The FDA Announces Two More Antacid Recalls Due to Cancer Risk

Two more companies recalled their ranitidine drugs, generic forms of Zantac, over concerns they may contain a carcinogenic substance.

That burning feeling in your chest after you eat a heavy meal could be heartburn. Or it could be worry over the drugs you’ve taken to treat that heartburn. Among the top medical stories of 2019 was the discovery of contaminants in common medicines, and ranitidine—best known as Zantac—took up a large share of those headlines. A cancer-causing substance known as NDMA has been repeatedly found in one of the most popular antacid drugs in the United States.

The scary news continues in 2020. On Wednesday, the Food and Drug Administration announced voluntary recalls of prescription forms of ranitidine by two generic drug companies, Appco Pharma and Northwind Pharmaceuticals, bringing the total number of ranitidine recalls to 14 in the past five months. The agency also reported that Mylan
Pharmaceuticals recalled three lots of Nizatidine (Axid), a similar drug, again because of NDMA.

This week’s recalls are a new cause for alarm for the 15 million Americans who take ranitidine at prescription levels, and the millions more who regularly take lower-dose, over-the-counter versions. More than 60 million Americans experience heartburn at least once a month. Zantac was once the best-selling drug in the world.

Bianca Ryan, the season 1 winner of America’s Got Talent, took to Twitter after the voluntary recalls this fall: “I'm literally hyperventilating, like, I've been taking Zantac every single day for the last 10 years for my GERD,” she wrote, referring to gastroesophageal reflux disease, a frequent or more serious form of heartburn, which occurs when acid from the stomach flows up into the esophagus “So—what do I use now?! And they found what in it?!”

For people worried about past use of Zantac and cancer risk, here’s some backstory and a bit of perspective.

Last year, Adam Clark-Joseph, cofounder of the mail order pharmacy Valisure, ordered ranitidine syrup, prescribed to treat reflux in his infant daughter. The pharmacy distinguishes itself by testing every batch of drugs it sells for impurities; earlier, it had found a potential carcinogen in valsartan, a blood pressure medicine. When the ranitidine tested positive for NDMA, Valisure tested other formulations from other manufacturers. “Every batch of every bottle of every manufacturer showed the same results, tremendously high formation of NDMA,” says CEO David Light.

Light says the findings point to an instability with the drug that, in the right conditions, could produce NDMA—for example, if heated. (Valisure heated its ranitidine to 130 degrees Celsius, or 266 degrees F. A car on a hot summer day could reach 140 F.) Valisure reported the results to the FDA, which took exception to the testing methods, saying that its testing at lower temperatures had resulted in much smaller amounts of NDMA. Still, the agency responded to the larger issue, announcing nine voluntary recalls on September 13 with the explanation that “early, limited testing has found
unacceptable levels of NDMA” impurities in samples of ranitidine. Even as it argued that a “third-party laboratory” used a method “not suitable for testing ranitidine,” it said it would update its own investigations (without adding heat).

Light stands by Valisure’s testing methods. “We used those conditions to underscore the point that it’s fundamentally unstable,” he says. Valisure also conducted tests with simulated gastric fluid (at body temperature, 37 degrees Celsius) and added sodium nitrite, simulating a diet with high levels of the common preservative found in processed meats, and found high levels of NDMA. The nitrite is an important component (the N) in the creation of NDMA. (Some vegetables, smoked fish, and dairy products also contain nitrates and nitrites.)

The FDA’s own tests with simulated gastric fluid didn’t show formation of NDMA—but they didn’t add sodium nitrite. “There is also some evidence that there may be a link between the presence of nitrites and the formation of NDMA in the body if ranitidine or nizatidine is also present,” the FDA acknowledged on December 4. “Because of this, consumers who wish to continue taking these drugs should consider limiting their intake of nitrite-containing foods, such as processed meats and preservatives like sodium nitrite.” At the same time, the FDA asked manufacturers to expand their testing and check every lot of ranitidine and nizatidine for NDMA and withhold lots with detected levels above what the agency considers acceptable for daily use.

So what’s the upshot? Many countries, including Canada, Switzerland, and Germany, pulled ranitidine from stores. In the US, the decision to halt all sales of ranitidine fell to individual companies, and major drug chains such as CVS, Walgreens, and Walmart yanked the over-the-counter versions. The FDA advises people to consult with their doctors about switching medications.

The Zantac cancer scare didn’t just hit home for people with heartburn. On breast cancer forums, patients wondered whether they had been harmed by Zantac—and whether they should stop taking it. In a blog post, Breastcancer.org shared the news with its 200,000 members along with some
reassurance that the FDA said the levels detected would be “unlikely” to increase the risk of developing cancer.

Breast cancer patients and survivors latched onto other words in the FDA’s advisory. “I've been taking ranitidine twice a day for more than five years. So it was no comfort to read on Sept 13th that the FDA warned about the Probable Carcinogen in Zantac,” said one posting. “The operative word, for me, is PROBABLE!”

Already, several lawsuits have been filed asserting that Zantac caused cases of cancer. Valisure has submitted a Citizen Petition to the FDA, asking the agency to request recalls of all ranitidine and suspend sales in the United States.

The FDA says the NDMA levels they found in ranitidine were comparable to what people might be exposed to from eating smoked or grilled meat. But somehow, that just highlights the added dangers of foods Americans love—foods that often cause heartburn.

Of the antacid medications, only ranitidine and nizatidine, a similar antacid medication, have been recalled over NDMA. Experts point out that many other choices are available, including proton pump inhibitors such as Nexium, Prilosec, or Prevacid. More research needs to be done to answer important questions about the two antacid medications, says Caleb Alexander, a pharmaco-epidemiologist who is codirector of the Johns Hopkins Center for Drug Safety and Effectiveness. But the chance that any individual will get cancer from taking the heartburn drugs is low, he says. “Even if it raises one’s risk, these are still rare outcomes that we’re talking about,” he says.

Stephen Freedland, a urologist and expert in cancer prevention at Cedars-Sinai Medical Center in Los Angeles, had gotten into the habit of taking ranitidine if he had heartburn after a long day working in the operating room. He figures he took the antacid about once a week for the past year. So the news of NDMA came with a personal twist. “It’s important to keep things in perspective,” he says. “The goal is everything in moderation, not to get too anxious because anxiety has negative health consequences.”
Freedland has stopped taking ranitidine. Even better, he lost 12 pounds over the past several months and no longer has the bouts of heartburn. He is studying the impact of a low-carb diet on cancer prevention and allows himself an occasional grilled steak. After all, life is all about balancing benefits and risks.