Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

07 APR 2020

FDA ADVISORY
No. 2020-548

TO: **ALL CONCERNED LICENSED ESTABLISHMENTS AND THE GENERAL PUBLIC**

SUBJECT: **DIRECTIVES FOR RANITIDINE-CONTAINING PRODUCTS**

Last year, an impurity, N-nitrosodimethylamine (NDMA), which was classified as a probable human carcinogen (a substance that could cause cancer) was found in some ranitidine products distributed globally. In the Philippines, the innovator, Ranitidine (Zantac), in 75 mg Tablet, 150 mg Tablet, 300 mg Tablet, and 25 mg/mL (50 mg/2 mL) Solution for Injection (IM/IV) presentations were voluntary recalled by GlaxoSmithKline Philippines, Inc. due to the detection of the said impurity in these drug products.

With the recent developments of this impurity such as increasing levels over time in some ranitidine products as discovered by the United States (US) Food and Drug Administration (FDA), the FDA Philippines acknowledges the importance of appropriate testing in order to ensure the provision of good quality, safe, and effective ranitidine products. The following drug products were tested accordingly and confirmed to have levels of NDMA below the acceptable limit:

PRODUCT INFORMATION	REG. NO.
Ranitidine Hydrochloride 25 mg/mL Solution for Injection (IM/IV) (Siutec)	DR-XY31808
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Nelstac)	DRP-7171
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Ranistar)	DRP-7171-01
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Aglotac)	DRP-6135
Ranitidine (as hydrochloride) 25 mg/mL Sterile Solution for Injection (IM/IV) (Danitin)	DRP-1107
Ranitidine (as hydrochloride) 25 mg/mL Sterile Solution for Injection (IM/IV) (Dynastin)	DRP-1107-01
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Aciloc)	DRP-869
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Eastidine)	DRP-869-01
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Hacidac)	DRP-869-02
Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Apo-tin)	DRP-6304

Ranitidine (as hydrochloride) 25 mg/mL Solution for Injection (IM/IV) (Primudine)	DRP-6304-01
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Solution for Injection (Entac)	DR-XY29322
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Solution for Injection (IM/IV) (Ulcin)	DR-XY19686
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Qualran)	DRP-159
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Effedine)	DRP-159-03
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Zantricid)	DRP-159-04
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Amkodine)	DRP-159-05
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Geoxer)	DRP-159-06
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Westran)	DRP-159-07
Ranitidine (as hydrochloride) 25 mg/mL (50 mg/2 mL) Sterile Solution for Injection (IM/IV) (Ranipen)	DRP-159-09
Ranitidine (as hydrochloride) 150 mg Tablet (Contracid)	DRP-1237
Ranitidine (as hydrochloride) 150 mg Tablet (Ranae)	DRP-1237-01
Ranitidine (as Hydrochloride) 150 mg Tablet (Radine)	DR-XY32319
Ranitidine 150 mg Film-Coated Tablet (Zilatec)	DRP-4651
Ranitidine (as hydrochloride) 300 mg Film-Coated Tablet (Alcera)	DRP-4494
Ranitidine Hydrochloride + Tripotassium Bismuth Dicitrate + Sucralfate 84 mg/100 mg/300 mg Film-Coated Tablet (Albis)	DR-XY44001

However, as precautionary measures for other registered but not tested ranitidine products for human use, the FDA Philippines directs the following:

1. Immediate suspension of all operations (i.e., manufacture, importation, exportation, distribution, offer for sale) of concerned establishments, e.g., Marketing Authorization Holders (MAH), manufacturers, importers, exporters, distributor/sub-distributor, dealing with ranitidine products excluding those in the retail level. Ranitidine products currently available in the retail outlets can still be consumed;
2. Strict utilization of either Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS) or Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) as recommended by the US FDA for every registered ranitidine product showing the analyses, in available batches of both the drug substance/active pharmaceutical ingredient (API) and the finished product, to determine the presence of NDMA;
3. Submission of complete documents including the following:
    a. Certificates of Analysis of API and Finished Product
    b. Analytical Results
    c. Analytical raw data including chromatograms/spectra
    d. Other relevant data

4. Provision of these documents must be done by all affected MAHs/establishments within ninety (90) calendar days from issuance of this advisory through submission to cdrr_postmarketsurveillance@fda.gov.ph containing the subject: Ranitidine-*[Name of MAH/establishment]*. A list of your registered ranitidine products with its registration numbers and the complete address of every API manufacturer/supplier must also be reflected in the body of your e-mail.

Resumption of operations of affected ranitidine products shall depend on the compliance of its MAH and non-submission of required documents shall lead to regulatory action/s without prior notice. Furthermore, the FDA Philippines shall still stringently monitor all ranitidine products under Post-Marketing Surveillance.

Dissemination of the information to all concerned is requested.

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