**Generic Versions of Toprol XL, a Heart Drug, Are Recalled**

By [KATIE THOMAS](http://topics.nytimes.com/top/reference/timestopics/people/t/katie_thomas/index.html)JUNE 23, 2014



Dr. Harry Lever, a cardiologist at the Cleveland Clinic, said some patients taking a generic version of Toprol XL reported chest pains. Credit David Maxwell for The New York Times

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For years, Dr. Harry Lever, a cardiologist at the Cleveland Clinic, has been warning nearly anyone who would listen of his growing suspicions about generic versions of a widely used heart drug, Toprol XL.

Patient after patient, he said, would visit his office complaining of chest pains or other symptoms after switching from the brand-name version, made by AstraZeneca, to a generic product, often one made in India. When he switched them back to the brand — or to another generic — the symptoms disappeared, he said. Dr. Lever wrote a letter outlining his concerns to the [Food and Drug Administration](http://topics.nytimes.com/top/reference/timestopics/organizations/f/food_and_drug_administration/index.html?inline=nyt-org) in 2012, and this year, he traveled to Washington to try to get the attention of Congress.

Dr. Lever could not prove that the generic drugs were to blame. “You see enough people and you get a feel, but it’s anecdotes,” he said in an interview Monday. “It’s not science.”

Now, Dr. Lever is feeling a sort of sad vindication. Two large Indian manufacturers, Wockhardt and Dr. Reddy’s Laboratories, have announced recalls over the last two months totaling more than 100,000 bottles because their products were not dissolving properly — therefore probably not working as they should. The drug is a beta blocker that treats [high blood pressure](http://health.nytimes.com/health/guides/disease/hypertension/overview.html?inline=nyt-classifier) and heart ailments.

The recalls are the latest in a string of recent problems involving generic drugs, especially those made in India. Wockhardt, for example, is now banned from exporting drugs to the United States that were manufactured in two Indian plants where F.D.A. inspectors uncovered serious problems.

The number of recalled bottles is relatively small compared with the 38 million prescriptions for the drug, known generically as metoprolol succinate, that were filled in the United States in 2013, according to the research firm IMS Health. The recalls are considered Class II, meaning they may cause temporary health problems but are unlikely to pose an immediate safety threat. They come as the F.D.A. is taking a closer look at the quality of generic drugs, which now account for more than 80 percent of prescriptions in the United States. In February, Dr. Margaret A. Hamburg, the F.D.A. commissioner, traveled to India to express her concerns about the safety of medicines manufactured there.

The agency is also more closely studying all extended-release products, like the two recalled products, which are more technically difficult to make. Earlier this year the agency put a call out to researchers to investigate the efficacy of generic versions of metoprolol succinate, which is best known by AstraZeneca’s brand name, Toprol XL

Even as the agency has stepped up its scrutiny of generics, however, it has maintained its long-held position that generic drugs are generally as safe and effective as the brand-name versions.

Dr. Lever and other critics of generic drugs say the agency needs to be more frank about the potential downsides to generics. “The doctors in this country need to know what’s going on, because we’re ultimately writing the prescriptions and we’re responsible,” Dr. Lever said. “There’s been this assumption that one generic is the same as another. Not in this case.”

Representatives for Wockhardt and Dr. Reddy’s did not return calls or reply to an email seeking comment. Ralph Neas, the president of the Generic Pharmaceutical Association, the industry trade group, said the F.D.A. thoroughly vetted generic drugs and a “bioequivalence designation assures U.S. patients and caregivers that generic medicines, regardless of the geographic location of origin, are the same medicine with the same active ingredients as the brand but at a lower cost.”

Mr. Neas also noted that generic companies supported a 2012 bill that increased funding — through industry-generated user fees — to scrutinize generic manufacturing, especially overseas.

Generic manufacturers have repeatedly stumbled in their attempts to copy Toprol XL, which lost its patent protection in 2006. In 2008, Sandoz, a division of the drug maker Novartis, recalled its version of the product, and in 2009, the manufacturer Ethex followed suit, as part of a wider recall of its products for quality problems.

Drug-industry experts said the drug has encountered manufacturing problems because it is an extended-release tablet. As these drugs have grown in popularity in recent years, they have posed additional challenges to generic companies seeking to replicate them. Brand-name companies not only initially hold patents on the active ingredient but also on the way a pill releases a drug. So even if the generic companies can match the ingredient once the patent expires, they must come up with their own methods for release of the drug into the body that do not infringe on a separate patent. They are usually successful, but not always.

In another recent case, the F.D.A. decided in 2012 that an extended-release generic version of Wellbutrin, the antidepressant, was not the equivalent of the brand-name product and said it would take a closer look at how well generic companies were making extended-release drugs. Like the longstanding complaints about Toprol, consumers had complained for years that generic versions of Wellbutrin were not working properly.

Christopher C. Kelly, a spokesman for the F.D.A., acknowledged in a statement that “there have been challenges in consistently manufacturing” metoprolol succinate and said the agency had consistently monitored manufacturing of the drug to prevent problems. He said in 2013, the F.D.A. undertook a “multidisciplinary investigation” of the efficacy and quality of each of the versions of metoprolol succinate available in the United States. The agency concluded then that all of the versions, including those made by Wockhardt and Dr. Reddy’s, were bioequivalent to the brand-name version.

He said the recalls were the result of the companies’ own tests.