



Supply Disruption Alert

SDA/2019/005

Issued: 15 October 2019

Valid until: 15 January 2020

Ranitidine: all oral formulations – Supply Disruption Alert

Summary

- All oral formulations of ranitidine are anticipated to be out of stock, with no date for resupply until further notice.
- An investigation by the Swiss and German regulatory agencies and the US Food and Drug Administration (FDA), has 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.
- Although all oral formulations are expected to be out of stock, very limited supplies of unaffected oral ranitidine products may remain available and should be reserved for those patients in whom alternatives are not clinically appropriate.
- All other patients should be reviewed as repeat prescriptions are requested, and if ongoing treatment is required, be switched to clinical alternatives.
- 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.

Action

All healthcare professionals in primary, secondary or specialist healthcare services who prescribe or dispense ranitidine, should for:

Licensed use for gastrointestinal conditions

- Identify current patients prescribed ranitidine tablets, effervescent tablets and oral solutions, and:
 - Review to establish if ongoing treatment is still required.
 - If ongoing treatment is still required, then consider switching to an alternative treatment (see table below).

Please note:

- *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.*
- *It is recommended that 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.*

Specialist indications

- Consult specialist clinicians who use ranitidine to identify circumstances when ranitidine cannot be substituted with clinical alternatives.
- Reserve any remaining supplies of oral ranitidine for circumstances where specialists consider there are no clinically appropriate alternatives.

Prescribers should work in close collaboration with their pharmacists to understand which clinical alternatives are available.

Deadlines for actions

Actions initiated: Immediately
Actions completed: 15 January 2020

Product details

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

Background

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.

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. MHRA is continuing to investigate the issue alongside the European Medicines Agency (EMA).

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.

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.



Alternative formulations

Alternative products for the main indications of ranitidine in adults:

Before switching to another agent, review if patients still require treatment or could be stepped down to an antacid or alginate.

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 <i>*not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy</i> <u>Paediatric licence:</u> 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)	<i>*not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy</i> <u>Paediatric licence:</u> 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 <i>*caution as CYP P450 inhibitor; care with drug interactions- consult SPC</i>

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->



Distribution

If you are responsible for cascading these alerts in your organisation, these are our suggested distribution lists.

Trusts (NHS boards in Scotland)

CAS and SABS (NI) liaison officers for onward distribution to all relevant staff including:

- A&E consultants
- A&E departments
- A&E nurses
- Cardiologists
- Cardiology departments
- Cardiology nurses
- Cardiology, directors of
- Cardiothoracic departments
- Cardiothoracic surgeons
- Cardiothoracic surgery directors
- Chief pharmacists
- Clinical governance leads
- Clinical Procurement Specialists [NEW]
- Community children's nurses
- Community hospitals
- Community midwives
- Community nurses
- Coronary care departments
- Coronary care nurses
- Day surgery units
- Dermatologists
- Dieticians
- District nurses
- Gastroenterology departments
- Gastroenterology, directors of
- Gastro-intestinal surgeons
- Haematologists
- Hospital at home units
- Hospital pharmacies
- Hospital pharmacists
- Intensive care medical staff/paediatrics
- Intensive care nursing staff (adult)
- Intensive care nursing staff (paediatric)
- Intensive care units
- Intensive care, directors of
- Maternity units
- Medical directors
- Medical oncologists
- Medical oncology, directors of
- Midwifery departments
- Midwifery staff
- Neonatal nurse specialists
- Neonatology departments
- Neonatology directors
- NHS walk-in centres
- Nutrition nurses
- Obstetricians
- Obstetrics and gynaecology departments
- Obstetrics and gynaecology directors
- Obstetrics departments
- Obstetrics nurses
- Oncology nurse specialists
- Outpatient clinics
- Paediatric intensive care units
- Paediatric medicine, directors of
- Paediatric nurse specialists
- Paediatric oncologists
- Paediatric surgeons
- Paediatric surgery, directors of
- Paediatric wards
- Paediatricians
- Paediatrics departments
- Palliative care teams
- Paramedics
- Pharmaceutical advisors
- Pharmacists
- Purchasing managers
- Risk managers
- School nurses
- Special care baby units
- Supplies managers
- Walk-in centres

NHS England regional offices

CAS liaison officers for onward distribution to all relevant staff including:

- Community pharmacists

- General practitioners
- Nutritional nurse specialists
- General practice managers
- General practice nurses

Independent distribution

Establishments registered with the Care Quality Commission (CQC) (England only)

- Adult placement
- Care homes providing nursing care (adults)
- Care homes providing personal care (adults)
- Clinics
- Hospices
- Hospitals in the independent sector
- Independent treatment centres
- Nursing agencies
- Private medical practitioners

Please note: CQC and OFSTED do not distribute these alerts. Independent healthcare providers and social care providers can sign up to receive Supply Disruption Alerts directly from the Department of Health's Central Alerting System (CAS) by sending an email to: safetyalerts@mhra.gov.uk and requesting this facility.

Enquiries

England

Send enquiries about this notice to the DHSC Supply Resilience Team, quoting reference number **SDA/2019/005**

Email: supplyresiliencemd@dhsc.gov.uk