INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION

Preserving Sustainable Competition and Preventing Medicines Shortages

Comments from The International Generic and Biosimilar Medicines Association (IGBA) regarding FDA-2018-N-3272: Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions.

Long-term sustainability of the generic medicines industry is crucial to global public health and affordable, quality care. Each year, generic medicines provide consumers and citizens hundreds of billions of dollars in direct savings. Policymakers and advocates play an important role in preserving the environment that has allowed generic medicines companies to compete in the marketplace and bring accessible medicines to patients around the world.

The International Generic and Biosimilar Medicines Association (IGBA), representing member associations from the United States (AAM), Canada (CGPA), South Africa (GBMSA), India (IPA), Jordan (JAPM), Japan (JGA), Europe (Medicines for Europe) and Taiwan (TGPA), as well as associate member associations from Australia (GBMA), Brazil (ProGenericos), Mexico (AMEGI), Malaysia (MOPI) and Saudi Arabia (NCPI), very much applauds the United States (U.S.) Food and Drug Administration for its commitment to developing policy solutions to address shortages.

Access to medicine is an indispensable part of modern health care and ensuring healthy societies. However, medicines shortages have been reported across the globe, with increasing frequency. The U.S. is not unique in its experience with drug shortages, nor are the causes particular to the U.S. system. The drug supply chain is highly globalized and accordingly, FDA should consider how U.S. market challenges fit within global conditions. Although FDA's principal concern is for U.S. citizens, IGBA believes that medicines shortages are a global problem that needs to be tackled at a global level.

Shortages occur due to market conditions and policies that deflate the price of generic medicines below reasonable levels. If price falls below the break-even point, the most efficient manufacturer may have to exit the market, leading to a loss in supply. Even shortages due to manufacturing issues can be explained by economic forces that threaten the sustainability of the generic medicines industry as a whole; if the manufacturer elects to stay in a price-deflated market, lost revenues could lead to foregoing investment in facilities, putting the plant at greater risk for future manufacturing problems.

It is now increasingly recognized by both generic manufacturers and by key regulators [including the U.S. FDA, the United Kingdom (UK) MHRA, the German BfArM, the European Union (EU) EMA and the United Nations' WHO] that the biggest risks lie with injectable medicines required for essential anti-infective and oncology treatment. This type of production is particularly complex from both a

manufacturing and a regulatory compliance perspective and is highly consolidated at a global level. The reality is that there is limited incentive for manufacturers to invest further in increasing global supply under the current market conditions. A manufacturing problem in any part of the world can destabilize the supply of critical medicines other global regions. Recent domestic policy changes in China, where many active ingredients and intermediates are manufactured, have generated major supply constraints globally. For example, the Access to Medicine Foundation found that an explosion at a Chinese factory led to shortages of a critical intravenous antibiotic in the UK.[1] This experience shows us that there is a need to rethink the incentives – especially in major markets around the globe – to invest in greater capacity to supply essential medicines for public health.

Shortages are therefore a symptom of a fundamental sustainability challenge currently facing all generic drug manufacturers. Deflationary pricing and inflated costs result from global consolidation, regulatory barriers and insufficient or misguided government policy. While these forces take different forms in particular nations and markets, the detrimental effect on sustainability is universal.

Supply Chain Bottlenecks

The generic medicines industry is characterized by a large manufacturing base on one side, and a large patient population on the other. However, medicines are delivered to patients through a complex supply chain, passing through channels controlled by a small number of market actors. It is well established that a small number of buyers dealing with a large number of sellers possess market power and the ability to greatly influence – if not dictate – prices.

In the U.S., wholesalers' market power has deflated prices and created unsustainable incentives for manufacturers. Suppliers are often faced with decisions that narrow the manufacturing base (exit or merge), which increases the likelihood of shortages.[2] This dynamic occurs in the U.S. in part because only three wholesalers control nearly 90 percent of the market; in Europe, single-winner tendering and reference pricing function in much the same way, creating a bottleneck that reduces or eliminates market entry incentives. In Europe, many major national markets are now relying on one or two suppliers of essential medicines. Should those suppliers face a manufacturing issue, this would have a

[1] "Shortages, stockouts and scarcity: the issues facing the security of antibiotic supply and the role for pharmaceutical companies," Access to Medicine Foundation, 31 May 2018. Accessible at: https://accesstomedicinefoundation.org/publications/shortages-stockouts-and-scarcity-the-issues-facing-the-security-of-antibiotic-supply-and-the-role-for-pharmaceutical-companies

[2] According to the World Health Organization, a supplier base of at least three manufacturers per product is desirable to minimize the potential for medicines shortages. Medicines Shortages. WHO Drug Information. Volume 30, No. 2. 2016. Accessible at: http://apps.who.int/medicinedocs/documents/s22463en/s22463en.pdf.

negative effect on supplies in the rest of Europe and possibly even in the U.S. and other major global markets.

Many countries in Europe use tendering to award exclusive contracts to a small number of suppliers, or in some cases, a single supplier. This approach, well-intentioned to control the state's health care costs, crowds out other suppliers who might otherwise provide redundancy that reduces the risk of shortages. (Suppliers who do not win contracts are more likely to exit the market, unable to achieve sufficient scale based on remaining demand outside tendering agreements.) If tender winners experience manufacturing or other problems that affect their ability to produce the correct output, a shortage can occur. These policies can easily be changed by introducing criteria to ensure that multiple manufacturers can compete in procurement systems as was recently demonstrated by the multi-winner tender systems introduced in Italy and the UK to ensure long term competition and security of supply.

Manufacturers who choose not to exit a price-deflated market are stretched to their limit; it is not uncommon for generic companies to maintain a portfolio that contains some unprofitable products. Needless to say, a market cannot thrive under conditions that limit participants' ability to meet demand with adequate supply and hinder necessary investment in capital.

Regulatory Barriers

Regulatory barriers both obstruct entry and inflate costs. The generic medicines industry is accustomed to struggling with long lead times, country-specific regulatory requirements, and changing standards over time. However, if regulations are redundant between geographies or overly burdensome, it can increase the barrier to entry, resulting in too few manufacturers being willing or able to overcome that barrier. Additionally, recurring regulatory costs exacerbate deflationary pricing and threaten sustainability. Again, this phenomenon is not unique to the U.S.

More global convergence of regulatory systems would allow suppliers to enter more markets, reducing redundancy of requirements without compromising safety. Less complicated market entry would allow manufacturers to offset the "crowding out" posed by tendering with economies of scale achieved across several countries. Quickly responding to a shortage would also be more feasible under global harmonization. There are two concrete opportunities available to advance this construct. First, agree and fully implement GMP mutual recognition systems (like the EU-U.S. or EU-Canada agreements), which enable regulators to focus resources more efficiently. Second, advance progress on global development, which has already started on biosimilar development between the EU and the U.S. Such a system should be fully implemented for biosimilars and a similar policy should be developed for complex chemical products. This bilateral progress can later serve as a basis for global approaches (at least between countries with a high degree of regulation).

Chilly Competition Due to Insufficient or Misguided Policy

The generic medicines industry depends on policymakers who respond to a dynamic environment with polices that protect competition so that affordable medicines can continue to benefit society. When an imbalance occurs between innovation and access, policy must be swift and effective to correct course.

Patients are harmed when affordable generic medicines are unable to compete with expensive brand names in the marketplace. Strategic tactics by brands to block generic entry change over time, but consistently, this conduct increases litigation costs for generics companies, delays patients' access to

affordable drugs, leaves significant budgetary savings unrealized, and diverts regulators' precious resources from actions that would more efficiently benefit patients. Although these outcomes are a result of specific conduct by other firms, if left unchecked, the consequences are familiar: barriers to entry, a diminished manufacturing base, increased risk of shortages, and a negative impact on public health. Our industry is clearly experiencing these challenges today in the U.S., Canada and in parts of Europe, where the originator industry is using highly questionable strategies to delay competition from complex generics, value-added medicines and biosimilar medicines. These strategies undermine the competitiveness of our industry's massive investments in complex follow-on competition and limit our ability to keep older products on the market. Governments should take clear corrective action against all forms of ever-greening and restore healthy competition.

Governments should also resist increasing intellectual property standards in international trade agreements. These provisions delay or prevent market entry of generics and biosimilars around the globe, further damaging the viability of the generic and biosimilars medicines industries. The recently negotiated U.S.-Mexico-Canada Agreement is a prime example of this kind of anti-competitive increase in IP standards, which will have a significant detrimental impact on the generic and biosimilar medicines industries in those three countries and in all other countries where the affected companies do business. There are currently three trade agreement negotiations underway by the U.S., six by the European Union, and three by the European Free Trade Association. In each of these agreements, brand drug and biologic companies will seek to increase their monopolies, detrimentally impacting generic and biosimilar companies and the patients who need access to high quality affordable medicines, and further increasing the likelihood and number of shortages.

Following widespread media attention on the high cost of prescription drugs in the U.S., policies intended to make medicines more affordable have thus far targeted the generic medicines industry, a massive source of savings, rather than the brand industry, which is the overwhelming driver of drug spending. In 2017, generic medicines filled 90 percent of prescriptions but comprised only 23 percent of all U.S. drug spending, while brands accounted for 77 percent of costs while covering only 10 percent of prescriptions. Policies that aim to save money by targeting generics are paradoxical; not

only do these policies ignore the true cost-drivers, but they could unintentionally push cost-saving companies out of the market. In order to sustain the savings that generics bring forth, political leaders need to base policies on an understanding of the dynamics and challenges facing the market.

In Europe, governments have finally embraced the opportunity of biosimilar medicines competition (which is increasing access to biological medicines by 50-200 percent depending on the country) but there are still major gaps in the system. First, southern European countries with low generic penetration are slow to establish more effective generic prescribing policies. Second, hospital procurement and reference pricing laws are leading to extreme consolidation of suppliers on the market. This is a recipe for unsustainability and more risks of shortages.

The generic and biosimilar medicines industries have demonstrated over decades that access to quality medicines drive sustainable healthcare and better prevention of disease. But this industry can only deliver on these important public health objectives in a competitive environment that encourages and rewards a robust base of manufacturers that invests in new products and capacity. Responsive and well-crafted policy has the ability to balance innovation and access for a sustainable, healthy generic drug market. Timely and sufficient action to address unfair competitive conditions, in the U.S. and around the world, is essential to ensuring the sustained availability of affordable generic medicines.

About IGBA

The International Generic Pharmaceutical Alliance (IGPA) was founded in March 1997 as an international network of generic medicines associations. To reflect the evolving nature of the industry, in late 2015, IGPA incorporated under Swiss Law, and at the same time changed the name of the organization to the International Generic and Biosimilar Medicines Association (IGBA).

IGBA is committed to promoting generic and biosimilar medicines by exchanging information worldwide through constant dialogue with the ICH, WHO, WTO, WIPO and other international organization.

IGBA consists of the following associations:

- Association for Accessible Medicines (AAM-USA)
- Canadian Generic Pharmaceutical Association (CGPA-Canada)
- Generic & Biosimilar Medicines Southern Africa (GBM-Southern Africa)
- Japan Generic Medicines Association (JGA-Japan)
- Jordanian Association of Pharmaceutical Manufacturers (JAPM-Jordan)
- Indian Pharmaceutical Alliance (IPA-India)
- Medicines for Europe (Europe)
- Taiwan Generic Pharmaceutical Association (TGPA-Taiwan)
- In addition, the generic medicines associations of Australia, Mexico, Malaysia, Saudi Arabia, and Brazil are Associate Members