GLAXOSMITHKLINE Letter to Healthcare Professionals (Prescribers and Pharmacists)

Information about the recent Recalls of certain Zantac (ranitidine hydrochloride) medicines

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Dear Healthcare Professional,

Summary

- The purpose of this letter is to inform prescribers about a precautionary pharmacy/retail level recall of a number of batches of Zantac products (see Appendix I) which occurred on 23rd September 2019, as well as a further recall of Zantac 150mg Film-coated Tablets which occurred on October 2nd 2019. The reason for the recalls is the potential presence of a nitrosamine impurity (N-Nitroso dimethylamine (NDMA)) in ranitidine active substance batches used in the manufacture of Zantac.
- This letter is also being sent to pharmacists for their information. Pharmacies have already been sent the recall letters.
- At this time, no additional batches of the intravenous and syrup presentations of Zantac have been included in the second recall action (of October 2nd 2019) in accordance with the HPRA's instructions. The reason for this is the lack of available suitable authorised alternatives, and the need to maintain supply for paediatric and other patients who may require the IV or syrup products.
- The European Medicines Agency (EMA) has commenced a review of ranitidine medicines to assess whether patients using ranitidine are at any risk from NDMA and will provide information about this as soon as it is available.
- The HPRA is working with the HSE to identify, where possible and appropriate, suitable alternatives.
- There is no recommendation for patients who have Zantac to stop taking it and the patients should consult their prescribing physician. These recalls from pharmacy/retail level were precautionary while the issue continues to be investigated. However, it is likely that ranitidine containing products will be in short supply for the foreseeable future.
- This is an evolving issue and it is possible that a recall by GSK of the Zantac IV and/or syrup product batches may be required from the Irish market at a later date in agreement with the HPRA. An update in relation to these presentations will be provided in the coming days.

- The reason for the recalls is the following:
  - A nitrosamine impurity has been identified in ranitidine active substance batches manufactured at two sites.
  - This impurity, N-Nitroso dimethylamine (NDMA), is a type of N-nitrosamine compound. The general population may be exposed to unknown quantities of NDMA present in foods and beverages, tobacco smoke, herbicides, pesticides, drinking water, and

industrial pollution. In addition, nitrosamines may be formed from amines reacting with nitrites in the human body as a result of ingestion of these precursors separately in food, water, or air. NDMA is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals. NTP 14th Report on Carcinogens (2016)

- The pharmacy / retail level recalls were conducted as a precautionary action.

- Please note that Zantac 25mg/ml Solution for Injection / Infusion and Zantac 150mg/10ml Syrup should only be prescribed where no suitable alternative product is available. GSK will write to you again in the future when an update on this point is available.

Action Being Taken by GlaxoSmithKline

- The September 23rd 2019 recall action (on various Zantac products) has already been communicated to pharmacies and retailers. It included a number of batches, all of which were manufactured using the active substance sourced from one manufacturing plant.
- The recall letter for the October 2nd 2019 recall (Zantac 150mg Film-coated Tablets) was sent to pharmacists on October 2nd via email and is being mailed (via the post) to all pharmacies and retailers at this time. The batches concerned were manufactured using active substance from a second manufacturer.
- GSK is continuing its investigation into the potential source of the NDMA impurity. These investigations include continued engagement with the active substance manufacturers.
- GSK has engaged with external laboratories to conduct tests on active substance and finished product batches of Zantac in various dosage forms.
- GSK is committed to supplying high-quality products to patients and we sincerely regret any inconvenience caused to patients and healthcare professionals.
- GSK is aware of the review of Ranitidine by the EMA and will participate fully as required.

All adverse events should be reported directly to GSK by telephone on 1800 244 255 or to HPRA Pharmacovigilance, Earlsfort Terrace, Dublin 2: Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; email: medsafety@hpra.ie. Please share this information with other HCPs as applicable.

Further Information

- Information on these precautionary pharmacy/retail level recalls of ranitidine-containing products is available at the website of the Health Products Regulatory Authority (www.hpra.ie).

Contact(s) for Further Information or Questions

- For all questions, please contact, the Medical Department at GSK (Ireland) Ltd., 12 Riverwalk, Citywest Business Campus, Dublin 24 on (01) 4955000.

Yours sincerely,

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GSK