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IN FOCUS

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FDA and Drug Prices: Facilitating Access to Generic Drugs

A variety of proposals to address high drug prices have been introduced in legislation and by the Trump Administration in its blueprint to lower drug prices. According to a Food and Drug Administration (FDA) analysis, the price of a drug is associated with the number of generic manufacturers on the market. As such, absent new legislation, FDA—the primary federal regulator of prescription drugs—can help reduce drug prices indirectly by facilitating competition. This In Focus describes selected FDA actions intended to lower drug prices through generic competition, and considerations for the 116th Congress. Proposals that would not involve FDA (e.g., price negotiation under Medicare) are not discussed.

Prescription Drug Regulation

Before a new drug may be marketed in the United States, it must be approved by FDA. To obtain approval, the sponsor (generally the manufacturer) must submit to FDA a new drug application (NDA) containing, among other things, data from clinical trials. The Federal Food, Drug, and Cosmetic Act (FFDCA) specifies the required contents of an NDA, provides for the conditions under which FDA may deny approval of an NDA, and prohibits certain acts with respect to drugs (e.g., adulteration, misbranding, and sale of counterfeit drugs). The law does not expressly require an NDA to include price information, does not authorize FDA to deny approval of an NDA because of price, and does not prohibit the marketing of a drug whose price may be considered too high.

Figure 1. FDA's Statutory Authority to Approve Prescription Drugs

NDA Requirements	Basis to Deny Approval
• Full reports of safety and effectiveness investigations • Full list of articles used as components of the drug • Full statement of the drug's composition • Full description of manufacturing methods, facilities and controls • Samples of the drug and its components • Specimens of the proposed labeling • Any required pediatric assessments • Patent information	• Submitted reports are not adequate to show safety • Test results show drug is unsafe or do not show drug is safe • Manufacturing methods, facilities, and controls are inadequate • Insufficient information to show the drug is safe • Lack of substantial evidence of effectiveness • Labeling is false or misleading • Application fails to contain required patent information

Source: FFDCA Section 505(b) and 505(d).

The FFDCA does not explicitly prohibit FDA from requiring drug manufacturers to submit pricing information, although the agency has consistently indicated that it does not have the authority to control or investigate drug prices. FDA can, however, affect drug prices indirectly by facilitating competition, specifically by (1) increasing access to generic drugs and (2) decreasing so-called "gaming" of existing statutory and regulatory requirements.

Increasing Access to Generic Drugs

Unlike brand-name drugs, generic drugs are approved under an expedited pathway created by the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act; P.L. 98-417). A generic drug manufacturer may submit to FDA an abbreviated NDA (ANDA), rather than a full NDA, demonstrating that the generic is the same as the brand drug (i.e., the reference listed drug or RLD). By relying on FDA's previous determination that the RLD is safe and effective, the generic drug company can avoid replicating costly clinical trials already conducted by the brand company. The Hatch-Waxman Act has been considered successful in increasing generic drug competition. Generics now account for 90% of U.S. prescriptions dispensed but 23% of prescription drug spending, while brand-name drugs make up 10% of prescriptions dispensed but 77% of prescription drug spending. According to the Association for Accessible Medicine's (AAM) *2018 Generic Drug Access & Savings Report*, in 2017, savings from generic drugs in the United States totaled $265.1 billion, including $82.7 billion in savings to Medicare and $40.6 billion to Medicaid.

Although FDA does not have explicit statutory authority to regulate drug pricing, the agency can prioritize the review of certain ANDAs, thus allowing a lower-priced alternative onto the market more quickly. In June 2017, as part of its Drug Competition Action Plan, FDA posted on its website a list of off-patent, off-exclusivity drugs for which there are no approved generics and announced its intent to expedite the review of ANDAs for drugs on this list until there are three approved ANDAs for each RLD. These actions were codified by Title VIII of the FDA Reauthorization Act of 2017 (P.L. 115-52). In its manual of policies and procedures, FDA specifies which ANDAs it will prioritize for review (e.g., ANDAs for "sole source" drugs or for drugs in shortage); the cost of the brand drug is not listed as a consideration for prioritization. To promote competition, FDA is evaluating the feasibility of drug importation from other countries in the case of price increases for sole source off-patent, off-exclusivity drugs. FDA also can increase access to generic drugs by helping manufacturers comply with statutory and regulatory approval requirements. The agency has issued various guidance documents and held public workshops to facilitate the development of generic drugs, including complex generics.

Decreasing Gaming

Despite the successes of the Hatch-Waxman Act, certain practices have emerged that may be disrupting the law's intended balance between innovation and competition. FDA has taken action to address two such practices used by brand companies to delay approval of generic competitors:

(1) misuse of required risk evaluation and mitigation strategies (REMS), and (2) filing of citizen petitions.

REMS

FDA may require a REMS, under specified conditions, for certain drugs that it otherwise may have kept off the market due to safety risks (FFDCA §505-1). As part of a REMS, a drug manufacturer may be required to impose restriction on a drug's distribution via one or more elements to ensure safe use (ETASU). An ETASU is a restriction on distribution or use that is intended to (1) allow access to those who could benefit from a drug while minimizing the risk of adverse events, and (2) block access to those for whom the risks would outweigh the potential benefits. An ETASU could require, for example, that pharmacies that dispense the drug be specially certified or that the patient using the drug be subject to monitoring. A brand drug and its generic must use a single, shared system of ETASU, but FDA may waive this requirement for the generic drug if (1) the burden of creating a single, shared system outweighs the benefit, or (2) an aspect of the ETASU for the RLD is claimed by an unexpired patent or is a method entitled to protection, and the generic applicant certifies that it sought but was unable to obtain a license for use of the ETASU.

The FFDCA prohibits the brand company from using ETASU to block or delay approval of an application. However, FDA, the Federal Trade Commission (FTC), and other stakeholders have reported that some brand companies are using REMS to prevent or delay generic drugs from entering the market. First, to obtain approval of an ANDA, the generic manufacturer must demonstrate to FDA that, among other things, the generic is bioequivalent (absorbed at the same rate and to the same extent) to the brand drug; this testing requires a sufficient quantity of the brand-name drug. Second, even when a generic company has acquired the necessary samples, conducted the required testing, and obtained FDA approval, challenges in negotiating a single, shared system of ETASU also can delay the generic drug from entering the market. Brand companies have justified their refusal to sell samples to competitors by citing safety concerns (e.g., that the generic company may not ensure safe use of the drug) and liability concerns (e.g., the brand company could be held liable for any injuries caused by the generic product, which could result in regulatory action against the RLD).

FDA has attempted to address misuse of REMS through its existing authorities. In December 2014, FDA issued draft guidance outlining the steps that an ANDA sponsor should take to obtain a letter from FDA to the brand company, indicating that the ANDA sponsor's proposed bioequivalence testing protocol is comparably as safe as the applicable ETASU, and that it would not be a violation of the REMS to provide the product samples for such testing. However, FDA cannot compel a company to sell samples to another sponsor, and the guidance has been described by AAM as ineffective. FDA has published on its website a list of drugs for which it has received sample access inquiries related to limited distribution of the brand drug; the list includes the name of the brand company and number of inquiries received. FDA has issued one draft guidance to facilitate the submission and review process for shared system REMS and another describing how and when FDA will consider waiving a single, shared system requirement, and how generic drug applicants can request a waiver.

Citizen Petitions

The citizen petition process allows interested stakeholders, including drug companies, to bring concerns to FDA's attention. A petition can request that FDA take certain action (e.g., require warnings on a drug's labeling) or that FDA delay an administrative action (e.g., approval of an ANDA). Due to concerns about misuse of citizen petitions, FFDCA Section 505(q) was enacted. It prohibits FDA from delaying approval of a pending application based on a citizen petition or stay of action (SOA) request unless the agency determines, upon reviewing the petition or SOA, that a delay is necessary to protect the public health. FDA may deny at any time a petition that was "submitted with the primary purpose of delaying the approval of an application" and that "does not on its face raise valid scientific or regulatory issues," but has never done so.

Although citizen petitions have rarely delayed specific generic drug approvals, FDA has expressed concern that petitions are being submitted with intent to delay generic competition and that because of the 150-day deadline by which FDA needs to take final action on a petition, they take resources away from other work. In October 2018, FDA issued a revised version of its draft guidance "Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the [FFDCA]." Unlike the earlier draft, it includes a list of factors FDA intends to consider in determining whether a petition has been submitted to delay application approval (e.g., submission of serial petitions raising issues that could have been addressed in the original petition). Per the draft guidance, if FDA determines that a petition has been submitted with the primary purpose of delaying an application, it will refer the matter to FTC and will highlight those determinations in its annual reports to Congress.

Considerations for the 116th Congress

FDA is using its existing authorities to facilitate competition and indirectly tackle high drug prices. However, Congress may consider expanding FDA's authority to affect drug prices. For example, Congress could revisit legislation from the 115th intended to keep brand companies from using REMS to prevent or delay generics from entering the market. The Fair Access for Safe and Timely (FAST) Generics Act of 2017 (H.R. 2051) and the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2017 (S. 974, H.R. 2212) each would have established a mechanism for a generic company to obtain samples of the brand drug for testing purposes, although in different ways. These bills are further described in CRS Report R44810, *FDA Risk Evaluation and Mitigation Strategies (REMS): Description and Effect on Generic Drug Development*). Regarding 505(q) petitions, Congress may consider codifying aspects of FDA's draft guidance or establishing monetary penalties for entities that file serial petitions with the primary purpose of delaying competition. Congress also may consider, among other things, explicitly authorizing FDA to require drug price

-related information as part of an NDA, for purposes of approval or otherwise, or to prohibit high drug prices.

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