FDA/CDER SBIA CHRONICLES
MAY 15TH, 2014

Drug Shortages – Make an Impact

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Saline. Trace Elements. Zinc injection. Nitroglycerin. Propofol. Cyanocobalamin. Methylphenidate. Leucovorin. And the list goes on. The common denominator? These drugs are all needed to address serious medical conditions, and have all experienced supply issues. The reasons or causes for drug shortages are wide in range, and solutions vary for each situation. However, with the help of the pharmaceutical industry, FDA can make breakthroughs in preventing and resolving drug shortages.

The Problem: FDA is concerned about the high incidences of drug shortages in the U.S., especially for drugs that are manufactured by a few firms and lack optimal therapeutic substitutes in adequate supply. Shortages may involve drugs that address serious medical conditions, which can translate into delaying or denying much needed patient care. Shortages may also cause physicians to prescribe second-line alternatives that may be less effective and at higher risk than first-line therapies.

The source of drug shortages may include: product quality concerns, manufacturing problems, difficulty in acquiring component parts or active pharmaceutical ingredients, increases in demand, or shipping delays.

Industry Assistance: The number of drug shortages increased from 62 in 2005, to 178 in 2010, to 251 in 2011. This increase was concerning to FDA. After working with stakeholders to discuss the issue, FDA took action. This resulted in a decrease to 117 shortages in 2012 and a further decrease to 44 new shortages in 2013. Manufacturers can play a critical role in decreasing the impact of shortages by notifying FDA of incidents that may result in a drug shortage or potential disruption in supply. Preventing drug shortages has been, and continues to be, a top priority for FDA. In 2011, early notification by manufacturers allowed the FDA to help prevent shortages of 195 drugs. That number rose to 282 in 2012, and in 2013 there were 170 prevented shortages.

The FDA Safety and Innovation Act (FDASIA) of 2012 requires all manufacturers of covered drugs to notify FDA of potential discontinuances. The prior law applies only to sole manufacturers. Manufacturers are required to report information about shortages to FDA, and are required to report the reasons for shortages and the expected duration of shortages on the FDA website. Title X of FDASIA lists the mandatory reporting requirements for manufacturers. FDASIA makes clear that manufacturers are required to report discontinuances to FDA regardless of whether they intend to discontinue the product permanently, or are facing only a temporary interruption of supply, at least 6 months prior or as soon as practicable.

FDA published a proposed rule for public comment in November 2013 to help implement FDASIA's expanded notification requirements. Among other things, the proposed rule would extend the notification requirement to most manufacturers of biological products. Manufacturers should notify the Agency as soon as they become aware of an issue that may result in a potential supply disruption.

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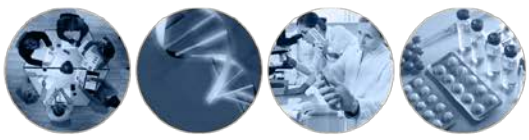

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FDA also encourages:

- Maintenance of compliance with current good manufacturing practice (CGMP) requirements and ensuring that suppliers of ingredients, components, and substances used in the manufacture of the products meet standards of safety and quality sufficient to ensure that the final drug or biological product is safe and effective
- Implementation of well-defined risk management systems at all layers of the supply chain, and continuous evaluation and investment in manufacturing operations, and
- Contingency planning by manufacturers.

If your firm would like to source any drugs in shortage in the U.S., please send the following information to the Drug Shortages Staff (drugshortages@fda.hhs.gov) for consideration:

- List of products available
- Address of manufacturing facility
- Whether the facility has been inspected by FDA
- Contact information

FDA's Role: The Drug Shortage Staff (DSS) within the CDER Immediate Office works closely with many FDA offices, outside experts and drug manufacturers to help prevent, alleviate or resolve drug shortages so medically necessary drug products are available for healthcare professionals and patients. Once the DSS becomes aware of a potential drug shortage, they work with pharmaceutical manufacturers to manage the shortage. For products that are in shortage or may progress to a shortage, FDA may expedite review of submissions from manufacturers. These submissions may support a marketing application for a new product (a New Drug Application (NDA) or Abbreviated New Drug Application (ANDA)), or may support manufacturing changes for existing products (for example, a supplemental application for a new manufacturing site). In addition, FDA may:

- Help drug firms qualify additional manufacturing sites or raw material supplies, if those drug firms are interested in having additional manufacturing capacity;
- Identify alternate manufacturers who can initiate or increase production;
- Help manufacturers qualify new or additional sources of raw materials;
- Advise/consult with drug firms on resolution of manufacturing issues
- Use temporary enforcement discretion for alternate sources of drug products, after ensuring the drug does not pose undue risks for U.S. patients, and ensuring it is manufactured in a facility that meets FDA quality standards.
- Approve extended dating to help increase supplies until new production is available.
- Discuss with industry contingency plans for additional manufacturing sites, production lines, and suppliers
- Meet with new companies interested in making drugs that are vulnerable to shortage.

By working closely with manufacturers who are experiencing problems, as well as potential alternative manufacturers, and by exercising regulatory flexibility in appropriate cases, FDA has had a substantial positive impact on the shortage situation. And industry plays a critical role in helping FDA to prevent and control drug shortages.

Until summer,
Renu Lal, Pharm.D.
CDER Small Business and Industry Assistance

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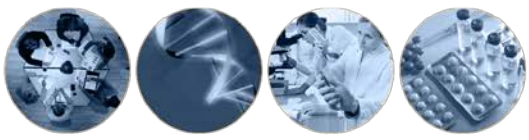

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