Similarly, patients with arterial clots might be pretreated with aspirin or the blood clot preventer Plavix (clopidogrel, Bristol-Myers Squibb and Sanofi), and those with vasospasm could be started on nitrates to open up the artery.

The suspension of ponatinib also raises questions about whether the accelerated approval process exposes patients to excessive risk. However, it appears as if the process worked well in this case, says Milne.

“This issue only came to the FDA’s attention a few weeks ago, and they acted on it quickly,” he says. “It shows that they are increasing the ways they can make decisions in the post-marketing scenario.”

**Strategic Plan Aims to Curb Drug Shortages**

The U.S. Food and Drug Administration (FDA) has released a strategic plan to strengthen its response to imminent and existing drug shortages, as well as a proposed rule requiring manufacturers of drugs and biologics to alert the agency to the impending discontinuation of any products or interruptions in manufacturing that could deplete supply.

The “Strategic Plan for Preventing and Mitigating Drug Shortages,” released on October 31, explains that early notification of manufacturing disruptions gives the FDA time to work with drug companies to help resolve such disruptions, identify other companies that might be able to increase production, and expedite inspections and reviews of product submissions from drugmakers that might help prevent or ease shortages.

The plan also calls for incentives for manufacturers to improve the quality of their drugs and facilities.

“The FDA can only do so much,” says Erin Fox, PharmD, director of the drug information service at University of Utah Health Care in Salt Lake City. “We know that many of the ongoing problems are related to poor manufacturing quality and companies not investing in their factories over time.”

One manufacturer, Ben Venue Laboratories in Bedford, OH, announced in October that it would permanently cease all drug production by the end of 2013. The company had halted production and spent more than $350 million since 2010 to repair and upgrade its facilities, but declared that the ongoing investment needed to overcome its challenges is too great for it to continue.

“That took away some of the hope that some of the shortages are going to be resolved quickly,” says Fox. She notes that Ben Venue was the only U.S. manufacturer of thiopeta, which is used to treat ovarian, breast, and bladder cancers and lymphomas. For now, the FDA is allowing an imported replacement, the brand-name drug Tepadin, from Italian drugmaker Adienne, although the logistics of purchasing it further complicate the situation. The proposed rule, released on the same day as the strategic plan, implements the early notification requirements included in the 2012 Food and Drug Administration Safety and Innovation Act. It requires manufacturers to alert the agency about potential drug shortages at least 6 months prior to permanently discontinuing a drug or interrupting its production. If that isn’t possible, manufacturers should do so “as soon as practicable” but no later than 5 days after the disruption. The proposed rule also spells out the types of products covered and the information to be reported.

Unlike an interim rule currently in force, the proposed rule would extend to manufacturers of biologic products, such as monoclonal antibody products and vaccines.

Janis Abkowitz, MD, president of the American Society of Hematology, applauded the inclusion of both drugs and biologics in the proposed rule. Shortages, she says, have been particularly troublesome for hematologists because “many of the drugs most vulnerable to shortages—older, generic sterile injectables—are used to treat blood disorders,” including cancer.

Early alerts about possible disruptions in drug supplies since 2011 have helped prevent some shortages. In 2012, shortages of more than 280 drugs were averted, and reports of new shortages dropped to 117, from 250 the previous year.

At the end of September, says Fox, 294 drugs were in short supply, 31 of which were cancer drugs.
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