U.S. Drug Shortages: Sterile Injectables

At Pfizer, we recognize that preventing and addressing drug shortages is vital to ensure patients have the treatments they need for optimal health. Manufacturers, policymakers, regulators, and others must work together with urgency to address the underlying market dynamics that create an environment ripe for drug shortages, with the goal of creating a more sustainable and supply-resilient market in which these critical and essential products are available. We urge all stakeholders to acknowledge that manufacturing high quality medicines requires a sustainable commercial model in order for this market to function reliably for patients and health care providers. Addressing the economics of this market will help bring continuity to the drug supply.

Background on Drug Shortages and Sterile Injectables

Drug shortages are defined as a period of time when the demand or projected demand for a drug exceeds the supply of the drug, which translates into patients being unable to receive needed therapies. Shortages are a continuing problem in our healthcare system and have impacted a wide range of therapies, both branded and generic, over the past decade. While drug shortages can occur in all areas of the pharmaceutical supply chain, it is particularly acute in the generic sterile injectable (GSI) market.

Generic sterile injectable medicines are critically important to patients and to the overall healthcare system, as they are used every day in intensive care units, emergency departments, and operating rooms in hospitals across the country to provide potentially lifesaving care. As a major supplier of over 600 generic sterile injectable medicines, including chemotherapies, antibiotics, parenteral nutrients, anesthetics, and many others, Pfizer is acutely aware of the market dynamics that contribute to sterile injectable drug shortages.

Challenges That Contribute to Drug Shortages

While GSI medicines are both crucial and ubiquitous in our healthcare system, they are complex, challenging, and expensive to manufacture. Pharmaceutical companies must make constant investments to meet evolving regulatory standards and to modernize facilities to maintain a high level of quality manufacturing. Increases in costs for equipment, wages, raw materials, distribution expenses, and other related inputs also contribute to making these medicines expensive to produce.

However, despite the investment required to reliably supply these important and complex products, GSI medicines are often sold at a low price compared to innovative products. Consequently, high manufacturing costs coupled with low prices often create unsustainable market dynamics that make the GSI market more susceptible to drug shortages.[1] GSI medicine prices are driven downward as a result of manufacturers having to compete for market access via a limited number of Group Purchasing Organization (GPO) contracts. GPOs purchase GSI medicines on behalf of hospitals, and often focus on securing the lowest-price product as the sole criterion for awarding a contract to a manufacturer. [2] Significant consolidation among GPOs and wholesalers has created a limited number of buyers who wield enormous power over manufacturers because of their market reach. Three GPOs cover over 90% of U.S. hospitals, down from at least six in the past decade alone; in addition,

[1] According to recent research from IQVIA, shortages are more common for medicines with very low list prices.
[2] Hospitals are reimbursed through Medicare Part A for GSI medicines as part of an overall diagnosis related group capitated cost, thus hospitals working through GPOs have an incentive to secure the lowest price possible for GSI medicines.

three primary wholesalers manage all the distribution. [3] Since generic medicines are often interchangeable, they mainly compete on price alone. Focusing only on price has incentivized GPOs and wholesalers to prioritize cost-cutting measures with little regard for the impact on long-term sterile injectable supply and consequent continuity of patient care. Moreover, manufacturers, even after cutting prices to obtain favorable market access, are unable to rely on a consistent volume over the term of the contract, as GPOs are permitted to contract with other manufacturers if they offer a lower price.

As a result of these market dynamics, GSI medicine manufacturers often exit the market when they are not awarded a contract or when prices fall to a point where manufacturers can no longer make the required investments to maintain quality manufacturing standards to produce GSI medicines. With fewer, or in some cases only one, manufacturers remaining in the market for a given product, it only takes one problem or issue to arise, whether it's, for example, a quality concern, a natural disaster, or a raw material supply issue, to cause a drug shortage.

Solutions to Help Prevent and Address Shortages

Pfizer is deeply concerned about drug shortages and the impact on patients and the health care system overall. We work to provide patients with a consistent and reliable supply of high-quality medicines and make the investments of time and resources to meet our goal of full recovery when shortages occur even when those shortages occur due to another manufacturer's supply situation. We urge all stakeholders to acknowledge that manufacturing high-quality medicines requires a sustainable commercial model in order for this market to function reliably for patients and health care providers. Addressing the economics of this market will help bring continuity to the drug supply. We will continue to work with policymakers to mitigate drug shortages and advance long-term policy solutions.

Improve the Long-Term Sustainability of the Generic Sterile Injectables Market

- *Targeted payment reforms in Medicare & Medicaid:* Payers, including the Medicare and Medicaid programs, can play a key role in supporting a more sustainable market for GSIs by evolving reimbursement systems that impact these medicines.

- *Exempt GSIs from government mandated discounts* such as the 340B Drug Pricing Program and the price inflation penalties established by the Inflation Reduction Act for medicines to prevent continued erosion of already unsustainable margins.

- *Establish requirements for long-term contracting and limitations on off-contract purchasing* to provide greater demand certainty for manufacturers. It is critical to find ways to ensure volume commitments in contracts to give manufacturers greater predictability, such as bonus payments to hospitals that engage in contracting procedures that support supply reliability. Procedures that should be considered include minimum contract terms, ensuring a certain percentage of volume is purchased over the term of the contract, and a limit on off-contract purchasing.

- *Require redundant or contingent suppliers,* especially for essential medicines. Sole-source contracts should be avoided for medicines on the FDA essentials medicine list to ensure there are multiple suppliers to accommodate demand increases or absorb a disruption that may occur with one manufacturer.

[3] Amid drug shortages, FTC to probe the role of middlemen - STAT (statnews.com)

Establish Manufacturing Incentives for Generic Sterile Injectables

- *Federal grants for manufacturing infrastructure upgrades* and increased public-private partnerships can serve a key role in enhancing U.S. manufacturing infrastructure and help avoid shortages. Given the costs and timeframes for building, expanding, or modernizing domestic manufacturing capabilities and processes, funding levels should be realistically set along with transparent criteria that permits all companies, regardless of size, to be rewarded grants.

- *Federal funding for the cost of direct loans and loan guarantees* could play a key role in supporting increased U.S. investments by vendors and suppliers, notably including those involved in active pharmaceutical ingredient (API) manufacturing for products with low economic viability. However, it is unrealistic that any one country can take on all aspects of domestic manufacturing, and it is critical to preserve a global supply chain to ensure flexibility and resiliency.

Continue FDA Regulatory Modernization

- *Continued FDA regulatory modernization efforts* are needed to address shortages by fostering approaches that leverage flexibility and acceleration of approvals for new manufacturing processes and sites.

- *International regulatory harmonization and reliance* is needed to reflect that medicine development, manufacturing, and distribution is a global enterprise. Manufacturers operate in an environment of varying and sometimes conflicting global regulatory requirements which may contribute to or exacerbate shortages. FDA should continue in its leadership role in the International Conference on Harmonization (ICH) and other forums to build on current progress, particularly for post-approval changes to manufacturing. Additionally, FDA should further expand mutual recognition agreements (MRAs) with mature global regulatory authorities to rely on inspection findings and respond more efficiently to shortages.

- *Encourage the adoption of innovative manufacturing technologies* which hold great promise in addressing some of the most challenging issues in medicine production. Currently, FDA only reviews manufacturing technologies with binding feedback to medicine sponsors during product-specific meetings or the review of a medicine or biologic application. This practice creates additional risk for sponsors using a new method of manufacturing across multiple product lines, and, therefore, disincentivizes adoption. Pfizer believes that programs such as FDA's newly announced Advanced Manufacturing Designation Program are a step in the right direction in this area, as it will create new pathways for sponsors to implement modern manufacturing processes that can help create a more resilient supply of medicines.[4]

Ensure Flexible and Resilient Global Supply Chains

[4] Advanced Manufacturing Technologies Designation Program (fda.gov)

- *Trade and cross-border policies need to ensure that supply chains are flexible* and provide for the efficient movement of raw materials and finished products. No single country can produce every health product it needs, so uninterrupted supply chains across borders are critical to global health security.

- *The US government should take steps to help manufacturers develop strategic alliances* and partnerships to improve resilience. For example, the Medical Supply Chain Resiliency Act would create a framework for the United States to negotiate agreements with trusted allies to address barriers to investment and trade in medical goods and inputs to medicine manufacturing and promote greater regulatory harmonization. [5]

- *Ensure government policies build trust* – including government-to-government agreements that enable innovation, manufacturing, and the free flow of goods across borders. They create the security, predictability, and trust that allows companies to partner and swiftly scale up in a crisis.

Additional Policy Proposals

- *Physical and virtual inventory buffers* have been recommended in several recent policy proposals; if implemented appropriately they can support supply chain resilience.
    - Regarding API and raw materials, government financing of surpluses is needed for API and other supplies to support surge manufacturing capacity in the event of a shortage. These inventories should be aggregated and reported at an anonymized industry level.
    - Regarding finished product buffer inventories, Pfizer believes there is potential for these to be helpful, as most supply disruptions of essential products tend to be short-term and can be mitigated through inventory buffers. Pfizer believes that wholesalers or distributors are best positioned to hold buffer inventory given their existing warehousing capabilities. Mandating buffer inventories to be held by either manufacturers or hospitals would lead to substantial increased costs for storage needs, creating additional financial exposure to manufacturers and hospitals, and could unintentionally incentivize excessive stockpiling by hospitals which could exacerbate supply challenges.

- *Hospital incentives to purchase from quality suppliers* have been discussed using manufacturer quality score cards so that GPOs and hospitals can better select suppliers on their ability to uphold supply agreements; however, this may not be sufficient to move purchasing away from considerations based solely on price. Moreover, careful consideration would be required to determine how a quality scoring system should be established to ensure overall fairness, that manufacturers are not unduly burdened, and that metrics used appropriately reflect manufacturing quality.

[5] Text - S.2115 - 118th Congress (2023-2024): Medical Supply Chain Resiliency Act | Congress.gov | Library of Congress