What You Need to Know: Understanding Prescription Drug Shortages

PhRMA member companies are committed to researching and developing safe and effective medicines for patients. Our members, who manufacture branded innovative medicines, are also dedicated to maintaining quality manufacturing and working closely with the U.S Food and Drug Administration (FDA), supply chain partners and health care providers to prevent and mitigate drug shortages.

These commitments include making significant and sustained investments in the design and maintenance of all aspects of their supply chains, including quality systems for manufacturing facilities and the careful selection and oversight of suppliers such as contract manufacturing organizations. As a matter of course, innovative biopharmaceutical manufacturers prepare for unforeseen events through robust, adaptable business continuity plans to help ensure they can meet the needs of patients, prescribers, health care facilities and public health authorities who depend on their medicines.

Causes of Drug Shortages

Drug shortages can occur for many reasons, including but not limited to:

- **Production delays and delays in receiving raw materials and components from suppliers:** Disruptions in the production process can occur when there are delays in acquiring components of drug products.

  These components can be key starting materials (KSMs) which include commercially available chemical substances that are combined with other substances to form drug intermediates, active pharmaceutical ingredients (APIs), which are substances or mixtures of substances that are intended to furnish pharmacological activity or other direct effects in the diagnosis, cure, mitigation or treatment of a disease, or other key components of a finished drug product. Delays may be caused by logistical hurdles such as a limited number of suppliers, geopolitical events or complications to global transportation efficiency; all of which can have a cascading effect on manufacturing timelines and, ultimately, the availability of medicines.

- **Natural disasters and public health emergencies:** Natural disasters as well as unforeseen public health emergencies, can severely impact both production facilities and the global supply chain. These events may damage infrastructure, disrupt transportation networks or create shortages of personnel, all of which can delay manufacturing processes and hinder timely distribution of critical medicines.

- **Significant changes in demand due to shifts in supply chain, clinical practice and market dynamics:** Disruptions in the supply chain or fluctuations in market dynamics, can further complicate the forecasting and availability of medicines, potentially creating shortages or surpluses. Changes in demand to due to shifts in clinical practice can also have an impact.

Generic Drugs More Likely to Face Shortages

According to FDA data, generic drugs make up 84% of drug shortages in the United States.[i]

Generic pharmaceuticals are highly susceptible to shortages due to ongoing challenges in the generic marketplace. Manufacturers often operate on very low profit margins, making it difficult to absorb disruptions in the supply chain or necessary manufacturing improvements. The Association for Accessible Medicines notes that external factors, such as market pressures, can make producing certain generic drugs financially unsustainable.[ii] Older, sterile generic injectable drugs are especially vulnerable, as they have few manufacturers due to economic challenges and limited production capacity because they require long lead times and complex manufacturing processes.[iii] If one manufacturer faces a problem or discontinues a product, it may be difficult for others to quickly ramp up production, leading to shortages.

Business practices of supply chain intermediaries, like pharmacy benefit managers (PBMs) and their group purchasing organizations (GPOs), can worsen these challenges.

PBMs have significant control of the prescription drug market allowing them to decide what medicines people can get and what they pay out of pocket. Because PBMs are often paid based on a medicine's list price, experts say they are incentivized to exclude and slow uptake of lower-cost generics in favor of medicines with higher list prices and larger rebates. Meanwhile, consolidation in GPOs—organizations that negotiate discounts by pooling the purchasing power of multiple health care providers—can have negative impact on generic manufacturers' ability to recoup costs. These anticompetitive practices can discourage the production of generics or willingness for manufacturers to enter the market altogether.[iv]

Steps Manufacturers Take to Avoid Drug Shortages

Innovative biopharmaceutical companies have extensive measures in place to help prevent and mitigate potential drug shortages, including:

- Globally resilient supply chains to help ensure continuous supply of innovative medicines to meet patient needs.
- Robust inventory management systems that address:
  - o Data on anticipated demand reflecting historical demand and supply data;
  - o Mitigation plans for products and raw materials and the processes used for manufacturing or distribution;
  - o Logistics planning to ensure continuity in the shipping of supplies;
  - o Risk management strategies, including alternative manufacturing locations or distribution routes and channels, emergency planning for things like emergency power generation and inventory reserves and ongoing maintenance and modernization of manufacturing facilities and quality systems.

Manufacturers and the FDA: Mitigating Drug Shortages

Manufacturers and the FDA work to address the underlying causes of shortages and to mitigate and avoid potential additional shortages. Companies and FDA also work to respond to surges in demand, including expedited approval of manufacturing changes in times of public health emergencies such as the COVID-19 pandemic.

The FDA itself has taken a range of measures to help address drug shortages, including expedited reviews of new drug and biologic applications, expedited requests to facilitate expanded manufacturing capacity and exercising regulatory flexibility and discretion to increase supplies of critically needed medications. For example, when a shortage occurs and a biopharmaceutical manufacturer has inventory that is close to expiry or already expired, the FDA may work with the manufacturer to expedite the review and approval of an extended expiration date where available data supports a potential extension of the expiration date.

PhRMA's Policy Solutions for Addressing Prescription Drug Shortages

The biopharmaceutical industry supports efforts to address the root cause of long-standing prescription drug shortages. Given most drug shortages are for generic medicines, particularly generic injectable medicines, we support:

- Public policies to spur increased infrastructure investments by generic manufacturers, which may include but are not limited to consideration of guaranteed purchasing commitments.
- Public policies focused on increasing supply chain resiliency, including working with trading partners to expand regional manufacturing capacity, as well as increased federal investments and public-private partnerships to support innovation in biopharmaceutical manufacturing processes.
- Tax and other investment incentives for new manufacturing facilities and the expansion and enhancement of existing facilities.

Impact of the Inflation Reduction Act (IRA) On Drug Shortages

The generic drug market is a low margin enterprise and becoming more so. Low profit margins have driven some manufacturers out of certain generic product lines, reducing diversification of manufacturers and making these products more susceptible to shortage. One study found that 40% of generic drugs had only one manufacturer, and the median number of manufacturers per drug was just two.[v] These findings appear consistent with analysis by the FDA and others, which suggests that some drugs have gone into shortage because manufacturers do not have strong financial incentives to begin or continue to manufacture them.

The government price-setting provisions in the IRA will only exacerbate this risk because there will be even tighter margins for generics looking to enter the market when the innovator medicine is under a price control.

Former FDA Commissioner Scott Gottlieb, MD, has stated that the government price-setting provisions in the IRA, including the inflation rebate provisions, are already contributing to underinvestment in safe and sustainable generic supplies.[vi] Without sufficient volume or revenue to justify entering the market, generic manufacturers may not do so, further diminishing resilience and redundancy in the generics market.

To effectively address drug shortages, all stakeholders—including manufacturers, health care providers, regulators, and policymakers—must collaborate to strengthen supply chains, streamline production processes and ensure equitable distribution to meet patient needs. Working together is essential to create sustainable solutions and mitigate future disruptions.

i IQVIA. Drug Shortages in the U.S. 2023. Available at: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/drug-shortages-in-the-us-2023

ii AAM. Drug Shortages: Causes & Solutions. June 22, 2023. Available at: https://accessiblemeds.org/wp-content/uploads/2024/11/AAM_White_Paper_on_Drug_Shortages-06-22-2023.pdf

iii Idib

iv ASPE. Policy Considerations to Prevent Drug Shortages and Mitigate Supply Chain Vulnerabilities in the United States. https://aspe.hhs.gov/reports/preventing-shortages-supply-chain-vulnerabilities

v Berndt ER, Conti RM, Murphy SJ. The Landscape of US Generic Prescription Drug Markets, 2004-2016. National Bureau of Economic Research. 2017. https://www.nber.org/papers/w23640

vi The Hill. Drug price caps in Inflation Reduction Act exacerbating shortages, Gottlieb says. May 21, 2023. https://thehill.com/policy/healthcare/4014551-drug-price-caps-in-inflation-reduction-act-exacerbating-shortages-gottlieb-says/