NHS Circular:
MSAN (2019) 6

Chief Medical Officer Directorate
Pharmacy and Medicines Division

Scottish Government
Riaghaltas na h-Alba
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16 October 2019

Dear Colleague

MEDICINE SUPPLY ALERT NOTICE

Medicine in short supply: Ranitidine Tablets, Effervescent Tablets and Oral Solutions

Priority: **Level 3**
Valid until: **15 January 2020**

Issue

1. All oral formulations of ranitidine are anticipated to be out of stock, with no date for resupply until further notice. This is as a result of an investigation by the Swiss and German regulatory agencies and the US Food and Drug Administration (FDA), which identified a contaminant, N-nitrosodimethylamine (NDMA), in samples of ranitidine active substance. All stock manufactured for the UK using the affected ranitidine active substance has been quarantined, whilst Medicines and Healthcare products Regulatory Agency (MHRA) investigations are ongoing.

2. All oral formulations are expected to be out of stock, although very limited supplies of unaffected oral ranitidine products may remain available. These should be reserved for those patients in whom alternatives are not clinically appropriate. Although some IV products are affected, there is sufficient unaffected IV stock available to meet current UK demand. This situation is currently under review and may change.

Affected stock

3. The following oral presentations of ranitidine are affected:

- Ranitidine 75mg, 150mg and 300mg tablets
- Ranitidine 150mg and 300mg effervescent tablets
- Ranitidine 150mg/5ml oral solution
- Ranitidine 75mg/5ml oral solution

Addressees:

For action
NHS Directors of Pharmacy
NHS Medical Directors
Pharmacy Primary Care Leads
Medicines Information Pharmacists
Community Pharmacy Scotland
NHS National Procurement
Scottish Prescribing Advisor Network

For information
Director Practitioner Services, NHS NSS
NHS Scotland Chief Executives
NHS Director of Finance

General Enquiries to:

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Actions

4. All patients receiving ranitidine tablets, effervescent tablets and oral solutions should be reviewed as repeat prescriptions are requested, and if ongoing treatment is required, be switched to clinical alternatives. Details of alternative treatments can be found in Annex A. This advice will be reviewed in January 2020.

5. It is recommended that:

- omeprazole is the first-choice proton pump inhibitor (PPI) where clinically appropriate, as there are currently sufficient supplies to manage an increase in demand;
- patients are **not** switched to alternative H2-receptor antagonists in the first instance as this may exacerbate a shortage of these products. Sufficient supplies will continue to be available to meet current demand;
- for specialist indications GPs consult with specialist clinicians to identify circumstances when ranitidine cannot be substituted with clinical alternatives; and
- any remaining supplies of oral ranitidine are reserved for circumstances where specialists consider there are no clinically appropriate alternatives.

Further background

6. An investigation by the Swiss and German regulatory agencies and the FDA, has identified a contaminant, N-nitrosodimethylamine (NDMA), a probable human carcinogen, in samples of ranitidine active substance. Several ranitidine products manufactured for the UK market may contain this active substance contaminated with NDMA.

7. The MHRA has requested that all UK manufacturers using active ingredient from this source quarantine all stock whilst further investigations are ongoing. To date, one supplier, GSK, has undertaken a Class 2 recall of all their ranitidine products (https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=10290) MHRA is continuing to investigate the issue alongside the European Medicines Agency (EMA).

8. Currently all but three UK manufacturers are affected by this situation, however this may change as the MHRA and EMA continue their investigations. There are insufficient supplies available from the unaffected manufacturers to continue to support current usage of oral ranitidine in the UK. Very limited supplies of unaffected oral ranitidine products may remain available and therefore the majority of patients will need to be switched to alternative products. This issue is affecting supplies globally.

9. Although some IV products are affected, there are sufficient supplies of unaffected ranitidine 50mg/2ml injection to meet normal UK demand. This situation is currently under review and may change.

Action

7. Health Board Medical Directors and Directors of Pharmacy are asked to cascade this Medicines Supply Alert Notice to general practices, community pharmacies, and other relevant professionals in their Health Board area.

8. Healthcare professionals are asked to note the content and actions outlined in this circular and Annexes.

Yours sincerely,

Rose Marie Parr
Chief Pharmaceutical Officer/
Deputy Director Pharmacy & Medicines Division

ANNEX A

Alternative products for the main indications of ranitidine in adults:

Acid suppressant	Formulation	GU/DU treatment	GU/DU prophylaxis	GORD	NSAID associated GU/DU treatment/ prophylaxis	Comments
Proton pump inhibitors						
Omeprazole*	Capsules, tablets and dispersible tablets: 10,20,40mg Injection 40mg	20-40mg OD	10-40mg OD (DU) 20-40mg OD (GU)	20-40mg OD (treatment) 10-40mg OD (long term management after healed reflux oesophagitis) 10-20mg OD symptomatic GORD	20mg OD (prevention and treatment)	Losec MUPS® not licensed for use via enteral feeding tubes, but extensive experience of using them in this way **not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy* Paediatric licence: Reflux oesophagitis treatment, symptomatic treatment of heartburn and acid regurgitation in GORD (>1yr); DU due to H Pylori (>4yrs)
Lansoprazole	Capsules and dispersible tablets: 15 and 30mg	30mg OD	UL (15-30mg OD) **¥**	30mg OD (treatment) 15-30mg (prevention) 15-30mg OD (symptomatic GORD)	30mg OD (treatment) 15-30mg (prevention)	No paediatric licence but used off label in this population Orodispersible tablets licensed for administration down NG tube
Pantoprazole	Tablets 20 and 40mg Injection 40mg	40-80mg OD	UL (20-40mg OD) **¥**	20mg OD symptomatic GORD 20-40mg OD long term management and prevention of relapse	20mg OD (prevention)	Paediatric licence above 12 years

Acid suppressant	Formulation	GU/DU treatment	GU/DU prophylaxis	GORD	NSAID associated GU/DU treatment/ prophylaxis	Comments
Esomeprazole*	Tablets, capsules 20 and 40 Granules 10mg Injection 40mg	UL (20-40mg OD) **¥**	UL (20-40mg OD) **¥**	40mg OD (treatment) 20mg OD (prevention and symptomatic treatment)	20mg OD (prevention and treatment)	**not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy* Paediatric licence: above 12 years for tablets, capsules (treatment of GORD) Granules: 1-11 years (GORD) >4 years (H Pylori) Granules licensed for administration down NG or gastric tube
Rabeprazole	Tablets 10 and 20mg	20mg OD	UL (10-20mg OD) **¥**	20mg OD (treatment) 10-20mg long term maintenance 10mg OD symptomatic GORD	UL	No paediatric licence
H2 antagonists						
Nizatidine	Capsules 150mg	150mg BD or 300mg OD	150mg OD	150-300mg bd	150 BD or 300mg OD (treatment)	No paediatric licence
Famotidine	Tablets 20 and 40mg	40mg OD	DU 20mg OD	UL	UL	No paediatric licence
Cimetidine*	Tablets 200, 400 and 800mg Liquid 200mg/5mL	400mg BD OR 800mg ON (up to 400mg QDS)	400mg ON up to BD	400mg QDS	UL	Paediatric licence >1yr **caution as CYP P450 inhibitor; care with drug interactions- consult SPC*

Key:, GU: gastric ulcer, DU: duodenal ulcer; PU: peptic ulcer; GORD: gastroesophageal reflux disease, UL: unlicensed
¥ Based on PPI dose equivalence table for severe oesophagitis in NICE guideline (CG184) update (2014): *https://www.nice.org.uk/guidance/cg184/chapter/Appendix-A-*

ANNEX B

CLASSIFICATION OF MEDICINE SHORTAGES

LEVEL	DESCRIPTION	POTENTIAL RESPONSES
Level one (low impact)	Supply problem with a short duration **(up to one month**) where immediately available measures are expected to be sufficient and there is minimal additional management requirement.	Business as usual. Response likely to involve using the same medicine. • Alternative strength/formulation available to meet demand, potentially from other suppliers.
Level two (medium impact)	Supply problem where alternatives in the same therapeutic class are available but which may require some management such as switching to those alternatives, which may include unlicensed medicines.	Business as usual. Response not likely to require a change in the class of medicine. • Alternative strength/formulation available but clinical advice is required to help manage the switch. • Alternative medicine in the same therapeutic class. • Unlicensed alternatives may be used. • Issuing a Medicine Supply Alert Notice.
Level three (high impact)	Supply problems where there are limited or no alternatives in the same therapeutic class and which require significant management, potentially including changes in clinical practice or operational direction or that have patient safety implications. Level three shortages also include level two shortages for medicines used in life saving conditions such as anaphylaxis or involving patient groups considered as vulnerable, such as neonates, paediatrics or people with learning disabilities.	Serious shortage situation. Response likely to require a change in the class of medicine. • Alternative therapeutic class of medicine available. • The use of a 'serious shortage protocol'. • Additional clinical advice. • Exceptional MHRA regulatory measures. • Issuing a Medicine Supply Alert Notice.
Level four (critical impact)	Supply problems where there is no viable therapeutic alternative and where responses may also require support from outside the health system and / or which trigger the use of national resilience structures.	Very serious shortage situation. Wider burden on NHS and public sector. • Non-medicine support provided to patients. • National Resilience procedures potentially activated – including links with agencies outside NHS. Additional project management or communications support may be required. • Issuing a Medicine Supply Alert Notice.