

Shortages of medicines: a complex global challenge

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Shortages of essential medicines, among them generic injectable chemotherapy agents, are causing increasing concern in the United States of America (USA).^{1,2} However, the problem is far wider, affecting other classes of medicines including injectable anaesthetic agents, such as propofol, intravenous nutrition and electrolyte products, enzyme replacement products and radiopharmaceuticals.³⁻⁵ Medicine shortages have also been noted in Australia and Canada.^{6,7} A recent commentary in a Belgian pharmacy journal claims that the problem is global – “from Afghanistan to Zimbabwe” – listing 21 countries affected by a variety of supply problems.⁸ A shortage of the injectable antibiotic streptomycin was reported in 15 countries in 2010, with 11 more countries predicting their stocks would run out before they could be replenished.⁹

This problem does not seem to be that new: concern about prescription medicine shortages was raised in the USA at least a decade ago.¹⁰ The American Society of Health-System Pharmacists' web site (available at: <http://www.ashp.org>) shows 208 products were not available, with another 114 shortages resolved and 21 products removed from the market in the USA (as of 9 December 2011). A November 2011 report from the IMS Institute for Healthcare Informatics showed that medicine shortages in the USA were concentrated in just five disease areas (oncology, anti-infectives, cardiovascular, central nervous system and pain management) and that more than 80% involved generic injectables.¹¹ However, on a global scale, other markets may be particularly “fragile”, failing to meet demands for suitable products, such as paediatric dosage forms for HIV/AIDS and tuberculosis.¹²

There is a wide range of causes for medicine supply shortages, some of which could be dealt with by government agencies. However, no medicines' regulatory agency can mandate that a manufacturer produce a specific product. Manufacturing quality problems have been implicated in shortages of products produced by a limited number of suppliers, such as

propofol,³ imiglucerase and agalsidase β and influenza vaccine.¹⁰ Overall, 43% of 127 shortages investigated by the United States Food and Drug Administration were attributed to manufacturing quality problems.¹³ Where manufacturing is dependent on a small number of facilities, shut-downs for various reasons may cause problems, as has been the case with some radiopharmaceuticals.⁵ Changes in procurement practices (such as insistence on World Health Organization prequalification status or registration with a stringent regulatory authority) may invalidate a previous supplier, as happened with streptomycin.⁹

Increased global demand, consolidation of generic production at a few sites, and changes in regulatory standards requiring upgrading of manufacturing plants are all possible reasons for shortages of injectable generic medicines in the USA.² The IMS Institute for Healthcare Informatics report showed that two-thirds of the products with supply problems only had three or fewer suppliers.¹¹ Gatesman and Smith have claimed that “the main cause of drug shortages is economic”, pointing particularly to perverse consequences of Medicare reimbursement policies, which have discouraged the use of low-cost generic chemotherapy agents; however, this assertion remains to be proven.¹ A report by the United States Department of Health and Human Services blamed “a substantial expansion in the scope and volume of products produced by the industry that has occurred over a short period of time, without a corresponding expansion in manufacturing capacity”.¹⁴ It pointed out that manufacturing capacity took time to establish, and that existing manufacturers appeared to be making “strategic decisions about where to deploy production capacity”. However, the causes of some shortages have not been identified.

In September 2011, the Council of the International Pharmaceutical Federation called on “all stakeholders, including governments, pharmaceutical manufacturers, pharmacy wholesalers, pharmaceutical

purchasing agencies, medicine insurance plans, pharmaceutical regulators and the pharmacy profession to urgently evaluate these issues and work to ensure continuity of medication supply so that the appropriate treatment of patients can be initiated and maintained”.¹⁵ The United States Food and Drug Administration states on its web site that it cannot require firms to report the reason for shortage or duration of the shortage or any other information about shortages. Draft legislation to address this issue has been brought forward in both houses of the United States Congress.^{16,17} A similar resource has been developed for Canada.⁷ However, a longer-term solution may lie in careful policy-making that avoids winner-takes-all procurement decisions, that promotes the development of a sustainable local and global pharmaceutical manufacturing capacity, and that identifies and protects particularly fragile markets. While there have been predictable libertarian calls for lifting price controls to promote investment,¹⁸ governments have a responsibility not only to ensure the quality of medicines and access to essential medicines, but also to create the necessary conditions for a sustainable, productive and responsible pharmaceutical industry. In this case, *laissez faire* will not suffice. ■

Acknowledgements

Both authors are office-bearers of the International Pharmaceutical Federation (FIP).

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