MINISTRY OF HEALTH

PHARMACY AND POISONS BOARD

PUBLIC UPDATE

Genotoxic contaminant, N-nitrosodimethylamine (N-NDMA) Impurity, in Ranitidine products

Ranitidine is a medicine used to treat and prevent ulcers of the stomach and intestine, and belongs to a group of medicines known as H2-Blocker. It works by reducing the amount of acid that the stomach produces.

Swissmedic, the National Medicines Regulatory Authority of Switzerland through the Swissmedic's Official Medicines Control Laboratory found low level of N-Nitrosodimethylamine (NDMA) a genotoxic impurity in Zantac injection solution 50mg/5ml batch number 669. The value of NDMA found was 0.3ppm relative to the active substance.

NDMA is a potent carcinogen in experimental animals by several routes of exposure, including through ingestion of drinking-water. NDMA has been classified by IARC as probably carcinogenic to humans. The mechanism by which NDMA produces cancer is well understood to involve biotransformation by liver microsomal enzymes, generating the methyldiazonium ion. This reactive metabolite forms DNA adducts, with most evidence pointing to O_6-methylguanine as the likely proximal carcinogenic agent.

From the above Switzerland action, the following other regulatory authorities across the world have taken various actions;

No.	Date	Country	Regulator	Action Taken
1.	16th Sep 2019 23rd Sep 2019	Switzerland	Swissmedic	GSK instructed to carry out pharmacy/retail level of all Zantac IV batches in Swiss market Swissmedic asked for recall of all ranitidine containing products from Swiss market
2.	12th Sep 2019	Singapore	HSA	1. Tested all locally available ranitidine products for the presence of nitrosamine compounds and found that the products contained NDMA, the APIs had been supplied by Dr Reddy's Laboratory India and Saraca Laboratory.

No.	Date	Country	Regulator	Action Taken
				2. HAS instructed GSK to suspend the wholesale supply and conduct class 2 (retail level) recall of Zantac products
3.	13th Sep 2019	USA	USFDA	Issued a statement alerting patients and health care professionals of NDMA found in samples of ranitidine
4.	14th Sep 2019	Finland	FIMEA	GSK instructed to implement Pharmacy/retail level recall of all Zantac products (Tablets, effervescent tablets and syrups) from the Finish market
5.	17th Sep 2019	Ireland	HPRA	Prepare to recall Zantac products manufactured using API from Saraca Laboratory from Pharmacies and retail levels in Irish market
6.	18th Sep 2019	Denmark	DMA	GSK requested to implement a pharmacy/retail level recall of all Zantac products (Syrups and injections) from Danish Market
7.	18th Sep 2019	Saudi Arabia	SFDA	GSK instructed to carry out a pharmacy/retail level recall of all Zantac products (Tablets, effervescent tablets, injections and syrups) from the Saudi Market

Based on the above and with the PPBs core mandate of ensuring the safety of Kenyans, the Pharmacy and Poisons Board has decided that;

a) All ranitidine containing products shall also be recalled (level 2 recall; recall up to retail pharmacies) and quarantined by their respective marketing authorization holders (MAHs) until proved to be safe.
b) There shall be no more importing of the ranitidine products into the country or sale of ranitidine containing products pending conclusion of regulatory investigations
c) Doctors should prescribe the available alternatives and patients should also use alternative medicines

CHIEF EXECUTIVE OFFICER
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