New Safety and Efficacy Information on Generic Cancer Drugs Labels

The FDA wants to give prescribers and patients access to the most up-to-date information to guide treatment decisions.

December 20, 2018 By Food and Drug Administration (FDA)

Statement from FDA Commissioner Scott Gottlieb, MD, and Director of FDA's Center for Drug Evaluation and Research Janet Woodcock, MD, on efforts to modernize generic drug labels while maintaining the efficiency of generic development

Protecting patient safety is at the core of the FDA's mission. All FDA-approved drugs have benefits and risks which must be weighed and balanced by health care providers and patients when making decisions about medical therapy. For our part, the FDA is committed to a thorough, science-based review of the data and information submitted by drug manufacturers and the corresponding product labeling. Our goal is to ensure that the benefits and risks are clearly articulated in drug labeling. That patients and providers have accurate information. And that the benefits outweigh the risks for the intended patient population.

We recognize the decisions surrounding which drug to use in a treatment regimen can be complex. And often cost plays a role in those decisions for patients and health care providers. We also know there are impacts of these decisions on the health care system overall. When looking at the broader impact of our regulations, the agency must weigh and balance the potential impact of our actions especially as it pertains to consumer access to high-quality, lower-cost generic medicines. These are matters of public health concern. One such issue the FDA has considered extensively over the past few years is the process by which drug companies update drug labels and communicate safety-related information for generic drugs.

In November 2013, the FDA proposed a rule (Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products), which, if finalized, would have allowed generic drug makers to independently — meaning, without prior FDA review and approval — update and promptly distribute new safety information in drug labels. This is something that currently only branded drug makers can do.

This rule, if implemented, would have allowed generic manufacturers to independently update their drug labels with new information. We heard from manufacturers that they believed this change would have imposed on them significant new burdens and liabilities. We heard arguments

that the proposed rule could impose new costs on generic manufacturers that might have raised the price of generic drugs to patients, potentially impacting patient access to generic medicines. And, among other challenges, the new policy would have resulted in labels for the same drug that varied between different generic manufacturers, for some period of time. This could have led to consumer and provider confusion.

Today, the FDA is withdrawing this proposed rule. At the same time, we're taking important steps to update the labels on certain generic cancer drugs with modern safety and efficacy information. This effort will help make sure that prescribers and patients have the most up-to-date information to guide treatment decisions and will broaden patient access to generic medicines.

These actions are part of our ongoing commitment to promote a framework that ensures that generic drug labels reflect up-to-date, science-based information to inform patients and providers; while also balancing the need to maintain a pathway for the development of generic drugs that is modern, efficient and low cost.

As with all decisions we make, we carefully weighed the potential benefits of this proposed rule against the challenges it could impose. We want to provide background on this process, the FDA's decision and the overarching public health considerations that were weighed. And, more broadly, we want to outline some of the current efforts the FDA is undertaking to help modernize generic labels.

Since that 2013 proposal, there's been an important and robust public debate. It included extensive public comments received on the proposed rule and during a related public meeting in 2015. This debate has resulted in the FDA carefully considering over the past few years policy approaches on how best to improve communication of important, newly acquired drug safety information to providers and patients.

We've carefully considered all of the feedback we received from the various stakeholders — both in favor of and against the proposed rule. We've evaluated whether there are more effective and efficient ways of keeping generic drug labels up-to-date with the latest safety information and helping to ensure that generic companies continue to engage in an appropriate level of post-market safety surveillance.

Fundamentally, we believe that the withdrawal of the proposed rule is in the best interest of the public; and that other steps that we're pursuing can achieve our goals.

For a multisource drug (typically an older drug that is available as both a generic and brand medicine), there are generally several manufacturers that will make a generic version. The question posed by the proposed rule was whether each drug maker should be able to independently update its label. In our review of the issue, we uncovered several hurdles that — if the rule was implemented — could compromise public health.

Avoiding Unintended Consequences

Among the challenges identified is the ability of generic manufacturers to collect safety information to inform label changes. We heard that generic drug companies don't generally receive or possess all the data necessary to evaluate post-marketing safety information to support these changes on their own.

Another significant issue raised by the proposed rule is the potential for marked differences, for some period of time, between generic labels and the brand products, as well as amongst each of the generic labels. This could potentially lead to patient and provider confusion. It runs contrary to the goals of the generic approval process, which requires generic medicines to have the same label as the reference listed drug.

Another unintended consequence of the proposed rule is the potential for additional or different warnings to temporarily appear in generic drug labeling compared to the brand drug — depending on the availability of information to various manufacturers and the timing of updates. Such differences, even if temporary, could undermine confidence in generic drugs and their therapeutic equivalence. We understand that the proposed rule may have also led to confusing, conflicting generic labels that were crowded with redundant safety information. Individual generic manufacturers might have added additional and at times superfluous information to their individual labels to avoid the risk of liability for failure to warn.

Importantly, we heard important feedback that the proposed rule, if finalized, would have imposed significant burdens on the generic drug industry, and that it could have led to an increase in the cost of generic drugs or the market exit of certain products and manufacturers, exacerbating the risk of drug shortages and resulting in a less competitive marketplace.

We don't want to take an action that may play a part in these unintended adverse consequences, including a risk that generic drug manufacturers would raise prices to consumers to absorb the cost of the new regulation, especially when there may be other more efficient ways to achieve the same public health goals.

For all these reasons, we're withdrawing the rule with the best interest of the public health in mind.

Irrespective of the withdrawal of this proposed rule, the FDA will remain steadfast in our important work to help ensure that health care providers and patients have the best possible information about the safety of all drug products. And let us be very clear — the withdrawal of the 2013 proposed rule does not change the ongoing obligations under the FDA's current regulations for all brand and generic drug manufacturers. These regulations already require drug manufacturers to take steps to update their product labels when new information becomes available that cause the label to become inaccurate, false, or misleading. This responsibility isn't only for brand drug manufacturers. It also applies to generic manufacturers. If a generic drug maker becomes aware of new safety information that's not already on the drug label, they must also report it to the agency. This action, in turn, can result in safety changes that are directed by the FDA and would apply to all versions of the drug.

This current and ongoing obligation for both brand and generic drug manufacturers serves an important public health function. New information regarding the risks and benefits of a drug may become available over time from various sources. This includes real-world data like post-marketing adverse drug experience reports and published literature. New information can make updates to product labels necessary.

Generic drug manufacturers can and are required to propose certain updates to product labels by submitting adequate information about the proposed safety-related change (in the form of a prior approval supplement). The FDA will then determine whether the change is appropriate and whether the label for the corresponding brand drug and other generic drugs should also be revised. This approach enables the FDA to consider how this new information may apply to other generics under the same reference or brand drug. It allows the agency to provide consistency across labeling by ensuring the information is applied to all relevant labels. We'll continue to work with generic companies to ensure they understand this obligation.

Same Goal, New Initiative

We're also advancing other initiatives to facilitate efforts to keep drug product labels up-to-date throughout the product lifecycle. To this end, the FDA has undertaken a new program to update the labels on certain generic cancer drugs with modern safety and efficacy information. Consistent with our current authorities, the FDA expects to play a more proactive role to identify and facilitate updates to these older generic drugs, to give prescribers and patients access to the most up-to-date information to guide treatment decisions.

This is an important undertaking, because having out-of-date drug labels can depress use of generic drugs, reducing consumer access to these lower-cost medicines. By one rough estimate, there are about 5,600 reference listed drugs that correspond to generic medicines. Where there continue to be approved brand versions of these medicines, the FDA can and will work with the brand companies to update labels. But, of these brand medicines that serve as reference drugs, 1,170 have been identified as discontinued or withdrawn by the brand drug manufacturers for reasons other than safety or effectiveness. For example, the brand drug may have been withdrawn as the result of a business decision. If the brand drug manufacturer has voluntarily withdrawn their marketing application, generics that reference the brand medicine can still be approved and marketed. But the brand drug manufacturer is no longer responsible for making any necessary label updates that generic applicants can follow. This means that some drug labels become frozen in time. Often these drugs may be older medicines. But many of these older drugs are still very useful in modern treatment regimens. For example, some of these drugs form the backbone of modern cancer regimens. We may seek additional resources and help from Congress to expand these efforts.

The agency intends to continue pursuing these and other efforts to help ensure that generic labels are accurate and up-to-date throughout the lifecycle of drug products. Helping to ensure the appropriate risk information is communicated to both health care providers and patients is an important responsibility for all drug manufacturers as well as the FDA. For our part, we'll continue to work closely with companies to help ensure that risk information is effectively communicated.

And we’ll continue to seek out modern and efficient ways to help ensure that both the risks and the benefits are being conveyed to patients.

This announcement was originally published on the Food and Drug Administration website on December 13, 2018.
