



SAFETY ALERT

DRAP SAFTEY ALERT NO. 14

SAFETY ALERT OF DETECTION OF NDMA IN RANITIDINE CONTAINING MEDICINES

UPDATE FROM US-FDA

Date: 6th of May, 2020

Target Audience:

- Healthcare Professionals.
- Patients, consumers or caregivers.

Problem or Issue:

On 1st April, 2020, United States Food and Drug Administration (US-FDA) through a press release announced that it is requesting manufactures to withdraw all the prescription and over-the-counter (OTC) ranitidine drugs from the market immediately. This was the latest step in an ongoing investigation of a contaminant known as N-Nitrosodimethylamine (NDMA) in ranitidine medications. This steps was taken after FDA has determined that the impurity (NDMA) in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity.

A very low level of NDMA was detected in ranitidine containing medicines by FDA in September last year, which triggered a recall of these medicines throughout the world including Pakistan. Drug Regulatory Authority of Pakistan (DRAP) at first halted distribution of all dosage forms of ranitidine containing medicines in September, 2019 which was followed by its recall throughout the country. A Safety Alert was also issued by Pakistan National Pharmacovigilance Centre (PNPC) on 2nd October, 2019. Subsequently, the case was presented in 293rd meeting of Registration Board, held from 6th to 8th January, 2020, which after thorough deliberation and based on the decision of FDA and EMA regarding ranitidine containing medicines, allowed its sale in Pakistan as long as the impurities (NDMA) is well within the daily limits (96 nanograms per day). Manufactures in Pakistan were also advised to test NMDA impurity in finished products of ranitidine containing medicines including already manufactured batches and accordingly inform DRAP if testing shows NDMA above the acceptable daily intake limit i.e. 96 nanograms per day.

Based on this new update from US-FDA, Registration Board in its 294th meeting decided that registration of all ranitidine containing products shall remain suspended. Meanwhile, status of ranitidine containing products will be reviewed in reference regulatory authorities and a comprehensive case shall be submitted before the Registration Board for its consideration. Further manufacturers/ importers of ranitidine containing products were directed to withdraw/ remove all stocks from market immediately.





Therapeutic Goods Affected:

Name: **All dosage forms of Ranitidine containing medicines.**

Ranitidine is a H₂ (histamine-2) blocker which decreases the amount of acid created by the stomach. It is used to treat heartburn, gastric and intestinal ulcers and treatment of gastro-esophageal reflux disease.

Advice for Patients and Healthcare Professionals:-

As the registration of ranitidine containing medicines in Pakistan still remains suspended and Registration Board, in its 294th meeting directed manufacturer/ importers to immediately withdraw the stock from the market, there would be shortage of these medicines in Pakistan. Therefore, patients taking ranitidine containing medicines should speak with their healthcare professional about other treatment options, as there are multiple drugs approved for the same or similar uses as ranitidine that do not carry the same risks from NDMA. Healthcare professionals are advised to carefully monitor the condition of patients and switch to other treatment option for the similar indication. To date, NDMA has not been found in famotidine, cimetidine, esomeprazole, lansoprazole or omeprazole containing medicines.

Both healthcare professionals and patients are requested to report any suspected adverse drug reactions with these medicines to **Pakistan National Pharmacovigilance Centre**, Drug Regulatory Authority of Pakistan through **DRAP Med Vigilance e-reporting system** [http://:https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=PK](http://https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=PK) or at npc@dra.gov.pk.

