ZANTAC FACT SHEET

ZANTAC RECALLED DUE TO POTENTIAL CANCER RISK

Recently, multiple ranitidine and Zantac manufacturers recalled their products due to concerns that they contain high levels of NDMA, a likely carcinogen.

On April 1, 2020, the FDA requested that all Ranitidine (Zantac) products be removed from the market.

CONTAMINATION OF ZANTAC WITH CARCINOGENIC CHEMICAL NDMA

Valisure, an online pharmacy that regularly tests the drugs it sells, detected levels of dimethylformamide (DMF) in blood pressure back in the spring of 2019. DMF is a solvent that can form nitrosamine impurities like N-Nitrosodimethylamine (NDMA)—which is classified by the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC) as a probable carcinogen.

The FDA had been investigating NDMA and other nitrosamine impurities in blood pressure and heart failure drugs since July 2018, and had recommended numerous recalls after discovering unacceptable levels of these contaminants.

Valisure's testing found NDMA levels in ranitidine pills at "extremely high levels" in excess of 3,000,000 ng per tablet. The FDA's established permissible daily intake of the toxin is 96 ng. On September 9, 2019, Valisure submitted a citizen petition to the FDA, requesting they take action to protect public health, including recalling all ranitidine products in the U.S. due to the concerns.

On September 13, 2019, the FDA published a safety communication warning that some ranitidine medicines, including Zantac, had tested positive for N-Nitrosodimethylamine (NDMA) in the lab.

Soon after that, Sandoz, a generic maker of the drug, recalled 14 lots of ranitidine hydrochloride capsules because of confirmed contamination of NDMA above levels deemed safe by the FDA. Those lot numbers are listed on the FDA's news site. Other generic makers like Glaxo-Smith-Kline and Dr. Reddy's Laboratories stopped shipping their ranitidine products but stopped short of implementing any recalls.

WHAT IS NDMA AND WHY IS IT IN ZANTAC?

NDMA was used to make rocket fuel years ago, but it was banned from that process after high levels of the chemical were found in the air, water, and soil samples around rocket fuel manufacturing plants.

NDMA may also be formed as a by-product of other manufacturing processes. According to the Centers for Disease Control and Prevention (CDC), humans can be exposed to NDMA through a wide variety of sources, including:

- The environment—the air, rivers and lakes, and soil
- Tobacco smoke, chewing tobacco
- Food—cured meat, beer, fish, cheese and other items
- Toiletry and cosmetic products
- Interior air of cars
- Household items like detergents and pesticides

NDMA can even form in the stomach during digestion of alkylamine-containing foods and has been detected in small amounts in breast milk. In addition to WHO and IARC, NDMA has been classified by the Environmental Protection Agency (EPA) as probably carcinogenic to humans, because it can modify DNA. Studies have shown the chemical to increase cancer risk in animal experiments.

The WHO notes had indicated that the results of human studies so far can't be used to "derive a quantitative risk of cancer". In a 2002 Chemical Assessment Document, the WHO reviewed studies that addressed NDMA's effects on humans and reported that "[i]n three of four case–control studies, there was a positive relationship with evidence of exposure–response for the intake of NDMA and gastric cancer...."

RECENT RANITIDINE & ZANTAC RECALLS

As of November 25, 2019, there have been 12 Zantac and ranitidine recalls, which include:

11/19/2019: Precision Dose recalls ranitidine oral solution, USP 150 mg/10 ml due to potential presence of N-Nitrosodimethylamine (NDMA) above levels established by the FDA. [source]

11/15/2019: Golden State Medical Supply (GSMS, Inc.) recalls ranitidine HCl 150mg and 300mg capsules due to potential presence of N-Nitrosodimethylamine (NDMA) above levels established by the FDA. [source]

11/8/2019: Amneal Pharmaceuticals recalls ranitidine tablets, 150 mg and 300 mg, and ranitidine syrup (ranitidine oral solution, USP), 15 mg/ml due to due to potential N-Nitrosodimethylamine (NDMA) amounts above levels established by the FDA. [source]

11/8/2019: American Health Packaging recalls ranitidine liquid unit dose cups due to NDMA impurity. [source]

11/6/2019: Aurobindo & DG Health recalls ranitidine due to NDMA impurity. [source]

10/25/2019: Novitium Pharma recalls ranitidine hydrochloride capsules 150 mg and 300 mg because it may contain N-Nitrosodimethylamine (NDMA). [source]

10/25/2019: Lannett Company, Inc. recalls ranitidine syrup (ranitidine oral solution, USP), 15mg/ml due to above levels of NDMA. [source]

10/23/2019: Dr. Reddy's, Kroger, Walgreens, and others recall ranitidine tablets & capsules for containing N-Nitrosodimethylamine (NDMA). [source]

10/23/2019: Perrigo Company plc recalls Ranitidine (all pack sizes) for the presence of N-Nitrosodimethylamine (NDMA). [source]

10/22/2019: Sanofi recalls all Zantac OTC products in the U.S. for possibly containing N-Nitrosodimethylamine (NDMA). [source]

9/25/2019: Apotex Corp. recalls 75mg and 150mg ranitidine tablets for containing a nitrosamine impurity called N-Nitrosodimethylamine (NDMA). [source]

9/23/2019: Sandoz Inc. recalled ranitidine hydrochloride capsules due to an elevated amount of an unexpected impurity, N-Nitrosodimethylamine (NDMA). [source]

4/1/2020: FDA requests removal of all prescription and over-the-counter ranitidine products from the market immediately. [source]

The FDA has so far labeled NDMA as an "impurity" found in Zantac, generic ranitidine, and other drugs, but Valisure disagrees, stating the carcinogen is a natural by-product of the ingredients used to make the drug.

Valisure believes it has discovered the link between Zantac and its generics to NDMA:

"Valisure's research, along with that of Stanford University and others, found that NDMA was the result of the 'inherent instability' of the ranitidine molecule. This means that all manufacturers, brand or generic, and all lots of ranitidine-containing medications are affected and could generate very high levels of NDMA in the human body."

Significantly, ranitidine interacts with the stomach in a warm environment, and that heat could potentially transform the drug into NDMA during the digestive process, though we are still waiting on studies to confirm this.

Meanwhile, France, Canada, Austria, and other countries have recalled all forms of ranitidine from their markets after detecting NDMA. On April 1, 2020 the FDA requested removal of all prescription and over-the-counter ranitidine products from the market immediately.

FDA testing and evaluation prompted by information from third-party laboratories confirmed that NDMA levels increase in ranitidine even under normal storage conditions, and NDMA has been found to increase significantly in samples stored at higher temperatures, including temperatures the product may be exposed to during distribution and handling by consumers. The testing also showed that the older a ranitidine product is, or the longer the length of time since it was manufactured, the greater the level of NDMA. These conditions may raise the level of NDMA in the ranitidine product above the acceptable daily intake limit.

TYPES OF INJURIES ASSOCIATED WITH ZANTAC

Types of injuries associated with Zantac and generic forms of ranitidine may include:

- Bladder cancer
- Brain cancer
- Colon and rectal cancer
- Esophageal cancer
- Intestinal cancer
- Kidney cancer
- Liver cancer
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer
- Stomach cancer
- Testicular cancer
- Uterine cancer

WHAT IS ZANTAC (RANITIDINE)?

Zantac, the most popular brand of ranitidine, is used to help reduce stomach acid. The medication is commonly prescribed to treat ulcers, gastroesophageal reflux disease (GERD), chronic indigestion, and Zollinger-Ellison syndrome. It comes in both over-the-counter and prescription strengths that may be taken by mouth or administered via injection into a muscle or vein.

Ranitidine belongs to a class of drugs known as H2 blockers that work by reducing the amount of acid the stomach produces. H2 receptors are present on the cells in the stomach lining. A histamine chemical normally stimulates these receptors to produce acid to the body help digest food. Ranitidine blocks these receptors, and prevents histamine from producing its normal effect, which causes the stomach to produce less acid.

The manufacturers of Zantac and generic ranitidine products have warned patients and healthcare providers about the following potential side effects, but to this day have never warned about any potential exposure to a carcinogen:

- Headaches
- Gastrointestinal side effects (constipation, diarrhea, nausea, abdominal pain)
- Drowsiness, dizziness
- Sleep problems
- Decreased sex drive
- Swollen or tender breasts (in men)
- At high doses, may affect liver function

COMMON ACID REFLUX MEDICATIONS INCLUDING RANITIDINE:

- Zantac
- Wal-Zan
- Heartburn Relief
- Acid Reducer
- Acid Control

FILING A ZANTAC LAWSUIT

Some plaintiffs have already filed lawsuits against the makers of Zantac and of generic ranitidine, and more are expected to be filed in the future. In September 2019, for example, five plaintiffs joined together to file a class-action lawsuit against Zantac manufacturer Sanoti-Aventis LLC and former owner of the rights to Zantac, Boehringer Ingelheim, which manufactured and distributed the drug between October 2006 and January 2017.

The plaintiffs claimed that the defendants failed to warn healthcare providers and the public about the dangers of taking Zantac, and did not reveal that Zantac could produce NDMA in the human body.