



20 December 2019

## **Medicine Supply Alert Notice**

### **Ranitidine: all formulations**

**Priority: Second update to MSAN (2019)22**

**Valid until: 20 March 2020**

### **Summary**

1. This supply disruption alert update supersedes the previous update (MSAN (2019)22 update) issued on 12 December 2019 and advises on the following.
  - **Ranitidine injection is back in stock and supplies are available to order from wholesalers.**
  - Ranitidine tablets, effervescent tablets and oral solution will continue to be unavailable with no date for resupply until further notice.
  - Clinical advice on alternatives to oral ranitidine in children has been produced by UK Medicines Information (table 2; see Annex B). This guidance is in addition to previous advice issued for the management of adults (table 1; see Annex A).
  - There are short term supply issues affecting alternative H2-receptor antagonists.

### **Advice and Actions**

2. All healthcare professionals in primary, secondary or specialist healthcare services who prescribe or supply ranitidine should consider the following advice to manage affected patients.

#### **3. Ranitidine injection**

- Prescribe ranitidine injection in line with local guidance.
- Do not stockpile.

#### **4. Oral ranitidine**

Continue to follow the advice issued in MSAN (2019)22 update from 12 December 2019, which is as follows:

##### **Licensed use for gastrointestinal conditions**

- Do not initiate treatment with oral ranitidine in new patients.
- Identify current patients prescribed ranitidine tablets, effervescent tablets and oral solution, and review to establish if ongoing treatment is still required.

- If ongoing treatment is still required, then consider switching to an alternative oral treatment (see table 1 for alternative acid suppressants in adults and table 2 for alternative acid suppressants in children).
- **It is recommended that, where possible, patients are not switched to an alternative H2-receptor antagonist in the first instance as this may exacerbate a shortage of these products. There are currently sufficient supplies of oral omeprazole to manage an increase in demand.**

#### Specialist / unlicensed indications

- Do not initiate treatment with oral ranitidine in new patients.
- Local specialists should be consulted for advice on alternatives for specialist / unlicensed indications and high-risk cohorts of patients.
- For clinical alternatives to oral ranitidine in paediatric patients, please see table 2.

#### Alternative H2 antagonists

- There are currently short-term supply issues affecting cimetidine, famotidine and nizatidine.
- Only prescribe these products as an alternative to ranitidine in patients in whom proton pump inhibitors (PPIs) are unsuitable.
- Prior to prescribing, prescribers should liaise with their pharmacists to understand local stock availability (including resupply dates) of clinical alternatives.
- Further information and updates on these shortages will be disseminated through primary and secondary care networks.

### **Additional Information**

5. At present, in Europe, all suppliers of ranitidine's active ingredient have had their Certificate of Suitability (CEP) suspended. Therefore, until regulatory investigations are complete, and an uncontaminated supplier of ranitidine active ingredient has been found, no further supplies of ranitidine will be manufactured.
6. It is important to note that the situation is dynamic and further supplies of ranitidine in all formulations and strengths cannot be confirmed. Further details will be shared as and when they are available.
7. The following presentations of ranitidine are affected:
  - Ranitidine 75mg, 150mg and 300mg tablets
  - Ranitidine 150mg and 300mg effervescent tablets
  - Ranitidine 150mg/5ml and 75mg/5ml oral solution

### **Enquiries**

8. Any enquiries should be directed to – [PharmacyTeam@gov.scot](mailto:PharmacyTeam@gov.scot) or [NSS.NHSSMedicineShortages@nhs.net](mailto:NSS.NHSSMedicineShortages@nhs.net)

## Alternative formulations

**Table 1: Alternative oral 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
<b>Proton pump inhibitors</b>						
<b>Omeprazole</b>	Capsules, tablets and dispersible tablets: 10mg, 20mg, 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)	<i>Not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy.</i> Losec MUPS® is not licensed for use via enteral feeding tubes, however there is extensive experience of using via this route in practice.
<b>Lansoprazole</b>	Capsules and dispersible tablets: 15mg 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)	Orodispersible tablets are licensed for administration via nasogastric (NG) tubes.
<b>Pantoprazole</b>	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)	
<b>Esomeprazole</b>	Tablets, capsules 20mg, 40mg 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> Granules are licensed for administration via NG or gastric tubes.
<b>Rabeprazole</b>	Tablets 10mg, 20mg	20mg OD	UL (10-20mg OD) ¥	20mg OD (treatment) 10-20mg long term maintenance 10mg OD symptomatic GORD	UL	

Acid suppressant	Formulation	GU/DU treatment	GU/DU prophylaxis	GORD	NSAID associated GU/DU treatment/prophylaxis	Comments
<b>H2-receptor antagonists</b>						
<b>Nizatidine</b>	Capsules 150mg	150mg BD or 300mg OD	150mg OD	150-300mg bd	150 BD or 300mg OD (treatment)	
<b>Famotidine</b>	Tablets 20mg, 40mg	40mg OD	DU 20mg OD	UL	UL	
<b>Cimetidine*</b>	Tablets 200mg, 400mg and 800mg Liquid 200mg/5mL	400mg BD or 800mg ON (up to 400mg QDS)	400mg ON up to BD	400mg QDS	UL	No data on crushing tablets <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->

**Table 2: Alternative oral acid suppressants for gastro-oesophageal reflux disease in children**

[Refer to BNFC or local paediatric formulary for other indications/off label use]

Before switching to another agent, review if patients still require acid suppression or if could be stepped down to an antacid

Acid suppressant	Formulation	Licensed age group	Dose	Comments
<b>Proton pump inhibitors</b>				
<b>Omeprazole</b>	Capsules, tablets and dispersible tablets: 10mg, 20mg, 40mg  <i>An unlicensed liquid is available as a manufactured special. However, there is only limited evidence of efficacy.</i>	> 1 year and ≥ 10 kg	<u>&lt;2.5kg</u> 0.7-1.4mg/kg to 3mg/kg/day  <u>2.5 – 7kg</u> 5mg to 3mg/kg/day (max10mg) <u>7 - 15kg</u>  10mg to 20mg OD  <u>≥15kg</u> 20mg to 40mg OD	<ul style="list-style-type: none"> <li>• Losec MUPS® tablets may be dispersed in water (do not crush tablet) for oral liquid administration. Halve 10mg tablet before dispersing for 5mg dose.</li> <li>• Losec MUPS® is not licensed for use via enteral feeding tubes, however there is extensive experience of using via this route in practice (NB: granules are approx. 0.5mm in diameter and tend to block fine-bore feeding tubes [&lt;8Fr])</li> <li>• Esomeprazole granules are licensed for administration down tubes ≥6 Fr.</li> <li>• <i>Unlicensed liquid may be required in age&lt;1 year with nasogastric (NG) or gastric tubes &lt; 8 Fr, or in patients intolerant/allergic to excipients in esomeprazole granules.</i></li> </ul> <p><i>Not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy</i></p>
<b>Esomeprazole</b>	Tablets, capsules, 20mg and 40mg	≥12 years	20-40mg OD	Granules licensed for administration via enteral feeding tube ≥6 Fr
	10 mg gastro-resistant granules for oral suspension	1-11 years	Weight 10 - <20 kg: 10mg OD Weight ≥20 kg: 10-20mg OD	<i>Not to be prescribed with clopidogrel due to risk of reducing its antiplatelet efficacy</i>
<b>Pantoprazole</b>	Tablets 20mg and 40mg	≥12 years	20 mg OD	
<b>Lansoprazole</b>	Capsules and dispersible tablets: 15mg and 30mg	No paediatric licence but used off label in this population	Off label use:  <u>Infant 2.5kg – 5kg</u> 3.75mg (1/4 of a 15mg tablet) OD  <u>5 – 10kg</u> 7.5mg (1/2 a 15mg tablet) OD  <u>10 - 30kg</u> 15mg OD  <u>&gt;30kg</u> 30mg OD	<p><u>Dispersible tablets</u></p> <ul style="list-style-type: none"> <li>• Excipients include aspartame.</li> <li>• Dose should be rounded to the nearest solid dosage form i.e. half or quarter of tablet.</li> <li>• Halve or quarter tablet before dispersing in water for oral liquid administration. Stir thoroughly before administration.</li> <li>• Licensed for administration via NG tube (can be dispersed in 10mL water and flushed through tube &gt; 8Fr).</li> <li>• For fine-bore tubes &lt;8Fr, dissolve contents of capsule in 8.4% sodium bicarbonate before administration).</li> <li>• Lansoprazole dispersible tablets are generally easier to use than omeprazole. When using feeding tubes of gauge under 8Fr in patients over 2.5kg.</li> </ul>
<b>Rabeprazole</b>	Tablets 10mg and 20mg	No paediatric licence	Off label use 1-11 years; <15kg: 5mg OD ≥15kg: 10mg OD ≥12 years: 20mg OD	Crushing is not recommended. Not suitable for enteral tube administration

Acid suppressant	Formulation	Licensed age group	Dose	Comments
<b>H2-receptor antagonists</b>				
<b>Cimetidine</b>	Tablets 200mg, 400mg and 800mg Liquid 200mg/5mL	>1year	<u>≥1 year</u> 25-30mg/kg per day in divided doses  Use in age < 1 year not fully evaluated; 20mg/kg/day in divided doses has been used	No data on crushing tablets.  <i>Caution as CYP P450 inhibitor; care with drug interactions-consult SPC</i>
<b>Nizatidine</b>	Capsules 150mg	No paediatric licence	<u>Off label use</u>  6 months to 11 years 5-10mg/kg/day in 2 divided doses  ≥12 years 150mg BD	Not suitable to be used via enteral feeding tubes, as whilst drug dissolves in water, excipients do not and may coat and block tube.
<b>Famotidine</b>	Tablets 20mg and 40mg	No paediatric licence	<u>Off label use:</u>  1 to ≤3 months 0.5mg/kg/dose OD  ≥3 months to <1 year 0.5mg/kg/dose BD  1 to 16 years 0.5mg/kg/dose BD (maximum 40mg dose)	Without crushing, tablets will disperse in 2 to 5 minutes. This process can be quickened by crushing and mixing tablets with water to for administration. No information available on giving resulting suspension via enteral feeding tubes.

**References:** SPCs, Handbook of Drug Administration via Enteral Feeding Tubes, The NEWT Guidelines for administration of medication to patients with enteral feeding tubes or swallowing difficulties, [Evelina London Paediatric Formulary](#), BNFC, Paediatric & Neonatal Dosage Handbook, 23rd ed

**Please note:** Any decision to prescribe off-label must take into account the relevant GMC guidance and NHS Trust governance procedures for unlicensed medicines. Prescribers are advised to pay particular attention to the risks associated with using unlicensed medicines or using a licensed medicine off-label.