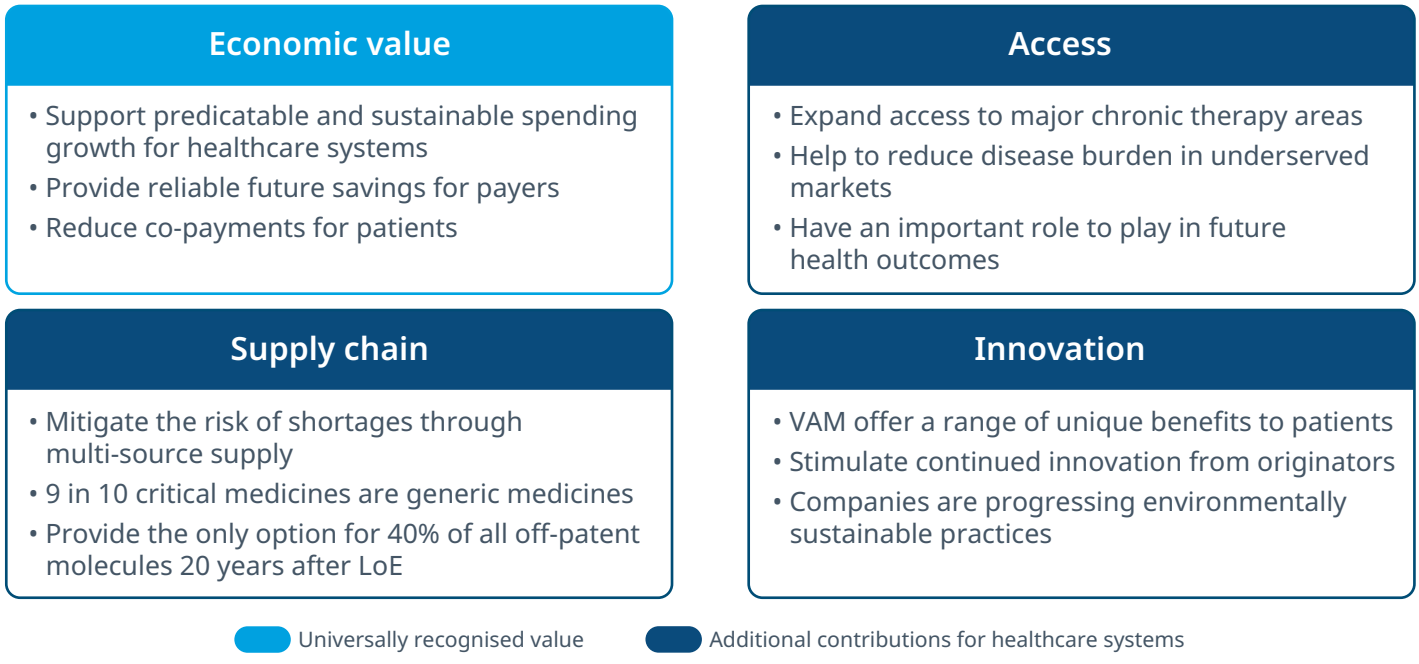


The report assesses the societal value of generic medicines in four novel dimensions, reflecting the changing priorities of European healthcare systems (Exhibit 3):

- **Economic value**: savings post-loss of exclusivity, but also comprising budget optimisation, savings long-term, and the impact of lower prices on medicine access throughout the EU.
- **Patient access value**: treatment of patients in areas which were limited by access restrictions. These areas can now be broadened to a greater patient population and the gains are measured by understanding the impact of genericisation on value, volume, and price on key therapeutic areas over time.
- **Value to the supply chain**: the role of generic medicines in supporting access to critical medicines, and supply chain security, evidenced by the proportion of generic medicines in the EU's critical medicines list and an investigation into the dynamics of shortages and the role that competition plays.
- **Value to innovation**: an important value provided by generic manufacturers represented by advances in delivery systems and production capabilities that can be optimised further by generic manufacturers.

Today, the value of generic medicines continues to be centred on affordability and access. However, while the generic medicine industry has long played a critical role in keeping budgets under control, it is important to recognise that the nature and extent of that role is now evolving.

Exhibit 3: Four value dimensions of generic medicines



Generic medicines support predictable and sustainable pharmaceutical spending

Over the past decades, the availability of generic medicines has contributed to cost containment in overall spending growth. Their availability and the effect of exclusivity losses in Europe have helped to offset the spending increase from branded medicines growth. This section describes the value of a sustainable generic marketplace in providing both short-term and long-term savings to healthcare systems.

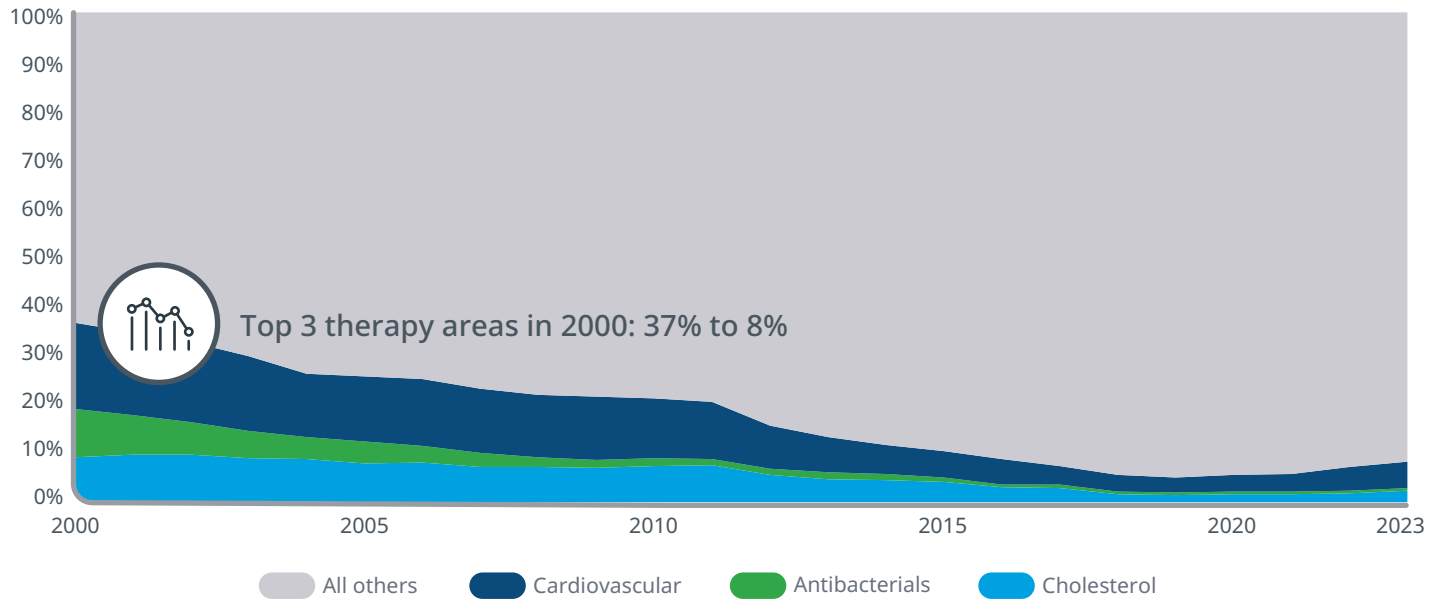
Generic medicines continue to deliver savings long after loss of exclusivity

While the short-term savings are the core component of the value of generics, savings can continue over long durations too if the system is managed sustainably. Since 2000, the expenditure on the largest therapy areas (i.e. cardiovascular, antibacterial, and cholesterol) has decreased from 37% of the total pharmaceutical expenditure to 8% because of the availability of generic treatments (Exhibit 4). The value of a sustainable generic marketplace to healthcare systems is one that permits not only short-term but also long-term savings.

Large opportunities for cost savings can be expected

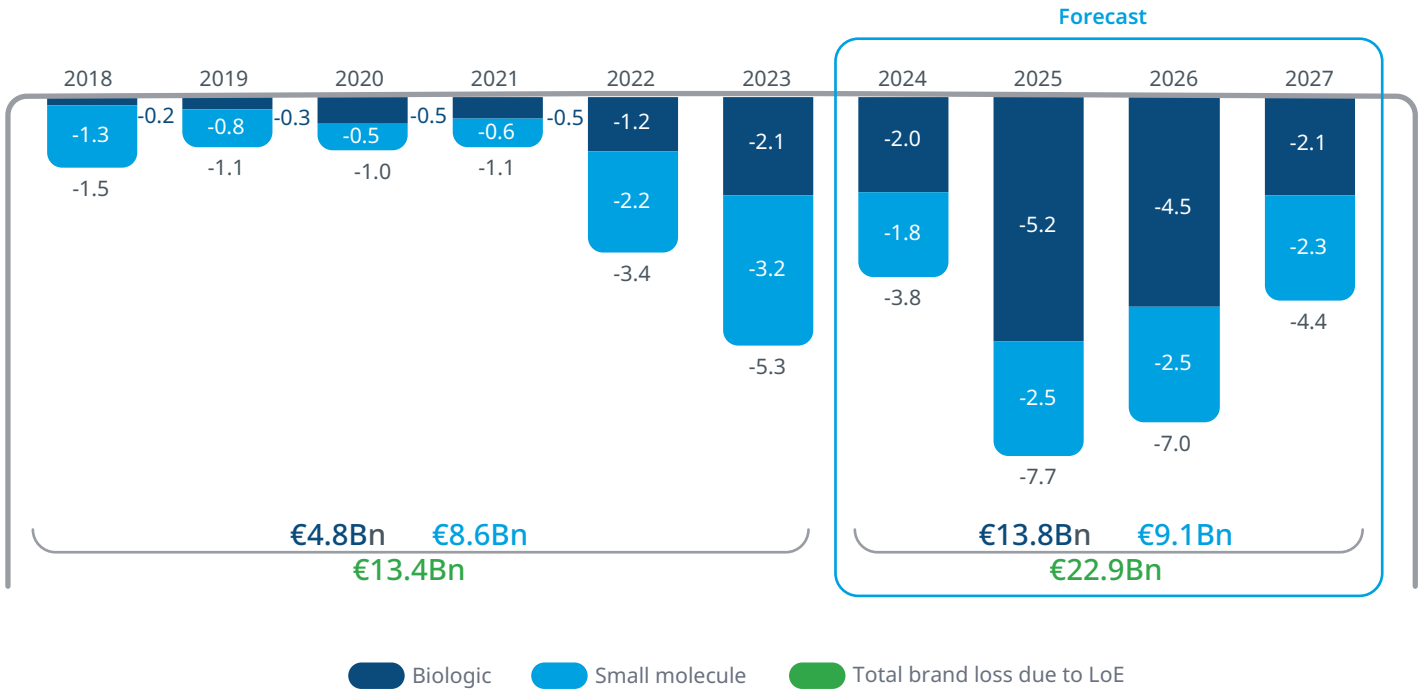
Major European markets have historically been dominated by small molecules, which has supported generic market growth. As the biologic market continues to mature, this figure is expected to fall from ~75% to less than 50% of upcoming losses of exclusivity (LoE) in the foreseeable future. However, the relative size of the small molecules facing LoE by 2027 is forecast at nearly €10bn, offering considerable opportunities for generic entry (Exhibit 5). Compared to biologic medicines,

Exhibit 4: EEA (+CH & UK) comparison of protected brand LC€ spend by medicine class, 2000–2023



Source: IQVIA Institute 25-year dataset (June 2023).
Notes: sales in LCEUR are calculated by applying annual exchange rate (2000–2023) to LCUSD sales data, and hence may be subject to fluctuations in exchange rates; Only includes non-biologic products. Protected brands include original protected brands, original new brands, upcoming LOE, and vaccines; EEA countries included: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden. LC: Local currency. Therapeutic areas are reported at the high class level. Cardiovascular is inclusive of all cardiovascular medicines (ATC1 = C) except antihypertensives and cholesterol therapies (lipid regulators), which have their own high classes.

Exhibit 5: EU4+UK impact of exclusivity losses 2018–2027, €Bn



Source: IQVIA Market Prognosis, Sep 2022; IQVIA Institute, Nov 2022. The Global Use of Medicines 2023: Outlook to 2027. Report by the IQVIA Institute for Human Data Science.
Notes: Sales in LCEUR are calculated by applying annual exchange rate to LCUSD sales data, and hence may be subject to fluctuations in exchange rates.

small molecules are more likely to attract competition, meaning that generic entry will continue to generate substantial savings in the future.[4] In total, the impact of exclusivity losses in EU4+UK markets from biologic medicines and small molecules will reach nearly €23bn by 2027, almost double the impact of the previous 6 years (Exhibit 5)

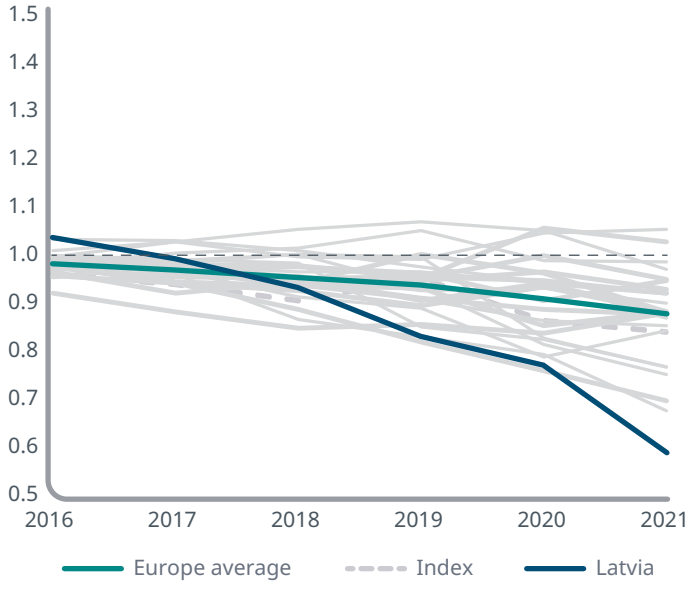
Generic entry contributes to reducing overall co-payments

Countries with high per capita healthcare expenditures often attenuate pharmaceutical costs for patients via co-payments, new reimbursement policies, and deregulation of certain therapies in order to reduce the impact on the healthcare system budget. In Latvia, despite near universal health coverage, publicly covered medicines are subject to co-payments determined by reimbursement levels. In 2016, medicine co-payments stood at 21% of their total cost, and in 2019, 36% of health expenditure in Latvia was paid via out of pocket, which was the second highest level in the EU after Bulgaria, and significantly above the EU average (15%).[5] However, in 2020, the government introduced a set of measures to reduce patients' co-payments for reimbursable medicines which included provisions to increase generic usage via mandatory INN prescribing.

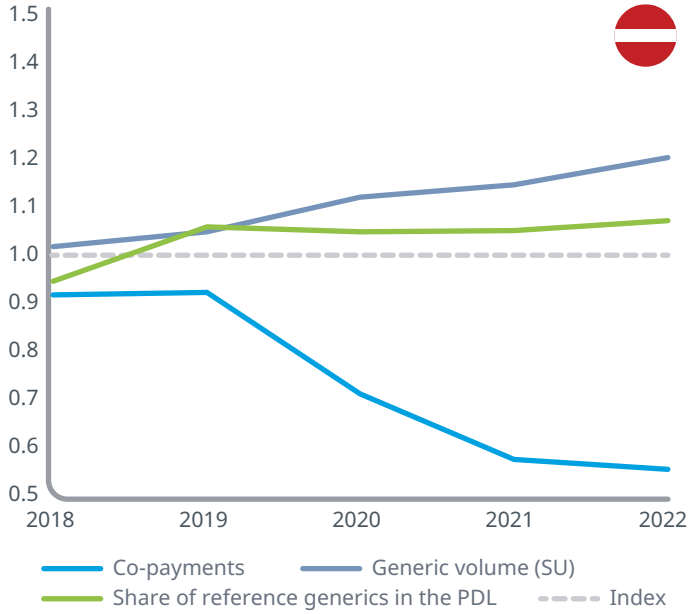
According to the Latvian Ministry of Health, in the 6 months that followed, co-payments generated from reimbursable medicines decreased by 48%, corresponding to an annual estimated per capita impact of around €6.25.[6] More recent data indicates that between 2018 and 2022 medicine co-payments decreased by ~50%, while generic volume increased by 23%. Importantly, the share of generic medicines included in the Positive Drug List (PDL) also increased by ~10% during this time, reflecting increased generic usage and consumption (Exhibit 6).

Exhibit 6: In countries with high co-payments, generic market entry is a driver of value for patients and payers

Share of co-payments in Europe as % of total health expenditure
(Rx only, data indexed to 2017)



Evolution of the Latvian generic market and medicine co-payments
(Rx only, data indexed to 2017)



Source: IQVIA MIDAS standard units (SU) MAT Q3 2023; OECD Statistics (accessed 28th November 2023). Rx only, Hospital and Retail data.
Notes: co-payments data was retrieved from the State Agency of Medicine, Republic of Latvia. The analysis only includes spend on prescription medicines.

Generic medicines are key access catalysts

Generic medicines have significantly contributed to increasing access to treatments in Europe, with considerable clinical benefits for patients. This section explores how generic medicines have been critical to not only increase access to key medication in Europe, but also improve health outcomes in key therapeutic areas.

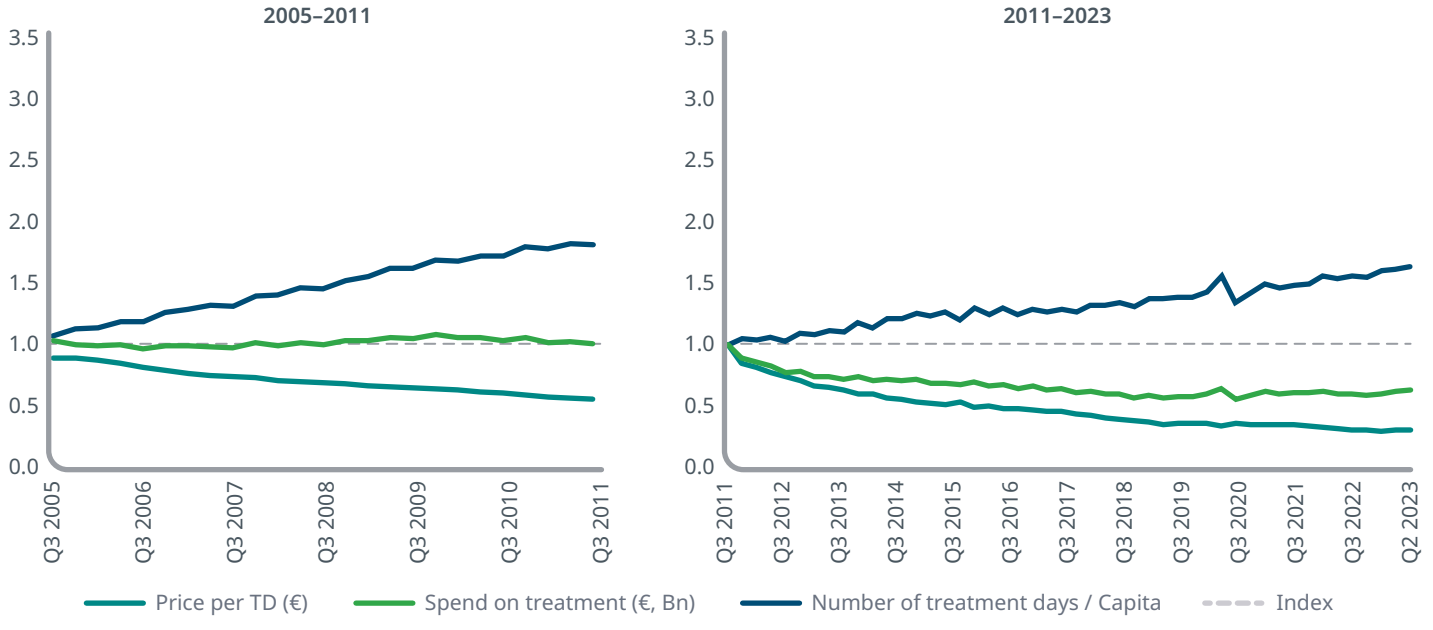
Generic medicines doubled access in chronic disease areas

Most studies published to date measure short-term savings in the years following competition at a molecule level, or the coming years, but rarely view the longer-term benefits from generic competition. This analysis shows the savings provided by generic medicines while ensuring that treatment volumes increase. In the past 20 years alone, the core seven therapy areas in 2000 were subject to the highest generic competition and have continued to provide savings while treatment volume has more than doubled (Exhibit 7).

Access benefits differ based on therapeutic category and market dynamics

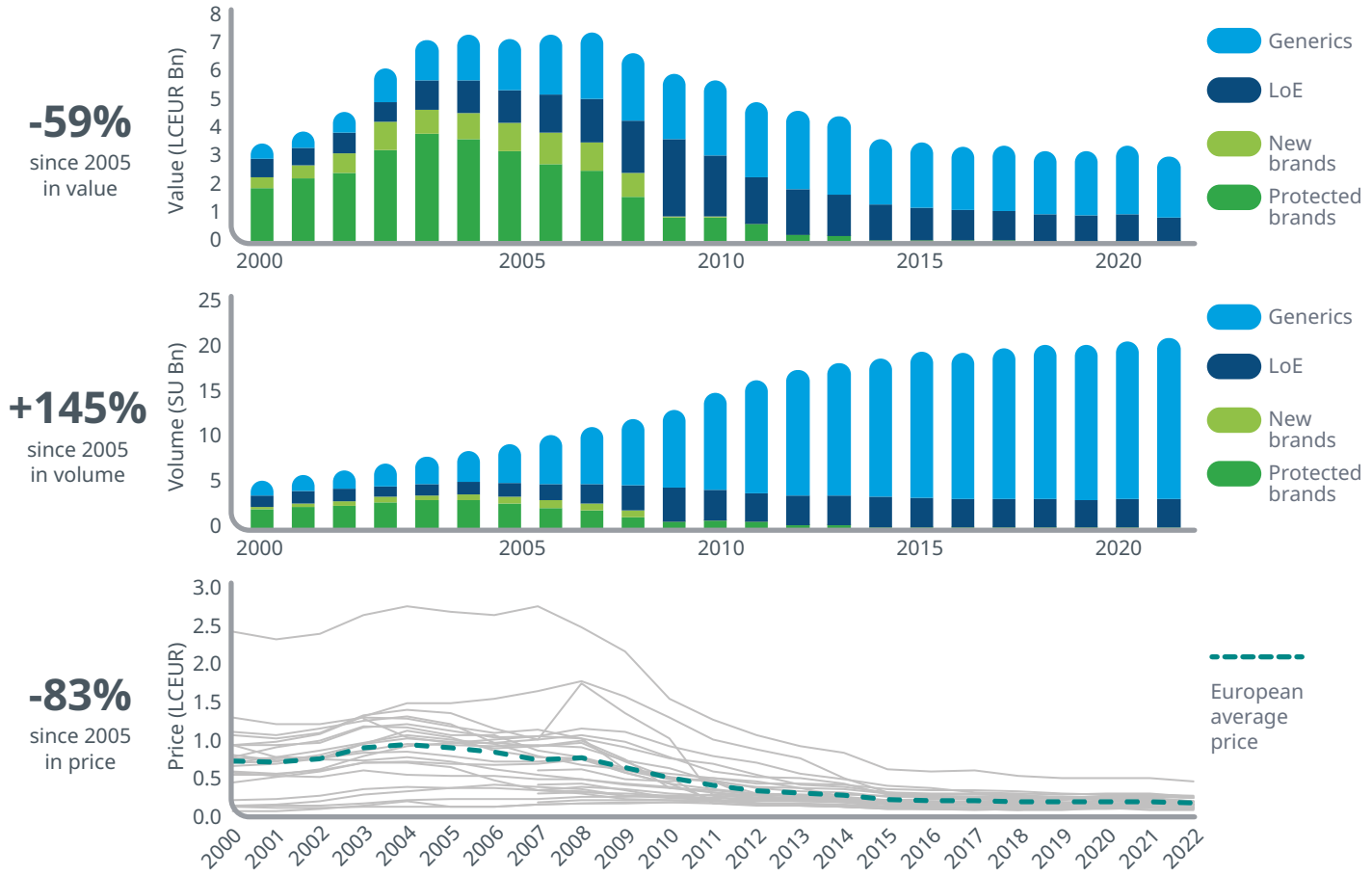
The effects of generic competition can vary considerably from country to country depending on price regulations, competitive barriers, the mix of molecules used, and distribution systems. To gain a detailed understanding of the impact of generic entry on both cost and access in different markets, the analysis of value, volume and prices was extended to all 27 EU + UK markets. This analysis finds that in some therapeutic categories, generic entry has been pivotal in supporting healthcare systems in increasing affordability and access. For example, since 2005 generic medicines have reduced the price of anti-ulcerants by 83%, while supporting a 145% increase in volume (Exhibit 8).

Exhibit 7: Evolution of therapy volume, price of treatment and overall spend on treatment in 7 therapy areas



Source: IQVIA MIDAS QTR Dec 2023; Selected therapy areas: Anti-depressants, anti-epileptics, anti-psychotics, anti-ulcerants, cholesterol regulators, narcotic analgesics and beta-blocking agents. Rx, retail, oral molecules only, combinations excluded; Includes 26 European countries; Normalized to population growth; Population data sourced from the World Bank. Note: Sales in LCEUR are calculated by applying annual exchange rate (2000–2023) to LCUSD sales data, and hence may be subject to fluctuations in exchange rates.

Exhibit 8: Generic anti-ulcerants reduce costs by almost 60%, while doubling access and reducing prices 6-fold

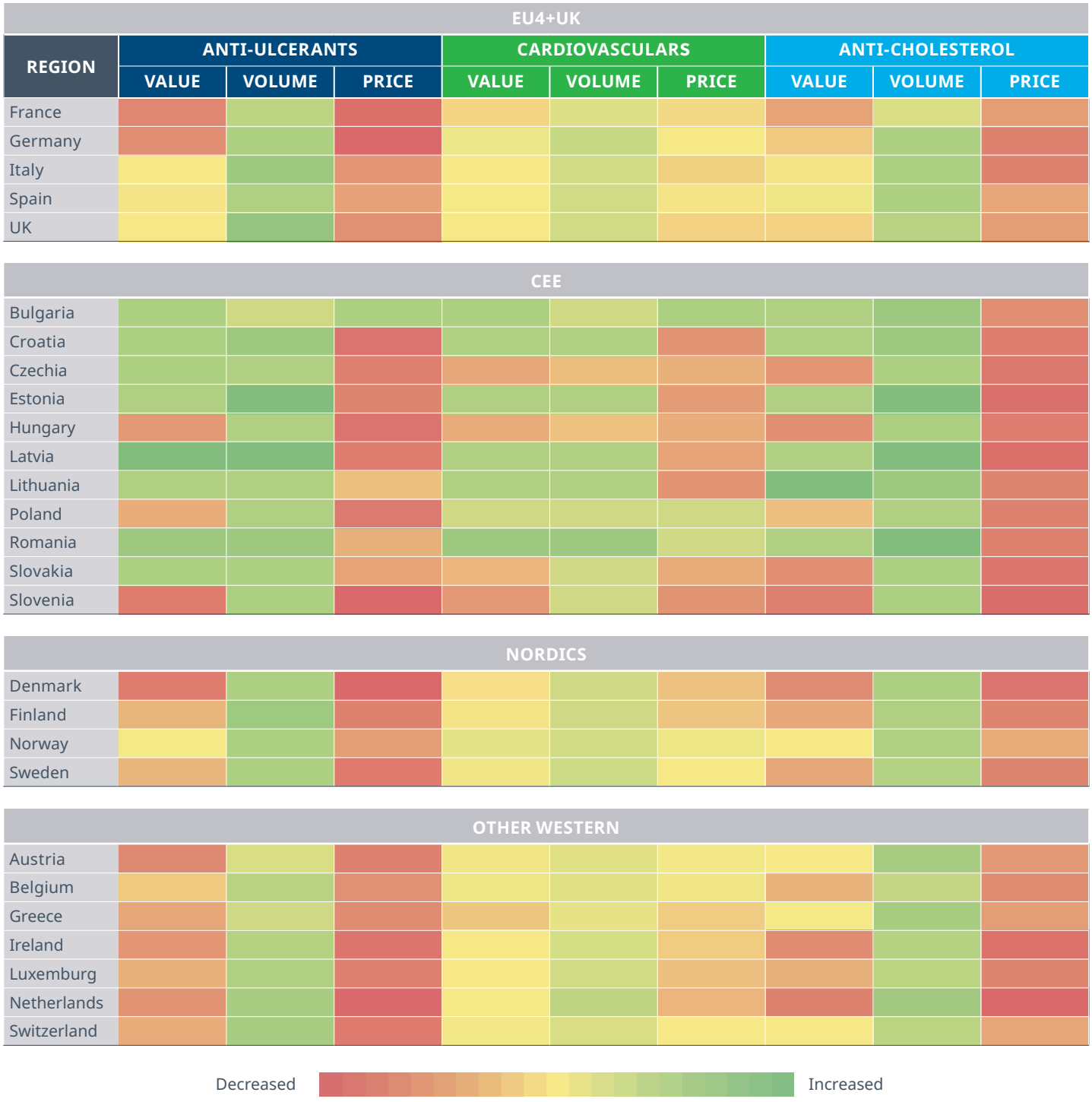


Source: IQVIA MIDAS long-term dataset. Chart notes: Sales in LCEUR are calculated by applying annual exchange rate (2000–2023) to LCUSD sales data, and hence may be subject to fluctuations in exchange rates; Only includes non-biologic products; Protected brands include original protected brands, upcoming LOE and vaccines, New brands include original new brands; LOE include drugs that lost patent protection; Generics include non-original branded products as well as drugs that are marketed using the molecule name. Standard unit (SU) refers to the number of doses of a product sold.

Data for cardiovascular and cholesterol therapies is broadly consistent. Prices of cholesterol therapies declined on average in all countries, yet, there was significant variation with regard to magnitude. Exhibit 9 shows that price decreases vary significantly across countries. Differences in market structures (notably the number of off-patent medicines) and prescribing practices likely explain these cross-country differences. The largest price declines were observed in countries that operate tender-like systems for generic procurement (i.e. Denmark, Sweden and Germany). However, the largest increases in access occurred in countries with only moderate price declines (i.e. Estonia, Lithuania, Romania). This shows that the potential benefits of the generics medicine industry cannot be maximised if the focus is on the lowest price alone. In addition, forced price reductions may impact the economic viability of market players and lead to voluntary withdrawals from the market, which would deepen medicines shortages and reduce access.

Since 2005 generic medicines have reduced the price of anti-ulcerants by 83%, while supporting a 145% increase in volume (Exhibit 8).

Exhibit 9: Country-level analysis of historical changes in value, volume and price



Source: IQVIA MIDAS long-term dataset (Dec 2023).
Notes: % change since 2007. Sales in LCEUR are calculated by applying annual exchange rate (2000–2023) to LCUSD sales data, and hence may be subject to fluctuations in exchange rates; Only includes non-biologic products; Protected brands include original protected brands, upcoming LOE and vaccines, New brands include original new brands; LOE include drugs that lost patent protection; Generics include non-original branded products as well as drugs that are marketed using the molecule name. Standard unit (SU) refers to the number of doses of a product sold. Dark green in the heatmap reflects instances where the % change exceeded 1000% (Latvia, Lithuania, Estonia).

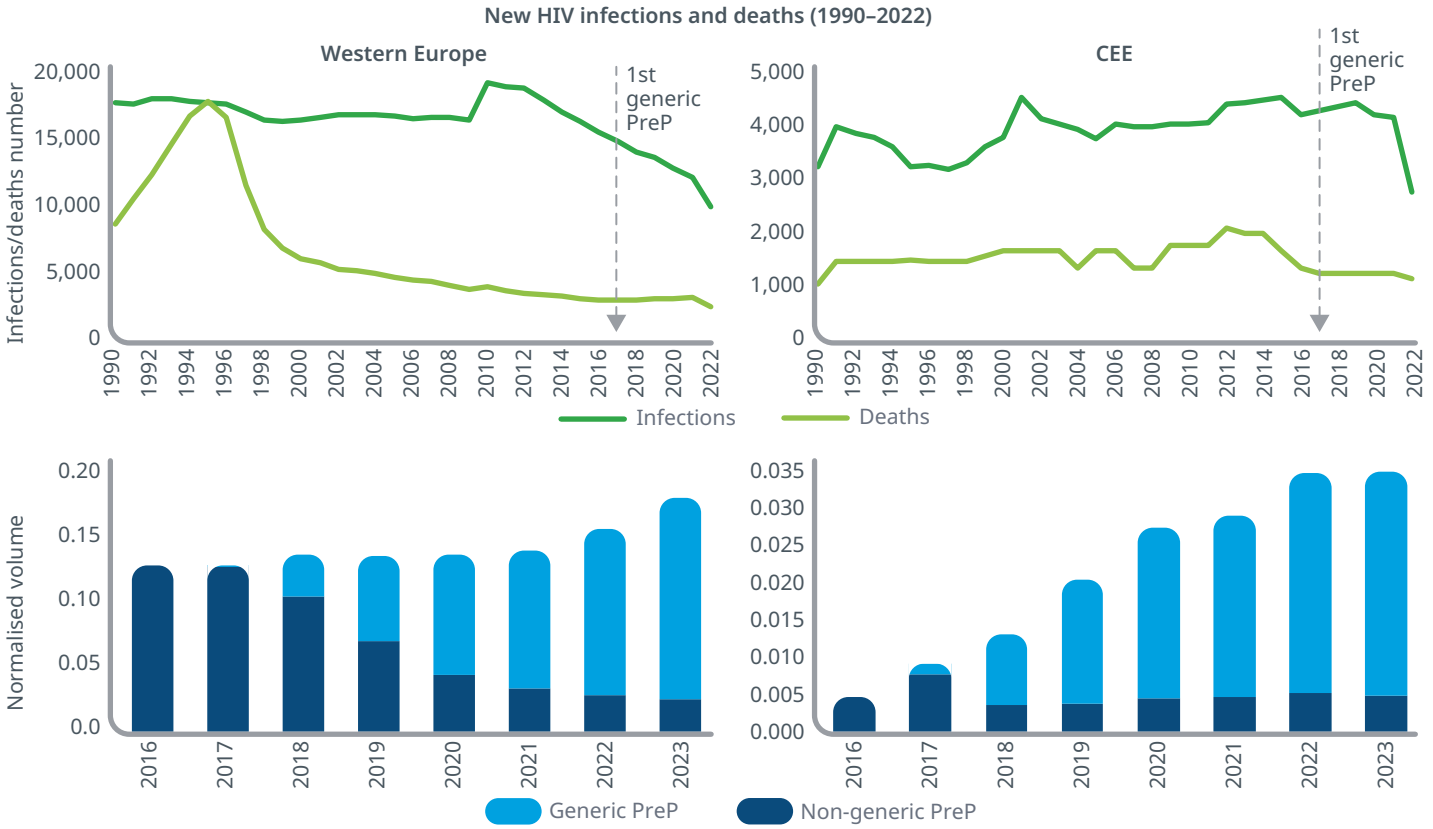
Generic medicines help to reduce disease burden in underserved markets

It is difficult to directly attribute health outcome improvements to medicines without a health economic assessment due to numerous variables however, in the European Union, new HIV infections have fallen by ~45% since the first branded PrEP, a prophylactic option for HIV prevention, was licensed in 2016.

Disparities in access mean that infections have fallen more slowly in CEE compared to Western European countries (Exhibit 10). The high cost of treatment is among the main reasons for limited access amongst HIV vulnerable populations in CEE countries. Currently, the EMA has approved two therapies for the use of PrEP: the combination of emtricitabine and tenofovir disoproxil fumarate (Truvada™), and, more recently, the injectable cabotegravir (Apretude™). However, in 2016, prior to the availability of generic medicines, only one therapy was available in Europe and available data shows that consumption was mostly concentrated in Western Europe where, in some countries, oral PrEP (emtricitabine and tenofovir disoproxil fumarate) is often available at no extra cost.[7]

In contrast, in most CEE countries PrEP therapies are not publicly reimbursed and out-of-pocket payments are required.[8] Research into the impact of generic availability of PrEP treatments indicate that countries with the lowest consumption of PrEP benefited the most from generic penetration. Exhibit 10 shows that following the commercialization of the first generic PrEP in 2017, the volume of PrEP therapies rose in both Western and CEE countries, however the sharpest increase is seen in the latter group of countries where treatment volume rose by nearly 35% in 5 years.

Exhibit 10: The entry of generic PreP has contributed to a significant reduction in HIV treatment access gaps across Europe



Source: IQVIA MIDAS; UNAIDS epidemiological estimates (accessed on 7th December 2023). Western Europe= Austria, Belgium, Denmark, Finland, France, Greece, Germany, Ireland, Italy, Luxemburg, Netheralnds, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom. CEE= Bulgaria, Croatia, Czechia, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Serbia, Slovakia, Slovenia. Analysis based on all 3 EMA authorized products for HIV prevention (PreP) as of 14th December 2023. Note: volume is in standard units (SU) and was normalized by country population data (source: World Bank, accessed on 7th December 2023).

Such examples illustrate the importance of generic medicines in enabling healthcare providers to afford access to new therapies where access barriers remain high, producing additional savings for healthcare systems through the indirect effects associated with improved population health.

Generic medicines have an important role to play in future health outcomes

In the near future, generic medicines will continue to play an important role in expanding treatment access in underserved markets. Hepatitis C is an important example due to the impact on people living with the disease, indirect societal costs, and the high cost to the healthcare system of under-treatment.

The disease affects ~15,000 people in Europe and with the notable exceptions of Denmark, France, the Netherlands, Scotland and Slovenia, which developed their first hepatitis C policies between 1997 and 2007, most of the current national hepatitis policies in Europe are recent and were developed in the wake of the Action 2030 plan for viral hepatitis.[9] Gilead's breakthrough medication sofosbuvir (Sovaldi™) is expected to face competitor generic entry in the next few years and thus generic companies are well-placed to seize the opportunity to fill treatment gaps and improve access to essential health products.

Generic medicines also have the potential to improve health outcomes in major therapeutic areas, such as hypertension. Past research suggests that increased utilisation of generic medicines was one of the key factors behind the significant fall in hypertension-related mortality in Germany (by 50% between 1998 and 2010).[10] However, underutilization of treatment guidelines and slower generic penetration in smaller markets mean that generic medicines still have a significant role to play in improving health outcomes. These examples highlight that to fully benefit from budget savings and population health benefits brought about by generic products, rapid generic uptake in volume terms and effective price competition among generic medicines producers should be facilitated.

Generic medicines support supply chain resilience

70% of medicines consumed in Europe are generics, and their large network of suppliers is of fundamental value to the supply chain and the wider pharmaceutical sector. This section explores the importance of generic medicines in supporting healthcare demand in Europe at normal and enhanced levels of need.

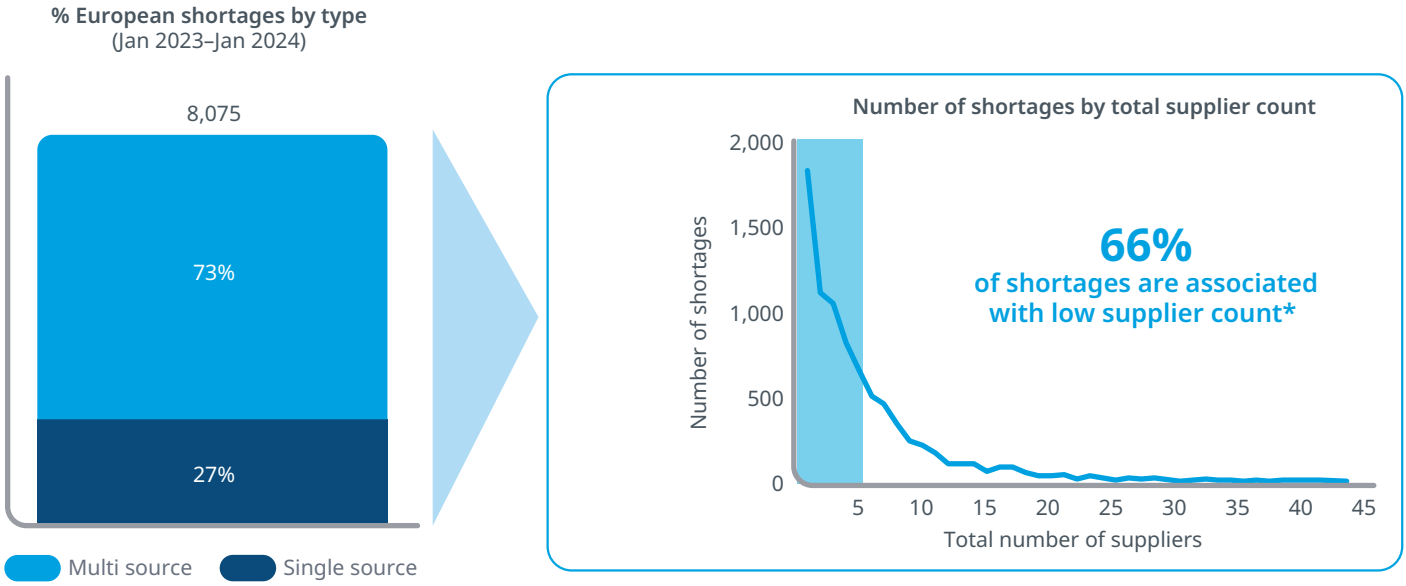
Multisource generic products mitigate the impact of shortages

Supply chain security has become a focus for governments around the world, with medicines shortages increasing in patient-critical therapies. Although the role of generic medicines in bolstering the pharmaceutical supply chain is increasingly recognized, their broader contributions to supply chain security are often overlooked.

Shortages of innovative and protected products are rare, however medicines shortages in the generics segment operate differently to those in the protected segment. With off-patent products, often multiple manufacturers can redistribute stock and meet demand within a country experiencing a shortage. For more complex shortages on products with few suppliers, volatile demand, and ultra-low prices, these dynamics do not always fill the gap, highlighting the benefits provided by a healthy competitive environment. To further illustrate the impact of this, there have been significant frictions in the supply of olanzapine in the UK after its price dropped to its lowest level in 2016 and the number of suppliers fell from 5 to 2. Although a subsequent increase in price was followed by new market entrants, re-establishing original supply volumes took up to 6 months.[11]

With off-patent products, often multiple manufacturers can redistribute stock and meet demand within a country experiencing a shortage.

Exhibit 11: The existence of multisource (MS) products is able to fill the gaps in European markets after shortages are reported



Source: IQVIA analysis. Chart notes: data is limited to total reported medicine shortages in all EU27 countries between January 2023 and January 2024. *Data includes both single-source and multi-source products. 'Low supplier count'correspondes to instances where the product is provided by <5 suppliers in Europe. The analysis does not account for the relative number of molecules, but does highlight the increased risk of shortages with low numbers of ccompetitors which is linked to the size of the market.

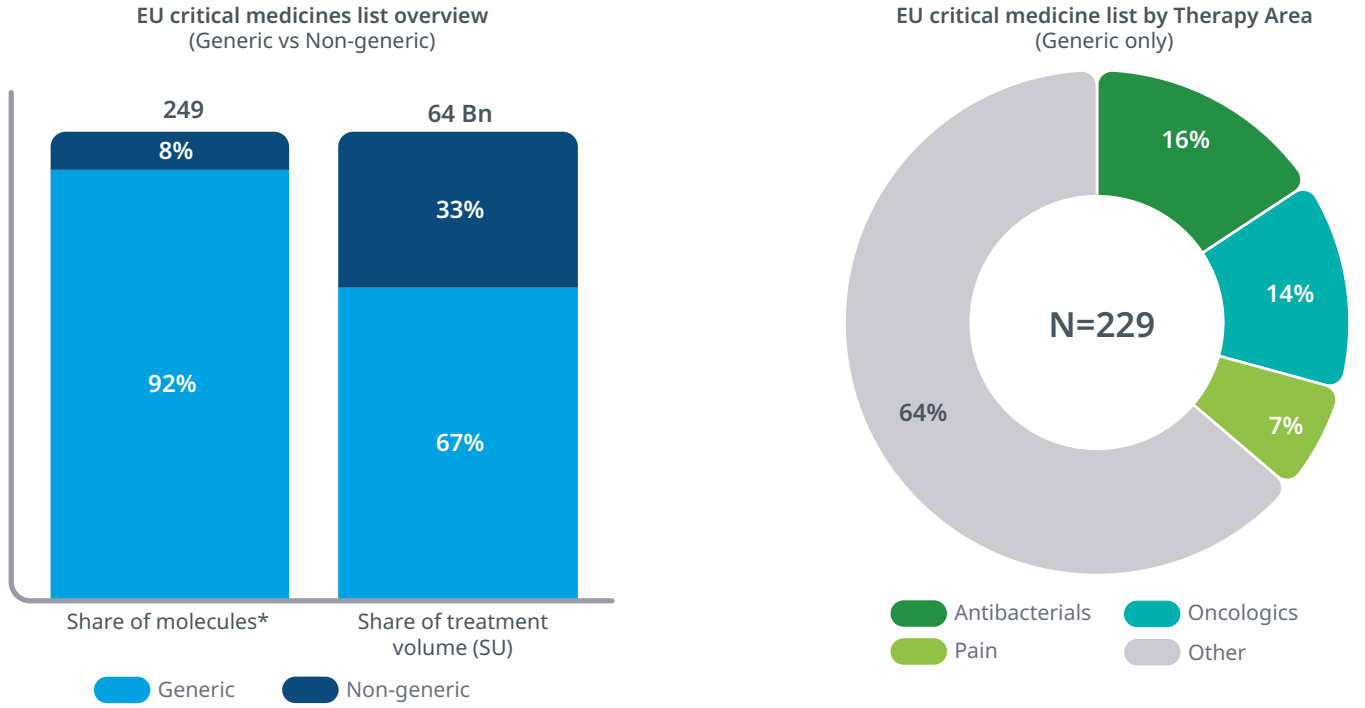
Importantly, the number of competitors for a given product has an impact on the risk of shortage (Exhibit 11). Over two thirds of all reported shortages between January 2023 and 2024 stemmed from medicines with low supplier count (i.e. less than 5 suppliers) in Europe, indicating that achieving continuity of supply requires sustainable levels of competition. Unlike protected brands, generic medicines are typically multi-source, with several generic medicine manufacturers producing the same product. This strengthens pharmaceutical supply chain resilience at times of increased demand.

9 in 10 critical medicines are generic medicines

The EU list of critical medicines contains human medicines whose continued supply is considered a priority in the EU, to avoid serious harm to patients and help healthcare systems function. 92% of the European Commission's list of critical medicines for major events and/or public health emergencies are generic medicines (Exhibit 12). The list includes both innovative and generic medicines for human use covering a wide range of therapeutic areas, including antibacterials. oncologic and pain therapies, which together represent almost 40% of all generic medicines included in the critical medicines list (Exhibit 12).

It is important to note that prior to the newly created European critical medicines list, some countries developed their own critical medicines lists. While the products included vary and the purposes of these lists differ, the national picture of generic medicines remains the same. Generic medicines are ~80% of the molecules and ~90% of volume of European countries' critical medicines list. For the most common INNs on European national critical medicines lists, there are rarely fewer than 5 competitors operating in each country.

Exhibit 12: Generic medicines are critical components of the EU critical medicines list



Source: IQVIA MIDAS Q3 MAT 2023; https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/medicine-shortages-and-availability-issues/availability-critical-medicines#ema-inpage-item-64278.
Notes: *Analyses based on 249/268 active substance-ATC-5 code pairs included on the Union list of critical medicines published on 12th December 2023, due to data coverage; Includes EU27+NO, CH, UK markets. Bn= billion, in standard units (volume).

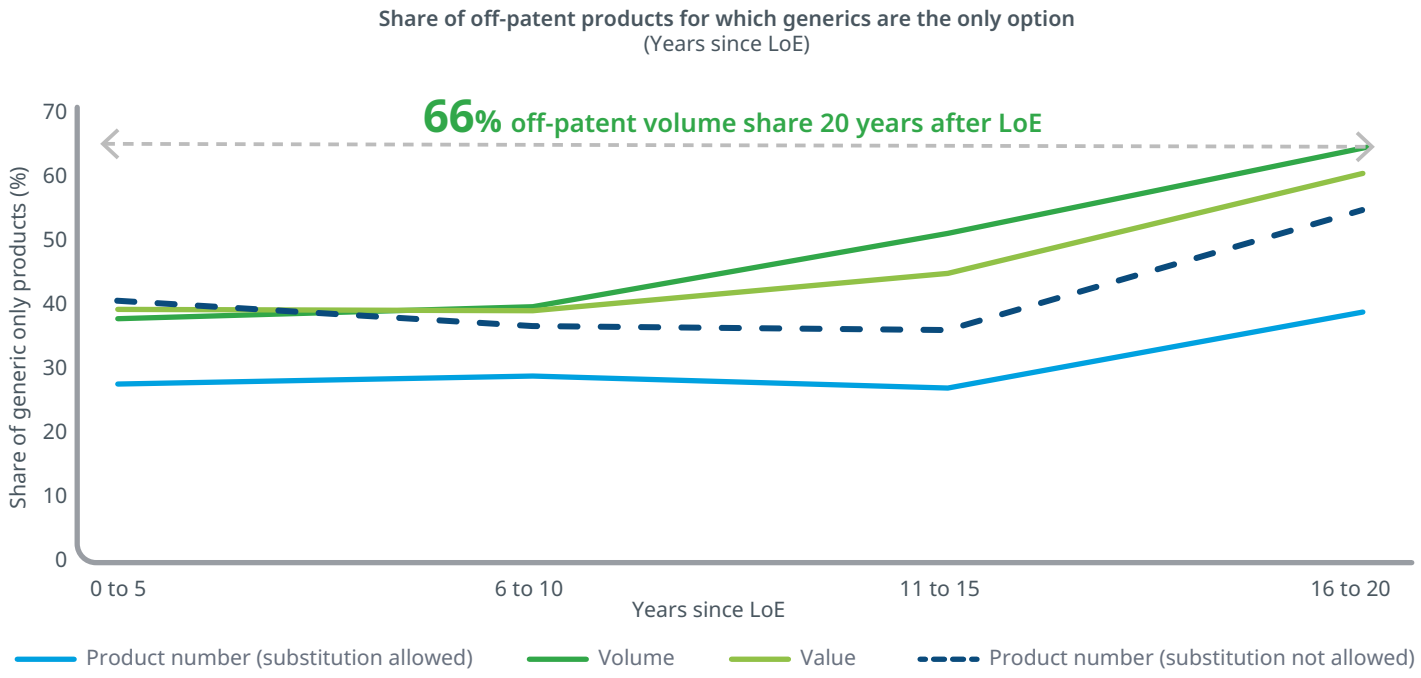
After loss of exclusivity, generic medicines are often the only option

The supply chain security provided by generic medicines continues long after loss exclusivity as generic medicines can often be the only available treatment option.
In many European markets, automatic substitution occurs for generic products meaning that the market share of the originator molecule will decline, replaced by competitors.

Regardless of which substitution policies are present in each market, available data suggests that generic medicines are often the only option for off-patent products. In countries where substitution is legally allowed, 40% of all off-patent products (in absolute numbers) are only available as generic medicines 20 years after LoE, representing 66% of the off-patent market by volume and 62% of the market by value (Exhibit 13). In countries where generic substitution is not allowed, the picture only differs slightly. Of all the off-patent products available on the market, 52% are generic only.

92% of the European Commission's list of critical medicines for major events and/or public health emergencies are generic medicines (Exhibit 12).

Exhibit 13: Generic medicines are often the only option, regardless of whether substitution is allowed



Source: MfE 'Market review: European generic medicines markets' (2023); IQVIA MIDAS Q3 2023; IQVIA Ark Intelligence 2023.Hospital and Retail. Rx only; INN insights (excl. vaccines, Inn insights not assigned, hospital solutions, diagnostics and ATC V products). Includes EU27+NO, CH, UK markets. Value=sales in EUR. Substitution not allowed= countries where generic substitution is not allowed (Austria, Bulgaria and Croatia). Note that 'generic only' products include instances where the product is supplied by both innovative brand and generic manufacturers, however the volume share of the originators is <25% of the total in standard units.

In summary, instances where generic medicines offer the only therapeutic option for a given molecule highlight the importance of the segment to patient care beyond simply savings and access.

Generic manufacturers continue to invest in Europe

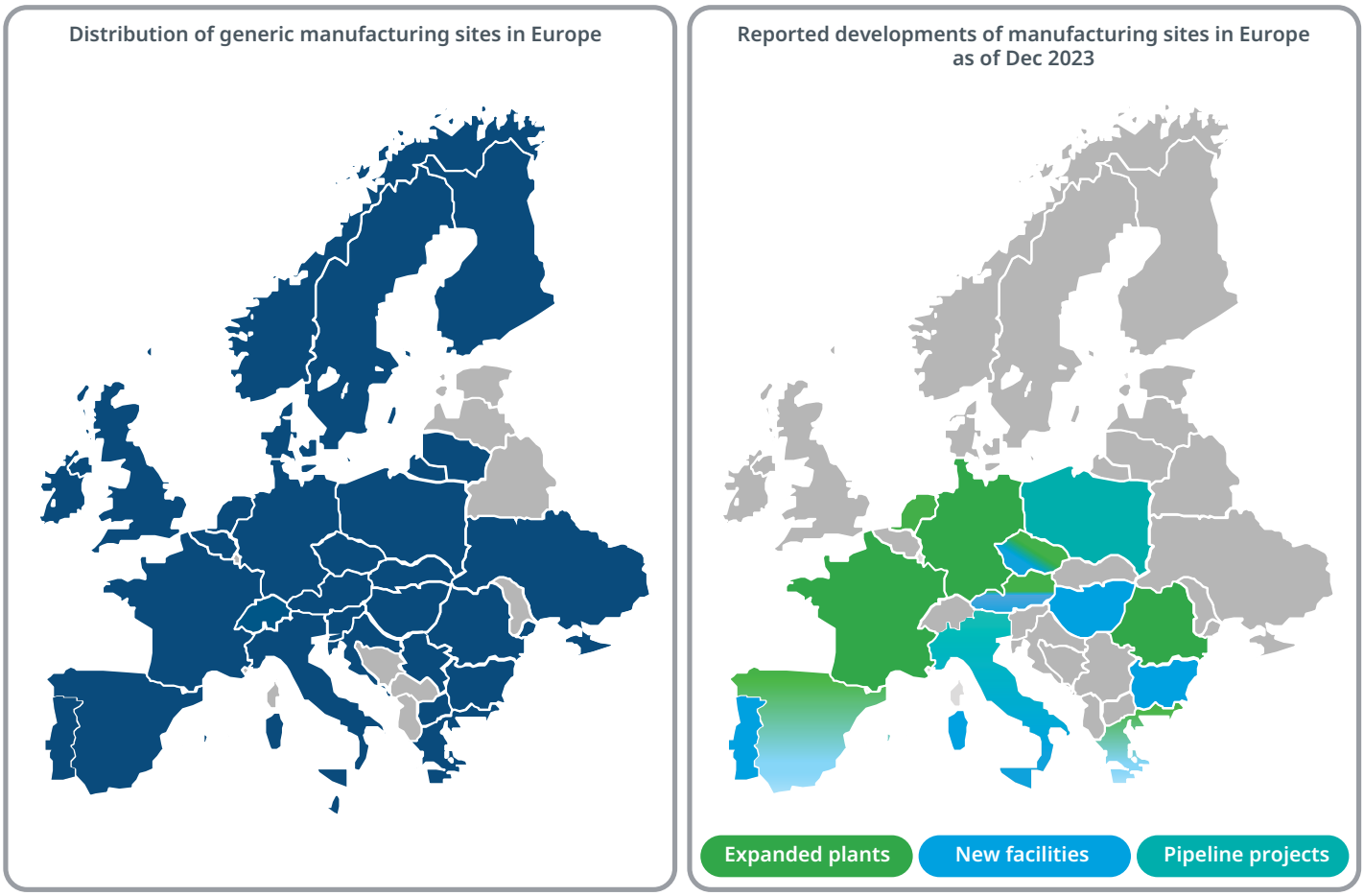
Reshoring of manufacturing sites has been a discussion topic since COVID-19, with many tender criteria now asking for a level of European manufacturing. In line with the European Commission's objective of supply chain security, there is a growing recognition among generic manufacturers of the importance of local manufacturing and supply chain strengthening. This has raised efforts from the generics sector to support the pharmaceutical supply chain in its most critical areas.

The generic medicines industry alone comprises over 400 manufacturing sites in Europe with over 20 projects currently underway across Europe to support manufacturing.[12] However, the development complexity is high since the relative size, current location of plants, and importance of sites is commercially sensitive (Exhibit 14).

In Austria, Sandoz's recent €200 million investment in penicillin manufacturing facility underscores the continued commitment of generic manufacturers to guaranteeing sustainable access to antibiotics in Europe.[13]

Generic manufacturers are also continuing to invest in API manufacturing at a time when the global production share of APIs in Europe has fallen from 53% to 25% between 2000 and 2022.[14] Companies are attempting to improve their processes, with some maintaining a minimum of two suppliers for every starting material[15] as alternative sources.

Exhibit 14: New generic medicine manufacturing investments in the EU



Source: IQVIA GS&AR; Egualia, Osservatorio Nomisma Su Il sistema dei farmaci generici in Italia 2023 (accessed on 12° December 2023); Medicines for Europe, Off patent industry new investments in EU manufacturing (2023); press releases and company websites.

Despite increasing investment in Europe, generic manufacturers are still facing challenges from overseas players. Although the market penetration of non-domestic generic medicine manufacturers in Europe has lagged that of the US, increasingly Indian and Chinese-based manufacturers are looking at the European generic medicine market with greater interest. Low production costs and a different patent protection system confer competitive advantages which can place the European generic manufacturing industry at disadvantage. Grants, low-interest loans, and export incentives generate cost advantages which cannot be obtained within the EU. These market dynamics can expose European generic manufacturers to unsustainable levels of competition as overseas players are able to drive down prices and gain market share in price-only tendering systems.

The generic medicines industry alone comprises over 400 manufacturing sites in Europe with over 20 projects currently underway across Europe to support manufacturing.[12]

The off-patent sector supports innovation

Generic companies support innovation both indirectly through savings that are then used to fund further innovation, but also directly by innovating in manufacturing approaches, product improvements, and through improved environmental practises to have wider patient and societal benefits.

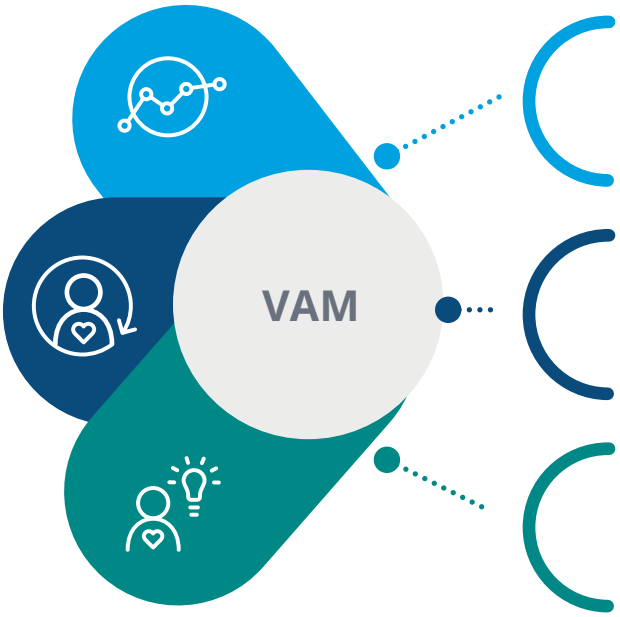
VAMs directly offer a range of unique benefits to patients

Value-added medicines (VAMs) are medicines based on known molecules that address healthcare needs, and deliver relevant improvements for patients, health care professionals and/or payers. They represent an opportunity to expand access to patients, while improving health outcomes.

While there is no dedicated approval process in Europe, the US offers well-established regulatory processes defining eligibility, submission criteria and exclusivity protection, via the 505(b)(2) pathway. The number of approvals obtained via this pathway can be used as a proxy to measure the pace at which the industry is evolving in Europe. Current data suggests that off-patent innovation has progressed rapidly in the last decades, moving from small-step innovation (i.e. new salts, new excipients), to leveraging advanced technologies and new treatments in often neglected therapeutic areas, ultimately improving outcomes for patients.

As an example, recently launched VAMs can range from alternative dosing forms for patients[16] no longer responding to their regular therapy, to products with improved pharmacological profile[17], which enable effective treatment for more patients, or with reduced side effects allowing patients to continue their treatment, instead of switching to more expensive options.[18] A summary of the major categories of VAMs are shown in Exhibit 15. These examples showcase some of the improvements that can be made to off-patent products by manufacturers other than the original developer that can have a benefit to the healthcare system.

Exhibit 15: Value-added medicines case studies from Europe



Superior efficacy

Dasatinib Zentiva: compared to dasatinib monohydrate, this product delivers the active ingredient irrespectively of the acidity in the stomach which enabled effective treatment for an additional 20% of patients.

Reduced side effects

Methotrexate Medac: this once-weekly subcutaneous injection offers reduced side effiects compared to the oral formulation allowing patients to continue their treatment for longer, instead of switching to more expensive treatments, with financial gains for healthcare systems.

Improved therapeutic option

Legicon: direct delivery into the intestine circumvents the limitations of erratic gastric emptying and short plasma half-life of levodopa, providing a therapeutic option for advanced PD patients that no longer respond to oral treatments.

On another level, VAMs enable the development of safer ways to administer medicines, so that physicians and patients are exposed to lower risks of accidents. For instance, in 2021 the launch of a ready-to-dilute, higher strength formulation for a widely used oncological treatment eliminated additional handling steps, reducing patients' contamination risk and waiting times.[19] Finally, beyond addressing unmet clinical needs, it is important to highlight that VAMs can also support healthcare systems in achieving improved efficiency and savings. For example, a recently published report by the UK's Department of Health and Social Care indicates that the increased use of ready-to-administer products could free up over 1 million hospital beds a year, helping the health system to achieve an estimated financial benefit of £346 million each year.[20]

Generic companies are progressing environmentally sustainable practices

While this is not unique to the generics sector, generic manufacturers are also exploring new approaches to meet environment, social and corporate governance (ESG) targets.

Several companies have developed novel approaches to link both climate and access to medicine targets to a sustainability-linked bond (SLB).[21] Some of these targets are not only associated with a reduction in both Scope 1 and 2 greenhouse gas (GHG) emissions, but also to an increase in access to essential medicines particularly for patients in low- and middle-income countries (LMICs). These efforts are increasingly being recognised by the industry.[22,23]

Manufacturers are also exploring how new production processes that can help them to reduce their carbon footprint. Continuous manufacturing (CM), for instance, not only allows companies to speed up development timelines for new medicines, but also represents an important advancement as separate production stages lead to significantly higher carbon emissions. At present, several companies have already invested in developing CM lines.[24] Additional innovation comes from the implementation of new sustainable solutions to offset emissions. In 2023, one generic manufacturer announced plans to complete one of the largest solar panels installations in Czech Republic at their local manufacturing site.[25] More recently, another company introduced the first electric vehicle of its kind – weighing more than 12 tons with cargo – in Slovenia.[26]

Generic savings cycle continues innovation

Savings generated from generic entry can be deployed to cover the costs of newer, innovative medicines that support new standards of care and improve health outcomes. This process permits innovation as payers are able to reinvest back into new innovations in pharma, healthcare technology, or staffing. If the pressure is only on costs without any holistic recognition of the true role of generic medicines in the healthcare ecosystem, then this innovative potential may not be fully maximized in the future.

Savings generated from generic entry can be deployed to cover the costs of newer, innovative medicines that support new standards of care and improve health outcomes.

Challenges and long-term outlook

Summary:

- **Spending on top 3 therapeutic areas has decreased from 37% to 8% since 2000**
- **The size of the small molecules facing LoE by 2027 is forecast at nearly €10bn**
- **Generic medicines have doubled access in chronic disease areas**
- **Nearly 70% of shortages are linked to products with less than 5 suppliers**
- **9 in 10 of Europe's critical medicines are generic medicines**
- **Generics are the only option for 40% of all off-patent molecules 20 years after LoE**

Over the past decades, it is unlikely that government and payers would have met the growing demand for medicines without the savings generated by generic medicines. Today generics are in use in all facets of healthcare and can only be replaced at enormous additional costs for society. Given the Europe's ageing populations[27], financial challenges, increased burden of chronic disease, and a surge in innovative treatment options, the contributions that generic medicines offer to health systems are increasingly important.

Generic medicines entered the European market in the 1980s and 1990s, supported by government policies favoring their adoption. In the following decades, the loss of patent protection for blockbuster medicines led to substantial healthcare savings, however subsequent cost containment policies have caused a sharper focus on their cost-saving potential at the expense of other contributions. The continued sustainability of the generic medicine industry is not a foregone conclusion and requires further consideration. While the core purpose is to deliver savings, viewing generic medicines solely as a cost-saving mechanism can limit their ability to deliver long-term benefits. Pricing pressures could limit the provision of older products as the commercial viability becomes limited but can also incentivise progression onto newer treatment classes if these are available.

The role of generics has grown in the post-COVID-19 era to one that supports Europe's supply chain resilience. An understanding of the role in critical medicines, and a need for greater European manufacturing presence was not a priority in previous decades. Managing medicines shortages effectively, expanding Europe's manufacturing footprint, and developing environmentally conscious approaches to products and manufacturing processes will add new costs in the short-term. Despite clear benefits, the willingness for continued investment and willingness to pay remains uncertain.

The focus on patient access, affordability, supply chain security, and environmental considerations come with an element of cost in their provision which is borne by different stakeholders. Manufacturers look for rewards for investments that add competition, stimulate innovation, and meet Europe's social agenda.

The changing landscape and proposition provided by the generic medicine sector raises new questions to be answered:

1. What can healthcare systems do to optimize past and future savings from off-patent opportunities provided by generic molecules?
2. Is it possible to balance access to smaller volume products that have limited commercial viability but remain valuable treatment options?
3. How can a greater supply security be ensured for Europe, and what are the implications on current prices?
4. What are the potential risks of reshoring and what challenges does the sector face?
5. How can the economic and societal value provided by the sector be translated into futureproof generic medicine policies supporting investment in the sector?

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