Written evidence submitted by BGMA (PHA0069)

A briefing on medicines supply issues: why do they exist and how best to reduce and mitigate their impact from an industry perspective?

Executive summary

- Supply issues have grown since the start of 2022 and now they are double what they were in 2021.
- Although historically high (96 medicine shortages in December 2023), this does need to be put in context. These represent 2.41% of all presentations in the Drug Tariff and used in the NHS. Often an alternative is available, such as a different form or strength, or a second line treatment.
- There are well-developed policies and levers in place to mitigate shortages where they do happen, and we have suggested several ways these can be enhanced (page 5).
- But the growing incidence of supply issues is in part due to an underestimation by some in Government of the importance of generics to the NHS, with 4 out of 5 Health Service medicines being generic and saving the taxpayers billions each year.
- This lack of prioritisation has been evident in the decline in the MHRA's performance in the last few years, with licensing timelines routinely doubling from 12-15 months to 24-30 months or longer. This means there are less medicinal products reaching the market to provide effective competition, maximise NHS savings, and boost resilient supply to the market, even where shortages exist. Government must prioritise and demand a return to the MHRA's previous service levels in 2024.

What are generic and biosimilar medicines?

BGMA members supply 4 out of 5 medicines used by the NHS. The BGMA represents the interests of UK-based manufacturers and suppliers of off-patent generic and biosimilar medicines. We represent 8 of the top 10 suppliers (by volume) to the NHS, with our members supplying over 2 million packs of medicines to the NHS every day. We are proud to be a key partner to the NHS.

Generic[1] and biosimilar[2] medicines, which are regulated to the same standards of quality, safety and efficacy as originator versions, are supplied to the market after the patent on the originator medicines has expired. Because generic and biosimilars are often over 80% less expensive than the originator versions[3], they make up 80% of NHS-prescribed medicines, saving the NHS approximately £13bn per annum on its medicines bill[4]. This makes generic, and increasingly biosimilar medicines, the bedrock of the NHS, providing life-saving and life-enhancing treatments to millions of people every day.

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[1] A generic medicine contains the same active ingredient as the equivalent original branded drug, and is marketed once the originator's patent protection has expired. Generics are authorised to the same standards of safety, quality and efficacy as original branded drugs, and have to demonstrate in clinical studies that they are bioequivalent to the original product: i.e., they deliver equal medical benefits to the patient. Generic medicines are therefore normally interchangeable with the equivalent branded drug. (www.britishgenerics.co.uk)

[2] "Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities. Due to the variability of the biological system and the manufacturing process, biological medicines may show a certain degree of variation, even between batches of the same product. A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing medicine. A biosimilar contains a version of an active substance of an already approved biological medicine, which is referred to as the reference medicine. Similarity to the reference medicine must be established based on a comprehensive biosimilar comparability exercise, such that they do not have any meaningful clinical differences from the reference medicine in terms of quality, biological activity, safety, efficacy and immunogenicity" (https://www.england.nhs.uk/wp-content/uploads/2019/05/what-is-a-biosimilar-medicine-guide-v2.pdf)

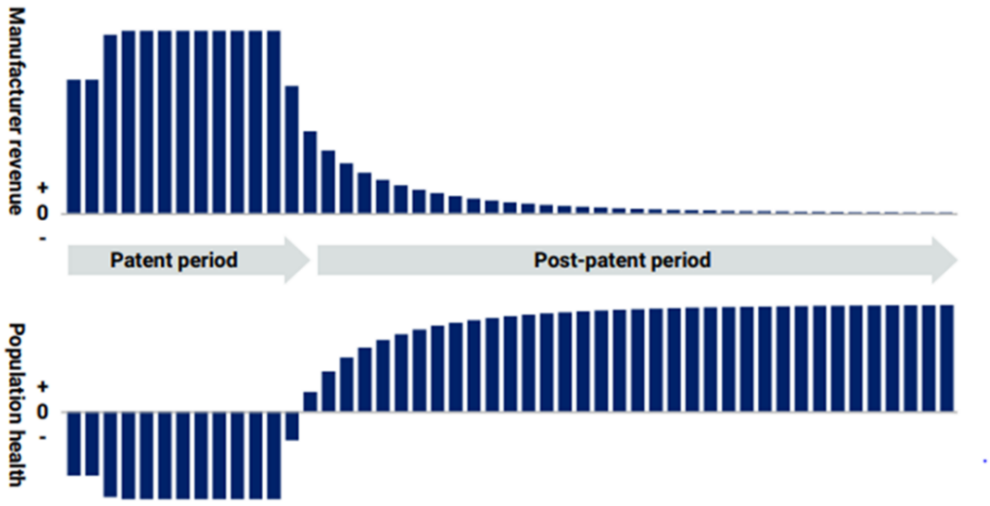
[3] https://www.oxera.com/wp-content/uploads/2019/06/Oxera-study-on-the-supply-of-generic-medicines-in-the-UK-26-June-2019.pdf

[4] NHS BSA, Prescriptions Dispensed in the Community in England: https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fnhsbsa-opendata.s3.eu-west-

Indeed, the stark NHS and population health or patient benefits provided by patent expiry and the onset of generic and biosimilar competition is presented emphatically by the country's foremost three leading academic bodies[5] on medicines policy: *"During the on-patent period, revenue mainly accrues to the manufacturer due to the drug's monopoly protection. During this period, NHS patients experience a health deficit as the new medicine's benefits are outweighed by the impact on other NHS services. After the patent period, NHS patients start receiving significant net benefits from the availability of cheaper generic or biosimilar versions of the medicine".*

The graph in the same academic study also clearly depicts the clear benefits to patients and the NHS when generic and biosimilar medicines enter the market.

Figure 2. The value profile of new pharmaceuticals from a manufacturer and NHS perspective



The UK benefits from the lowest average manufacturer selling prices in Europe[6]. This is because the UK typically enjoys high levels of competition and low barriers to entry once a marketing authorisation or medicines licence application has been secured. Having a competitive market doesn't just deliver lower prices, plurality of supply can often act as a safety net when one or more manufacturers encounter supply problems. As we shall note, data obtained from DHSC suggests that these have been slowly rising since 2022.

Around 25% of the over one billion packs of generic medicines used by the NHS each year are made in the UK. This is a high-tech industry that supports more than 26,000 good-quality jobs in a dozen major facilities around the UK. The remainder largely comes from India and the EU.

What is the supply issue situation now?

We track the incidence of supply issues based upon the data compiled by the Department of Health and Social Care and NHS England, which is then presented on the Specialist Pharmacy Service website for use by pharmacists and NHS commissioners.

The trend is towards more current supply issues. On a local level, we know that medicines shortages are among the top items of some Integrated Care Boards' risk registers. The figure during our last December 2023 analysis stood at 96 recorded supply issues covering medicinal products[7]. This appears

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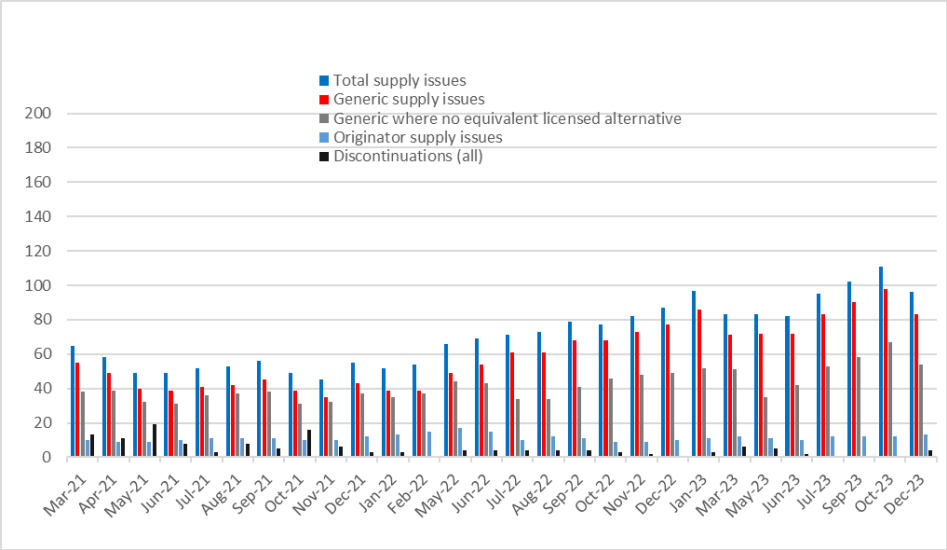
2.amazonaws.com%2Fpca%2Fpca_additional_tables_2021_22_v001.xlsx&wdOrigin=BROWSELINK

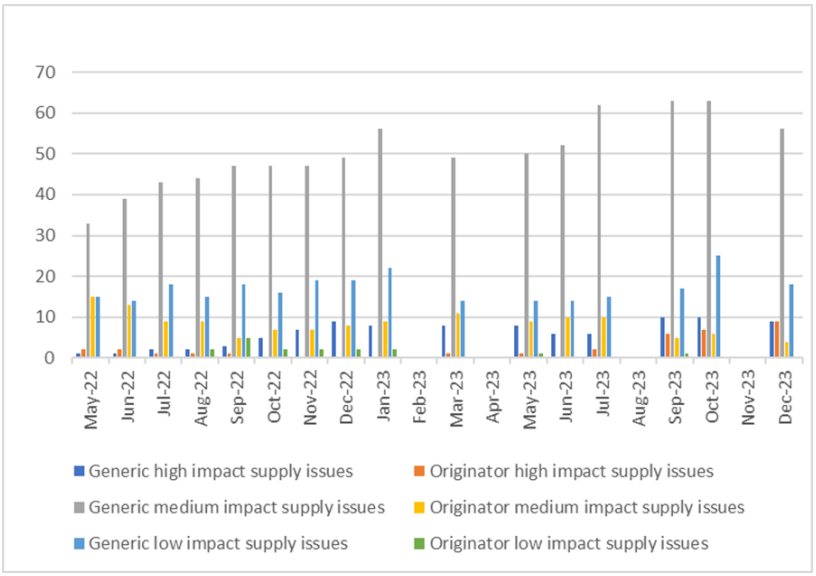
[5] The LSE, York University and the London School of Hygiene and Tropical Medicine, June 2023

[6] https://www.oxera.com/wp-content/uploads/2019/06/Oxera-study-on-the-supply-of-generic-medicines-in-the-UK-26-June-2019.pdf

reduced from an Autumn 2023 high but is still around double the lowest point in 2021. The below graph shows the number of supply issues since January 2021[8]. In both graphs below, the vertical indices track the number of medicinal products with supply issues.



The right graph categorises the level of impact upon the NHS, including potentially patients, as a result of these individual supply issues. The categorisation will depend, for example, upon the duration of the supply issue, the alternatives available in the market supplied by other suppliers, alternatives available within the same molecule, whether there are other treatments that can be used in place of the medicine under shortage, where and how the medicine is administered, whether a licensed version can be imported from another country, and the risk or potential health risks to the patient.



While the impacts upon individual patients are important and can be difficult for the person and their families and carers to manage, thankfully, this is often rare. That is largely because the DHSC, NHS and the supply chain do work effectively to minimise shortages and find additional or alternative sources. However, this can obscure the impact of supply issues and the effort this takes for the supply chain to mitigate, particularly for pharmacists. A recent example from a Local Pharmaceutical Committee in the north-east demonstrated that pharmacists could spend up to 12 hours a week sourcing replacements due to medicine shortages. This time could be spent in more productive ways supporting patients.

What processes and policies are currently in place to mitigate supply issues?

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[7] In very small instances, a molecule only is named on the SPS website and is counted as one, even where the issue with the molecule may affect more than one strength, form or pack size in which the molecule is provided.

[8] We record where there is no equivalent licensed alternative available for the pharmacist to dispense automatically. There may be alternatives such as a similar strength, a similar form of administration (capsules instead of tables) or another pack size, but this would normally require the doctor to authorise a change in script.

- There is a legal requirement for UK suppliers to notify DHSC as soon as they are aware of a shortage or potential shortage where their market share is above 20%.
- The very effective DHSC / NHS supply issues team provides a running log of current supply issues used across the NHS and by pharmacists, which note the duration and dispensing alternatives.
- The DHSC may also help expedite a company's pending marketing authorisation with MHRA to authorise a medicine that is in shortage, and it may help to expedite any customs issues in this country or using the UK Government's international embassy network.
- Parallel importers can be deployed to bring in licensed stock used in another European country, and medicines that are solutions may be made up in the UK by private or NHS-owned labs.
- Where stock is available beyond Europe, specials importers can be used to import batches into UK.
- DHSC may issue notices to stop the exportation of certain medicines for which there is a UK shortage (this does not cover specific manufacturing for export, but rather any trading of medicines that may take place at wholesaler or distributor level).
- In community pharmacy, where the price of a medicine may go up and pharmacists cannot recoup the cost of the drug plus the dispensing margin (the latter largely applies to unbranded generics as an encouragement to purchase the most cost-effective medicine from drug manufacturers on behalf of the NHS), DHSC in consultation with Community Pharmacy England may set a concessionary or temporary higher reimbursement price. This would be removed as prices start to reduce[9].
- For hospital supplied medicines, where the NHS is the direct purchaser of drugs, companies must carry 8 week buffer stocks beyond that used to meet demand for critical hospital-only medicines. There are penalties for non-supply against a framework agreement, even if the demand is higher than forecast, and there are increased reporting requirements for companies.
- A new Critical Imports Council has been established by Government that can take a strategic view on the importation of critical products including medicines.

The EU's proposed pharmaceutical package is seeking to replicate some of these reporting tools across the continent and we are seeing European countries hold more buffer stocks[10], as well as encourage more medicines manufacturing within EU through incentives.

Why are we seeing more supply issues?

We suggest further below a number of ways that the above policies and levers could be enhanced and added to. On a strategic level, falling resilience within the supply chain has been worsened because the generic and biosimilar market has not been a priority for Government, despite the huge reliance the NHS has on these medicines.

A failure to recognise the reliance of the NHS on generic medicines

Three years ago, we began explicitly warning the Government that the medicines regulator, the MHRA, was taking far longer to licence medicines than previously, effectively delaying competition and its substantial benefits to the NHS. The performance of the regulator has further deteriorated in this time, despite industry paying licence fees. Several years ago, a licence application took 12-15 months. Now a new licence takes on average 24–30 months or longer. This means that the NHS is in

[9] The extra spend on these concessionary medicines is then recouped by DHSC by very slightly dropping the reimbursement price NHS pays pharmacy for other medicines.

[10] While buffer stocks do provide added security, the more stock that is tied up in buffer stocks, the less efficient a supply chain can be in trying to resolve significant problems in one or more countries when they do arise.

some cases paying many millions more for some medicines than it could be. Delays to competition mean there are fewer suppliers in the market to pick up a supply problem, posing unnecessary and preventable risks to patients. One of our members is seeking to licence a product which is currently in shortage but that the MHRA will not fast-track. MHRA regulatory delays also prevent manufacturers making changes to their supply chains to increase capacity and speed up supply. This Autumn, action to reduce the generic and biosimilar backlog was deprioritised.

The Government launched its Life Sciences Vision in July 2021, in which we raised this issue. However, it excluded generic and biosimilar medicines – a surprising policy decision, given officials had had several discussions with the BGMA regarding the vision and the generic sector's significance and supply fragility. We wrote to the Prime Minister to state:

"Considering the Vision's commitment to 'reflect the diversity of the sector', it is astonishing that it ignores the manufacturers of four out of five medicines in the UK. This failure suggests only a narrow understanding of the UK's life sciences ecosystem – a narrowness that ultimately jeopardises the UK's medicines supply."

In September 2023, the global CEOs of the world's sixteen largest generic manufacturers wrote to the Prime Minister following the exclusion of industry from negotiating a new five-year medicines pricing agreement, called VPAG[11]:

"BGMA member companies manufacture in the UK 25% of the two million packs a day they supply to the NHS. Manufacturers must have confidence in the UK business environment to sustain and grow that direct investment in the UK. A determining factor in that confidence is the attractiveness of the UK as a Tier 1 priority market. Excluding our industry from the negotiations for VPAS, which profoundly impacts the commercial viability of many medicines and some companies in the UK, challenges your country's position as a priority market".

VPAG was agreed upon in late 2023, but since then, we are picking up reports that VPAG may include a wider list of medicines than envisaged because of an expanded definition of biological medicines including any treatments derived from living organisms. Were this to be the case, it could bring unbranded antibiotics, as well as other treatments, in competitive markets into the scope of the clawback and this could worsen the availability of some medicines.

Other reasons that we are seeing a growth in supply issues

- Manufacturer and distribution costs have risen in the last few years, reflecting rising costs for other products and services. This includes significant materials, packaging, energy and transport cost increases. As the trend of UK and global inflation eases, this may start to reduce.
- This has meant that the supply chain – at all levels from manufacturers, to wholesalers, to hospitals and community pharmacy – has sought to become more agile and efficient. This can be at the cost of reduced resilience, including carrying less stock. When a supply problem hits, this means each part of the supply chain is less able to make up the shortfall.
- In some cases, arguably longer and more complex supply chains – devised to provide the NHS with the most affordable medicines – do not always provide sufficient visibility to ensure that there is not enough time for the NHS and community pharmacies to respond to and mitigate the issue.
- In community pharmacy, we have, over the past few years seen an increase in concessionary priced products[12]. This is where DHSC provides a higher reimbursement price if the price of

[11] Voluntary Scheme for Branded Medicines Pricing, Access and Growth or VPAG
[12] https://cpe.org.uk/funding-and-reimbursement/reimbursement/price-concessions/

the product paid by pharmacy has gone up and is not sufficiently covered by the reimbursement price received by pharmacy. We understand that this increase may have happened at a similar time as the agreed overpayment to pharmacy during Covid-19 being recouped through flatter reimbursement prices, which may have exacerbated the numbers.

- NHS hospital tenders commonly do not provide sufficient time between award notice and the start date for manufacturers to make and supply the product. At least 16 weeks are needed to enable manufacturing capacity and supply to be secured to fulfil contracts. Sometimes half that or less has been provided. This increases the likelihood of supply problems.
- There is less transparency as to how suppliers gain licences and increase supply to meet demand for NHS-prescribed controlled drugs, such as those for cancer and end of life pain relief. These medicines come under the ambit of the Home Office and quotas submitted to and agreed by the International Narcotics Control Board.

What more could therefore be done to reduce shortages and lessen their impact when they do happen

- In 2024, the MHRA must prioritise a reduction of the generic licensing backlog, fund and commit to a return to most licences being determined within 12 months, and changes to existing licenses within 3 months.
- In community pharmacy, it will be important to ensure that the reimbursement that pharmacies receive from Government for the medicines they dispense commonly covers the cost of the medicine (plus the pharmacy margin).
- In hospital pharmacy:
    - It is important that tenders are awarded in good time so that suppliers can make the product for the contract duration in the right quantity. If buffer stocks are required, then that build up will take longer and that should also be factored in. Suppliers commonly need 16 weeks lead time, moving out to 20.
    - Where buffer stocks are held by contracted suppliers in other regions, incentives should be built in to encourage them to utilise these buffer stocks to fill a shortage elsewhere of another supplier. Currently, suppliers could be penalised for dipping into their buffer stock and not replenishing it quick enough that could affect future tender awards.
    - More suppliers should report supply issues to the NHS more quickly. The NHS should continue to encourage this through contract management and KPIs, and previous supply performance should become a more important factor in procurement award criteria.
- There needs to be easier links into the Home Office for suppliers to raise NHS-prescribed controlled drug shortage concerns and for issues around licensing and border control to be capable of being fast-tracked if the need arises.
- Of the life sciences manufacturing funding available[13], a greater proportion should be allocated to support (new and expanded) UK domestic production for generic and biosimilar medicines. Currently, nearly all funding is made available to originator treatments. The lack of at-scale facilities makes us less resilient to health emergencies and arguably less resilient in general.

Future issues to watch to ensure supply issues are minimised

These are issues not identified earlier, but which it will be important to monitor:

[13] In the recent Autumn Statement, the UK Government announced £520 million to support life sciences manufacturing. How this sum is distributed is not yet clear to us. Additionally, the new Investment Fund stemming from the December 2023 conclusion of a five-year branded medicines pricing scheme, VPAG, beginning in January 2024 may include £75m to support medicine manufacturing – the funding for which will come from the generics and biosimilar sectors, as well as those supplying on-patent drugs.

- The UK's exit from the EU has created challenges for supply across the UK, since the Northern Ireland Protocol threatened to separate GB supply from NI supply and render many products in NI unviable given the small volumes (the generic sector operates best at scale to achieve price efficiency). The Windsor Framework has corrected this, though all UK bound medicines have to bear the words 'UK only'. Where a batch is made for a small patient population medicine, it may be made up and packed to be supplied to the UK and other nations outside of Europe. This cannot now happen and may exacerbate products where there is small patient population.
- The NHS across GB is rightly seeking to develop plans to reduce the carbon footprint of the Health Service and the products that it procures, including medicines. We need to ensure that the ambitious targets – such as to reduce supplier emissions by 80% by 2039 in England[14] – are applied in an appropriate way. This will mean not only reducing avoidable unrecyclable packaging and the production and transport emissions which make and deliver drugs, but also to remake some medicines (green chemistry, including changing production processes, avoiding certain byproducts and minimising waste). While many manufacturers have begun this journey, it will create extra supply chain cost and complexity. Decarbonisation of the NHS supply chain must be balanced with ensuring the continued predictable and affordable supply of medicines. Greater alignment of what the NHS across the UK wants in its procurement will help to maximise both carbon reductions and cost efficiency.
- The Government has now established VPAG, a new voluntary pricing scheme for branded medicines[15]. The scheme places an annual cap on the level of NHS branded medicines spend from 2024-28 inclusive, with industry paying any overspend on the basis of the level of companies' collective annual sales. This is applied as a percentage rebate of each branded medicine prescribed on the NHS. There may be some cases where off-patent medicines are not viable with a clawback rate of up to 35% of revenues and DHSC will need to ensure that it is flexible to patient need while maintaining a robust system. As we note previously on page 5, if this scheme and its clawback on branded medicines does end up applying to classes of unbranded medicines operating in competitive markets, it could impact supply and availability.
- There is a pharmaceutical industry-wide proposal to make the Patient Information Leaflet available digitally such as through a QR code on the packaging (and for a paper version to be only provided to those who request it). There are numerous benefits, but the ePIL can help reduce shortages by allowing stock to be moved more easily between different markets.

[14] https://www.england.nhs.uk/greenernhs/a-net-zero-nhs/

[15] https://www.gov.uk/government/publications/2024-voluntary-scheme-for-branded-medicines-pricing-access-and-growth