December 2017

GENERIC DRUGS

FDA Should Make Public Its Plans to Issue and Revise Guidance on Nonbiological Complex Drugs

GAO Highlights

Highlights of GAO-18-80, a report to congressional requesters

Why GAO Did This Study

Generic versions of brand-name drugs provide substantial cost savings for patients and the U.S. health care system. FDA, an agency within the Department of Health and Human Services (HHS), has approved generic versions of NBCDs. Some industry stakeholders have asserted that, because it is difficult to assess equivalence for these complex drugs, there could be safety and efficacy problems that might not appear until after generic versions are on the market.

GAO was asked to assess FDA's process for reviewing generic versions of NBCDs. Among other things, this report (1) identifies the scientific challenges the review of generic versions of NBCDs may present and (2) identifies and evaluates the steps FDA has taken that may help address the challenges related to the review of generic NBCDs. GAO studied the literature and examined FDA product-specific guidance. GAO reviewed information related to the five NBCDs for which FDA had approved a generic version prior to fiscal year 2017. GAO also interviewed FDA officials and a nongeneralizable selection of 19 stakeholders, including brand-name drug sponsors, sponsors of generic versions of NBCDs that have and have not received FDA approval, and external expert groups.

What GAO Recommends

FDA should announce its plans to issue and revise product-specific guidance for drugs that are nonbiological and complex. HHS concurred with GAO's recommendations.

View GAO-18-80. For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov

What GAO Found

Certain drugs, referred to as nonbiological complex drugs (NBCD), have a more complex chemical structure than most other drugs. As a result, it can be more difficult to identify the physical and chemical properties of these NBCDs and, thus, more difficult to demonstrate that generic versions of these drugs are equivalent to their brand-name counterparts—a requirement for their approval by the Food and Drug Administration (FDA). To assess the equivalence of generic versions of NBCDs, drug company sponsors and FDA may need to take more steps compared with generic versions of noncomplex drugs. All but 2 of the 19 stakeholders GAO interviewed agreed that it is challenging to demonstrate equivalence. However, they disagreed about the extent of the challenges and whether those challenges could be overcome. For example, while some brand-name drug sponsors suggest it may be impossible to show that the active ingredient is equivalent between a brand-name and generic complex drug, some generic drug sponsors believe it can be done through advanced scientific methods.

GAO identified several steps that have been taken that may help address the challenges associated with reviews to determine equivalence of generic NBCDs to their brand-name counterparts. However, stakeholders disagreed about whether these steps have been sufficient. For example, to facilitate the entry of generic drugs on the market, including NBCDs, FDA issued product-specific guidance documents to industry, providing recommendations on how to demonstrate equivalence for certain products. While some stakeholders cited product-specific guidance as helpful, representatives of four brand sponsors said the guidance does not adequately address the scientific complexities of NBCDs. Further, guidance for some NBCDs was revised numerous times without any advance notification to industry, according to representatives of generic drug sponsors. Internal control standards for the federal government on communication state that sharing quality information with external parties is necessary to achieve an entity's objectives. FDA's good guidance practices regulation also specifies that the agency will publish a list of possible topics for guidance development or revision for the next year.

Although FDA publishes such a list annually, it does not include product-specific guidance documents. The lack of advance communication on guidance issuance and subsequent revisions can create setbacks for generic drug sponsors. For example, according to such sponsors, it may take considerable time, effort, and other resources for them to update their applications to market a generic drug in response to unexpected changes in guidance. This could delay or prevent the entry of some generics to the market.