



The unintended consequence of rewarding innovation? An assessment of medicine shortages across the UK and EU generics market

Nick Stringfellow, Senior Analyst at Lightning Health, has been closely monitoring the ongoing issues of medicine shortages in Europe that are disproportionately affecting generic medicines. He believes that more needs to be done to promote an equitable and balanced industry that pushes innovation and maintains supply of critical medicine.

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Pharmaceutical markets in both the UK and the European Union are experiencing huge change, with the UK set to turn rebates on their head in what is now a truly post-Brexit era, and the EU set to introduce the largest reformation to the pharmaceutical legislation in 20 years. Many of the proposed changes by both the UK government and the EU Commission aim to incentivise innovative medicines, ultimately relying on cost containment measures for mature, generic products to 'foot the bill'. However, with medicine shortages already a concern in both the UK and EU, these efforts are likely to exacerbate the unattractive and therefore heavily monopolised generics market, primarily recognised as the cause of such shortages.

Confirmation of the new Voluntary Scheme for Branded Medicines, Pricing, Access and Growth (VPAG), that came into force on 1 January 2024, sets into motion significant changes to the way in which rebates are calculated for manufacturers that opt out of the less popular Statutory Scheme (historically, over 90% of companies supplying eligible medicines to the NHS have been members of the voluntary scheme).^{1,2} Following the final publication of the policy on 14 December 2023, it has become clear that the aim of increasing access to innovative medicines for NHS patients is top of mind, but at what cost?

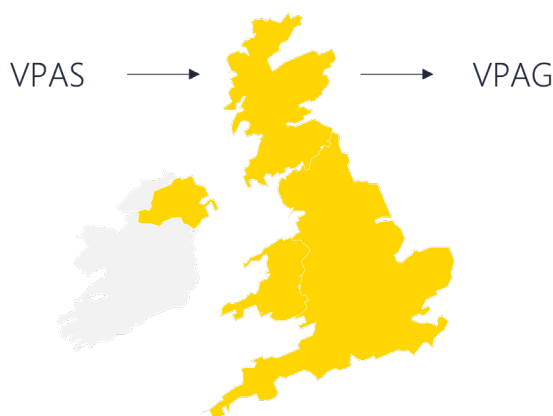
In an attempt to maintain similar cost savings to the NHS seen under the previous Voluntary Scheme for Branded Medicines Pricing and Access (VPAS) (26.5% rebate in 2023), while incentivising innovative medicines to ensure the UK stays a priority launch market, the new scheme sets differential rebates based on whether a medicine is considered 'newer' or 'older'. Newer medicines are defined as originator products that are either within their first 12 years post marketing authorisation or, while a Supplementary Protection Certificate remains in force for the active ingredient, if applicable. Such medicines will be subject to dynamic rebate rates, calculated based on the overspend above an agreed NHS growth rate. The allowed growth rate for newer medicines is projected to increase from 2% in 2024 to 4% in 2027 and 2028. The ABPI predicts that, under the new scheme, rates for newer medicines should fall to around 7.2% by 2028.³

Older medicines (i.e., any medicine that does not fall into the previous category) are subject to a Basic Payment Percentage representing a flat rate rebate of 10%.¹ In addition, a Top-up Payment is applied, calculated based on the Observed Price Decline each year (see table below). The maximum total rebate is therefore set to 35% for an older medicine with an annual price decline of 10% or less. Should an older medicine display a price decline of 35%, the total rebate would include only the basic 10% rate.

Observed price decline	2024	2025	2026	2027	2028
10% or less	25%	25%	25%	25%	25%
11%	24%	24%	24%	24%	24%
12%	23%	23%	23%	23%	23%
13%	22%	22%	22%	22%	22%
Each percentage point drop in observed price decline equates to a 1% point reduction in the Top-Up Payment Percentage until the percentage of observed price decline reaches 35%					
35% or more	0%	0%	0%	0%	0%

Prior to this system coming into full effect, between the 1 January and 31 March 2024, a transitional period will apply. During this, manufacturers will continue to experience a relatively high rebate of 19.5%, regardless of the age of the product. However, manufacturers should be aware that exemptions are available, including for: medicines containing a new active substance (not subject to a rebate for the first three years), SMEs that fulfil certain criteria, and Centrally Procured Vaccines and other Exceptional Central Procurements.

The only other rebate option for branded medicines in the UK comes in the form of the Statutory Scheme, which itself underwent a government consultation in July 2023.⁴ Under the reviewed scheme, rebates will be reduced from the record high of 27.5% seen in 2023 to a rate of 21.9% in 2024, 24.0% in 2025 and 26.8% in 2026. The original proposal included the introduction of a novel mechanism called the Life Cycle Adjustment (LCA) which, similar to the more recent VPAG, aimed to favour newer medicines. In order to do this, medicines at 12 years or more post marketing authorisation would be subject to rebates of up to 40% if deemed to be in an 'uncompetitive market' by the Department of Health and Social Care (DHSC). However, the proposed LCA mechanism led to unprecedented criticism from the pharmaceutical industry with over 20 industry leaders joining force to condemn the plan as completely unworkable.⁵ Many cited that the expected level of rebates under the LCA would compromise the industry's ability to invest in the UK, leading to a reduction in highly skilled jobs and ultimately having a negative impact on the UK economy. This led to the LCA mechanism as it stands being removed from the new scheme, with the caveat that the DHSC remains committed to ensuring sustainable spending on older medicines.⁴ A further consultation period is expected sometime in early 2024 to ensure that the Statutory Scheme is broadly commercially equivalent to the upcoming VPAG.



What trends can we see regarding rebate rates in the UK?

Under the current Voluntary Scheme, VPAS, rebates rose from 5.1% in 2021 to 15% in 2022 and reached a high of 26.5% in 2023.³ Under the upcoming VPAG, rebate rates for all medicines covered by the scheme will reduce to 19.5% in Q1 2024, prior to the introduction of differential rebates. By Q2 2024, newer medicines will be subject to dynamic rebates expected to be around 7.2% by 2028 based on a 4% allowed growth rate. By Q2 2024, older

medicines will be subject to rebates ranging from 10%-35% based on their percentage price decline from the previous year.¹ For manufacturers included in the Statutory Scheme, rebates are set to reduce from 27.5% in 2023 to 21.9% in 2024 before rising to 26.8% in 2026.⁴ However, manufacturers within the Statutory Scheme should remain wary of upcoming efforts to decrease rebates for newer medicines by increasing rebates for older medicines, similar to mechanisms seen in the VPAG.

What impact have the rebate rates had on the UK pharmaceutical market?

In November 2023, the BMJ released an article on the record number of problems the NHS has experienced with the supply of medicines.⁶ Of the 111 products deemed to be facing supply problems, branded generic drugs were disproportionately affected, as warned by the British Generic Manufacturers Association (BGMA). Branded generics made up around 50% of the drugs (55) facing supply problems, despite representing only 10% of prescribed products in the UK. Branded generics facing supply problems included hormone replacement therapies, contraceptives, antidepressants, and immunosuppressants. The main drivers for the rise in shortages in branded generics cited by the BGMA were the conditions imposed by both the current VPAS and Brexit. Therefore, particularly in the case of older branded generics, such supply issues are only likely to be intensified following the implementation of the VPAG, should manufacturers not be able to take significant price cuts, year on year.

How does the UK compare with current European trends?

With differential rebates for older and newer medicines under VPAG not coming into effect until April 2024, the UK entered 2024 with rebate rates for all medicines that were significantly higher than those under similar mechanisms in Europe.³ The 19.5% VPAG rate for early 2024 and the 21.9% statutory rate for the entirety of 2024 both exceed current rebate rates of 12% in Germany (set to reduce back to 7% during 2024, with the option for confidential discounts at the national level to replace part of the statutory rebate)⁷, 7.5% in Spain and 8.25% in Ireland. It is currently uncertain whether the proposed decline in rebate rates for newer medicines will be sufficient to temper warnings from the pharmaceutical industry regarding disinvestment in the UK, as its attractiveness as a priority market diminishes.

When comparing the state of the UK and Europe, one would hypothesise that lower rebates should make a market more attractive, build competition and limit the risk of drug shortages. However, the current state of medicine shortages in Europe has been recognised as a prioritised issue for the European Commission.⁸ This is due to various other factors faced by European countries that are contributing to drug shortages across the continent.⁹ Under the European tender system, many Member State governments use reference pricing to compare the price of drugs across markets, which may include the UK, to set a price benchmark prior to a tender being launched. Typically, the contract

is awarded to the manufacturer that responds with the lowest price, resulting in further downward pressure in subsequent tenders. Considering the unforeseen issue of the war in Ukraine driving up the cost of manufacturing and distribution, and an unwillingness of European markets to remove price caps, we see the thin profit margin for generic therapies becoming increasingly unsustainable. This has ultimately forced some European generics companies to either withdraw from the market or move the manufacturing process for some or all production to India and China. Both of these actions can increase vulnerability to medicine shortages in Europe (as highlighted during the COVID-19 pandemic).^{8,9} Furthermore, withdrawal of a manufacturer from the European market increases the market share of the remaining competitors.⁹ In Europe, this has led to the situation where some countries are relying on one or two generics manufacturers to supply certain off-patent drugs.

How has Europe worked to reduce medicine shortages?

There are some examples of EU countries introducing local policies in an attempt to control medicine shortages. In January 2023, Belgium adopted a Royal Decree under which, if certain conditions were met, the government could ban or limit the export of medicines from the Belgian market to other EU countries.¹⁰

The four cumulative conditions that must be met include:

The medicines unavailability has been observed by the Federal Agency for Medicines and Health Products

The drugs unavailability will last for at least one month

The administration of the drug is urgent and lack of the drug may lead to acute or chronic health deterioration

The drugs availability is not sufficiently compensated by other authorised drugs

Prior to the winter of 2023/24, the Austrian government, in cooperation with the Austrian Association of Full-Line Pharmaceutical Wholesalers, PHAGO, initiated stockpiling of medicines in order to avoid similar shortages to those experienced in previous winters.¹¹ 23 stockpiles were launched covering 10 critical drug types. Medications deemed as critical due to being subject to shortages in previous years included generic pain medicines such as ibuprofen and paracetamol.

At the EU level, various efforts to address medicine shortages through European cooperation were outlined in a communication by the Commission, published in October 2023.⁸ A New Voluntary Solidarity Mechanism has been established by the EMA and Member States. This aims to facilitate the redistribution of medicines on the European market from one Member State to another that is experiencing a critical shortage. On 12 December 2023, the EMA published the first Union list of critical medicines.¹²



This aims to allow the EMA and the Commission to analyse vulnerabilities in the supply chain and take proactive measures to avoid medicine shortages. The list includes both innovative and generic medicines, an important development considering there was previously no central EU system to track the supply of essential generic drugs in each country.^{9,12}

The Critical Medicines Alliance, an industrial policy pillar aimed to coordinate action at the EU level to address supply chain vulnerabilities, was launched on the 16 January 2024.¹³ The plan is to bolster production of critical medicines in the EU and diversify international supply chains to tackle shortages and reduce the EU's dependencies on third countries. The exact mechanisms underlying how this will be achieved remain vague. As an initial step, interested experts from Member States, industry, health professionals and civil society have been invited to take part in the selection procedure for the Alliance that runs until February 2024, with a view to participating in its meetings in Spring 2024. The Alliance may also pave the way for a possible 'Critical Medicines Act' in the future.⁸

How can we expect this area to evolve during the current Belgian EU Council Presidency?

As we move through the third month of the Belgian EU Council Presidency, it is clear through their involvement in the launch of the Critical Medicines Alliance, and the recent publication of the practical guidance to their upcoming health programme, that dealing with medicine shortages is quite literally 'top of the list'.¹⁴ Exactly how the Belgian Presidency plans to continue efforts to secure medicines within Europe may become clearer following the Conference on the Future EU Health Union planned for later this month.

One area that the Belgian Presidency has the rare opportunity to influence is how medicine shortages are addressed as the proposed Reform to the EU Pharmaceutical Legislation is adopted into policy. The current proposal introduces the requirement that all marketing authorisation holders have shortage prevention

plans in place with guidance published by the EMA on good industry practices to mitigate medicine shortages.^{15,16} However, without first addressing the current lack of manufacturers, particularly within the European generic markets, the reform is set to have limited impact in this area.

A further concern, that was highlighted during recent research conducted using the Lightning Insights Platform for ISPOR Europe 2023, is the perception by Central and Eastern European payers that a major benefit of the Reform will be cheaper pharmaceutical prices due to earlier generic market entry.¹⁷ Although it is easy to see why payers would favour the prospect of reduced market exclusivity, in the case where manufacturers are unable to meet certain conditions that extend the baseline exclusivity period, how this may impact medicine shortages must be considered. On the one hand, the Commission highlights their concern over medicine shortages through the efforts highlighted above and yet, on the other, they propose legislation that could intensify that very issue. Put simply, faster generic entry leading to spiralling prices within a market already plagued by a lack of generic manufacturer interest is unlikely to be the answer to the EU's battle against medicine shortages.

Fortunately, this is not news to the EU Council Belgian Presidency. During the second plenary session of ISPOR Europe 2023, Gloria Ghéquierre, advisor to Frank Vandenbroucke, the Belgian Health Minister, made it clear that low generic prices were recognised as a major contributor to the lack of competition with the European generics markets.¹⁸ Withdrawal of manufactures from Europe due to unsustainable profit margins, as explained earlier, has contributed to what was described in the session as 'the whole of Europe relying on only one or two manufacturers for some truly essential therapies'. With this thinking at the helm of the EU Council Presidency, there is the opportunity for the root cause of medicine shortages to be properly addressed.

One source of hope, which indicates a proactive approach towards mitigating medicines shortages, comes in the form of new, greener and more secure pharmaceutical production in Europe, spearheaded by the Belgian presidency of the EU Council.¹⁹ One example is a large-scale antibiotic manufacturing site inaugurated in November 2023, located in Kundl, Austria. The state-of-the-art facility is capable of handling the entire production pipeline in-house, leading to high-quality, EU produced antibiotics. The carbon emissions from the facility are estimated to have an equivalent reduced impact to the output of 12,000 households annually compared with previous processes. The facility is part of a strategy aimed at reshoring production back to Europe and removing the reliance on third country suppliers that can contribute to pharmaceutical insecurity and shortages.



"The fact that the Commission now considers the European production of older, basic medicines to be a matter of general public interest represents a complete paradigm shift and an important new milestone.

Frank Vandenbroucke

Belgian Health Minister¹⁹

However, the facility wasn't established on the usual economic basis for selecting a manufacturing site. 'The deal', which hinged on Austrian government concerns over antibiotic supply, required a promise of €50 million in subsidies to Sandoz with the prerequisite that the company would then create a fully operational antibiotic facility.^{20,21} The initiative that led to the facility being produced is an example of how, without public funding, manufacturing plants within Europe would not be economically viable. In contrast, it shows that, when an issue such as medicine shortages is deemed 'important enough', governments are able to take the steps to incentivise the industry and support supply chain security in Europe.

How can we expect the issue of medicine shortages to develop based on the current evidence?

We have explored the state of medicine shortages currently experienced by the EU and UK, described the contributing factors at play and, particularly in the case of Europe, explored the strategies in place to mitigate further problems.

In the case of the UK, the link between high rebate rates under the previous VPAS and the disproportionately high rate of medicine shortages for branded generics is clear. This acts as a worrying precursor to the upcoming market environment when the new VPAG comes into effect from 1 April 2024. This will inform whether the government's prioritisation of 'newer medicines' is a successful step towards innovation or a mechanism which backfires into unprecedented levels of medicine unavailability for the UK. In which case, the UK will likely look towards the efforts by the EU to assess their perceived success in ensuring the availability of essential medicines. However, unless these efforts are sufficient to stimulate the regeneration of a healthy, competitive generics market throughout Member States, it is unlikely they will succeed in addressing the underlying issues surrounding medicine shortages in Europe.

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