North Central London
Joint Formulary Committee

Supply disruption of oral ranitidine
Statement for NCL Primary Care

In October 2019, a shortage of oral formulations of ranitidine was declared in the UK following the identification of an impurity in samples of the ranitidine active substance. All stock manufactured for the UK using the affected substance has been quarantined as a precaution. As a result there will be stock shortages of all H_2-receptor antagonists availa ble in the UK (due to increased demand for the alternative H_2-receptor antagonists, and very limited supplies of unaffected oral ranitidine).

NCL has taken the position that this is an opportunity to review the requirement of these prescriptions for patients and where possible to de-prescribe. As such we have outlined the following actions for clinical teams:

1) **Patients in Primary care who request ranitidine will be reactively assessed for the clinical need of gastroprotection; those patients who do not require gastroprotection will be weaned off therapy.**
2) **Patients admitted into Secondary care on ranitidine therapy and have adequate stock of their own ranitidine should be allowed to continue treatment.**
3) **Patients running out of ranitidine (either during admission or estimated to run out shortly after discharge) should be assessed for the clinical need of ongoing treatment.**
    a) **Those who do not warrant ongoing gastroprotection should be weaned off therapy (with an oral antacid or alginate for symptom cover).**
    b) **Those that require long-term or life-long gastroprotective treatment under one of the indications listed in Table 1 can be switched safely to a recommended proton pump inhibitor.**
    c) **Other indications not listed in this document will require further input from Specialists in North Central London; these patients should remain on ranitidine treatment until further advice can be provided.**

1. Background

In September 2019, the EMA and FDA announced the detection of an impurity named NDMA in some ranitidine medicines at low levels.[1,2] It is known that NDMA is present in some foods and water supplies but is not expected to cause harm at low levels – the FDA stating that the finding from preliminary tests barely exceeded amounts found in common foods. At the time, both organisations declared that they would be evaluating the data to assess whether patients using ranitidine would be at any risk from NDMA. The disruption does not affect intravenous ranitidine.

In the subsequent weeks, manufacturers decided to recall their ranitidine products. In October 2019, the Department of Health and Social Care (DHSC) released a supply disruption alert[3], informing healthcare professionals in Primary, Secondary and Specialist care to identify patients on all oral formulations of ranitidine and review to establish if ongoing treatment is required, and if so, to switch to an alternative treatment.

At the October 2019 Joint Formulary Committee meeting, it was decided that a central response from the Committee would be beneficial in reducing variation in practice.

2. Indications where a switch toward PPI use is recommended

Ranitidine has been used for multiple indications and often this is for long-term use (and, in some cases, life-long). The supply disruption has been an opportunity to address the appropriateness of oral ranitidine for these indications.

The indications in Table 1 are those where it has been agreed that an initiation of a proton pump inhibitor (PPI) is appropriate, or a switch from ranitidine to a PPI is suitable (as long as there is no clinical reason for the patient to avoid a PPI, such as a true allergy). Ranitidine and PPIs have different risk/benefit profiles; in the absence of available H2-antagonists, clinicians are encouraged to give careful consideration before making a decision to provide alternative measures of gastroprotection in patients where the potential risks may outweigh the benefit of using a PPI (e.g. patients with history of bone fracture or decompensated liver disease). As with initiating any medicine the risk/benefit of PPI treatment should be considered against alternative options e.g. no protection or antacid.

The impact of this recall is that there will be an increased use of PPIs which are not without clinical risk e.g. increased risk of *C. difficile*. To mitigate the risks, all new prescriptions for a PPI must state the indication and duration of treatment in the patient's medical notes and the drug chart/prescription.

Affected supplies of oral ranitidine are expected to eventually return to circulation once the MHRA and associated manufacturers are satisfied that they are safe for use. When this happens, we would encourage that all patients switched from ranitidine to a PPI during this shortage are reviewed, and those patients that would benefit from ongoing therapy with a H_2-antagonist are switched back to ranitidine therapy, where absolutely necessary.

3. H_2-antagonist availability

For other indications not listed in this document, it has not yet been agreed between the Joint Formulary Committee and Specialists the most appropriate treatment protocol to be used in the absence of ranitidine. Patients should be reviewed for the need for an H2-antagonist, and an appropriate alternative should be chosen based on risk versus benefit (including the severity of symptoms, clinical interactions with current medicines, formulary status and optimisation of current treatments). There may be very small amounts of unaffected ranitidine, nizatidine, famotidine or cimetidine available, though their routine and continued supply throughout the ranitidine supply disruption cannot be guaranteed. Prescribers should liaise with their pharmacists to understand local stock availability of clinical alternatives.

Table 1: List of indications and recommendations agreed by Trusts where it is appropriate to use a PPI

Adults

Prophylactic indications

- Prophylaxis of gastrointestinal adverse events with NSAID
- Prophylaxis of gastrointestinal adverse events with oral corticosteroids
- Prophylaxis of gastrointestinal adverse events with anti-platelets
- Prophylaxis of gastrointestinal adverse events in patients taking dual antiplatelet therapy/ combined antiplatelet and anticoagulant therapy
- Patients taking direct oral anticoagulants (DOACs)
- Prophylaxis of gastrointestinal adverse events in transplant patients/acute transplant rejection on systemic steroids
- Prophylaxis of gastrointestinal adverse events in autoimmune hepatitis or alcoholic hepatitis responsive to steroids

Treatment indications

- Treatment of Gastro-Oesophageal Reflux Disease (GORD)
- Treatment of uninvestigated dyspepsia
- Treatment of functional dyspepsia
- Treatment of NSAID associated gastric or duodenal ulcer
- Treatment of Gastric/duodenal ulcer (not NSAID induced)
- Eradication of *Helicobacter pylori*
- Treatment of dyspepsia in pregnancy
- Hyperemesis Gravidarum
- Symptom management of oesophageal disorders whilst taking a Multikinase inhibitor (including Tyrosine Kinase inhibitors)

Enteral tube administration in adults (all indications)

- Enteral tube administration of PPIs in adults

Paediatric

Prophylactic indications

- Prophylaxis of gastrointestinal adverse events with oral corticosteroids in paediatrics

Treatment indications

- Treatment of Gastro-Oesophageal Reflux (GOR) and Gastro-Oesophageal Reflux Disease (GORD) in children and young people who can tolerate oral feeding
- Treatment of Gastro-Oesophageal Reflux (GOR), treatment of Gastro-Oesophageal Reflux Disease (GORD) or prophylaxis of gastrointestinal adverse events with oral corticosteroids in children and young people who are fed by enteral tubes.

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events with NSAIDs[1]	• Use a PPI in people at high risk of GI adverse events (which includes patients who have a history of complicated ulcer or >2 risk factors) • Consider a PPI in people at moderate risk of GI adverse events (which includes patients with 1-2 risk factors) • The risk factors for NSAID-induced gastrointestinal adverse events are: o Age over 65; o High dose of NSAID; o Prolonged requirement for NSAIDs; o Previous GI adverse reaction to NSAIDs without gastroprotection; o Concomitant use of medications known to increase the likelihood of upper GI adverse events (e.g. anticoagulants, corticosteroids or SSRIs/SNRIs); o History of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation; o Serious comorbidities, such as cardiovascular disease, hepatic or renal impairment (including dehydration), diabetes or hypertension; o Heavy smoking; o Excessive alcohol consumption.	**First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **Duration of treatment – for the duration of NSAIDs**
Prophylaxis of gastrointestinal adverse events with oral corticosteroids[2]	• Consider a PPI when gastroprotection is required in patients receiving oral corticosteroids who are at high risk of gastrointestinal bleeding or dyspepsia. • The risk factors for gastrointestinal adverse effects include: o History of gastroduodenal ulcer, gastrointestinal bleeding, or gastroduodenal perforation; o Older age; o Concomitant use of drugs that are known to increase the risk of gastrointestinal bleeding, such as NSAIDs, anticoagulants or SSRIs/SNRIs; o Serious comorbidity, such as advanced cancer. o Patients taking ≥30mg prednisolone or equivalent for >7days	**First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **Duration of treatment – for the duration of oral corticosteroids**

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events with anti-platelets[3]	• Patients at high risk of gastrointestinal adverse effects with anti-platelets can be prescribed a PPI • The risk factors for high risk gastrointestinal adverse effects include: ○ High dose of aspirin (>100mg daily); ○ Older age (especially >70 years); ○ History of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation; ○ Helicobacter pylori infection; ○ Concomitant use of medicines known to increase GI bleed risk (e.g. corticosteroids, NSAIDs or SSRIs/SNRIs). • For dual anti-platelet therapy or anti-platelet with anti-coagulant, see below.	**For low-dose aspirin, ticagrelor or prasugrel** Omeprazole capsules 20mg once daily OR Lansoprazole capsules 15mg once daily **For clopidogrel alone** Lansoprazole capsules 15mg once daily **(Avoid co-prescribing omeprazole or esomeprazole with clopidogrel)** **Duration of treatment – for the duration of anti-platelets**
Prophylaxis of gastrointestinal adverse events in patients taking dual antiplatelet therapy/ combined antiplatelet and anticoagulant therapy (including parenteral anticoagulant)[4,5]	• All patients requiring dual anti-platelet therapy should receive gastroprotective cover with a PPI • If it is essential for patients to remain on antiplatelet therapy whilst receiving an anticoagulant, then ensure gastroprotective cover with a PPI. • "Anticoagulant" in this section can refer to an oral OR a parenteral anticoagulant.	**First-line** Lansoprazole capsules 30mg once daily **Duration of treatment – at least for the duration of dual antiplatelet or antiplatelet/anticoagulant therapy**

Indication	Recommendations	Choice of medication and duration of treatment
Patients taking direct oral anticoagulants (DOACs)[4]	• Studies demonstrated a higher risk of GI bleeding with rivaroxaban (all doses), dabigatran 150mg or edoxaban 60mg daily compared to warfarin. • There is a higher risk of GI bleed when a patient is prescribed an anticoagulant in certain situations. Examples include: o A concomitant ulcer-causing treatment (such as NSAID, antiplatelet, corticosteroid, or SSRI/SNRIs); o A history of GI bleed or ulcer. • For patients at higher risk of GI bleeding, consider an alternative anticoagulant with a lower GI bleeding risk (e.g. warfarin, apixaban, LMWH). • A PPI may be considered in patients where there is concern of the risk of GI bleed. • When concurrent antiplatelet and anticoagulant is recommended by a Specialist, a higher dose of lansoprazole is advised.	**First-line** Omeprazole capsules 20mg once daily **Second-line** Lansoprazole capsules 15mg once daily **If concurrent antiplatelet unavoidable** Lansoprazole capsules 30mg once daily **Duration of treatment –the duration of "higher-risk" period (this is potentially long-term)**

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of Gastro-Oesophageal Reflux Disease (GORD)[6,7]	• Use a "full-dose" PPI first-line for 4-8 weeks in patients with GORD. • If symptoms recur after initial treatment, offer a PPI at the lowest possible dose to control symptoms. • Use a "full-dose" PPI for 8 weeks to heal severe oesophagitis • If the initial treatment for severe oesophagitis fails, consider switching to another "full-dose" PPI or a "high-dose" or the initial or alternative PPI • Offer a "full-dose" PPI as long-term maintenance treatment for people with severe oesophagitis, taking into account the person's preference and clinical circumstances. • For patients receiving long-term maintenance therapy with a H_2-receptor antagonist for severe oesophagitis and no clinical circumstances preventing the use of a PPI, switch the patients' therapy to the recommended "full-dose" PPI option. • If the patient fails to respond to maintenance treatment, consider an alternative PPI at "full-dose" or "high-dose".	**"Low-dose" PPI** **First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **"Full-dose" PPI** **First-line** Omeprazole capsules 40mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 30mg once daily **"High-dose" PPI** **First-line** Omeprazole capsules 40mg twice daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 30mg twice daily **Duration of treatment – Initially 4-8 weeks, then review**

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of uninvestigated dyspepsia[6,7]	• Review for medications contributing to dyspepsia and the need for ongoing treatment. • Offer the recommended "full-dose" PPI therapy for 4 weeks to patients with dyspepsia. • Offer *H pylori* testing to patients with dyspepsia. • Step-down PPI therapy to the lowest dose required to control symptoms. • For patients on long-term maintenance therapy with a H_2-receptor antagonist and no clinical circumstances preventing the use of a PPI, switch the patients therapy to the recommended "low-dose" PPI option.	**"Low-dose" PPI** **First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **"Full-dose" PPI** **First-line** Omeprazole capsules 40mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 30mg once daily **Duration of treatment – initially 4 weeks, then review**
Treatment of functional dyspepsia[6,7]	• In patients that have *H pylori* infection excluded, offer a "low-dose" PPI for 4 weeks. • If symptoms recur after initial treatment, offer a PPI at the lowest dose possible to control symptoms. • For patients on long-term maintenance therapy with a H_2-receptor antagonist and no clinical circumstances preventing the use of a PPI, switch the patients therapy to the recommended "low-dose" PPI option.	**"Low-dose" PPI** **First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **Duration of treatment – initially 4 weeks, then review**

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of NSAID associated gastric or duodenal ulcer[6–8]	• Wherever possible, the NSAID should be withdrawn if an ulcer occurs. • Test the patient for *H pylori* infection. • Use a "full-dose" PPI first-line to treat active ulcer for 8 weeks. • For patients continuing to take an NSAID after peptic ulcer healing, discuss the potential harm from NSAID treatment and offer alternative arrangements (e.g. lower-dose or PRN use). Review the need for NSAID use regularly (at least every six months). • For patients who continue on an NSAID following ulcer healing, prescribe alongside a PPI. • If ulcer healing fails, exclude non-adherence, malignancy, failure to detect *H pylori*, inadvertent NSAID use, other ulcer-inducing medications and rare causes (e.g. Zollinger-Ellison syndrome or Crohn's disease). • If symptoms recur after initial treatment, offer a PPI to be taken at the lowest dose possible to control symptoms.	**"Low-dose" PPI** **First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **"Full-dose" PPI** **First-line** Omeprazole capsules 40mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 30mg once daily **Duration of treatment – initially 8 weeks, then review**

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of Gastric/duodenal ulcer (not NSAID induced)[6–8]	• Test the patient for *H pylori* infection. • Offer a "full-dose" PPI for 4 to 8 weeks to patients who have tested negative for *H pylori* and do not take NSAIDs. • If ulcer healing fails, exclude non-adherence, malignancy, failure to detect *H pylori*, inadvertent NSAID use, other ulcer-inducing medications and rare causes (e.g. Zollinger-Ellison syndrome or Crohn's disease). • If symptoms recur after initial treatment, offer a PPI to be taken at the lowest dose possible to control symptoms.	**"Low-dose" PPI** **First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **"Full-dose" PPI** **First-line** Omeprazole capsules 40mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 30mg once daily **Duration of treatment – initially 4-8 weeks, then review**
Eradication of *Helicobacter pylori*[8–10]	• Use standard first-line combination therapy using a PPI and associated antibiotics • Patients that fail first-line therapy will generally be treated in Secondary care (using medications that may be restricted for Secondary care use).	**For a list of *H pylori* eradication regimes, please see the page of "recommended regimens for helicobacter pylori eradication" in the** BNF **Pepto Bismol® restricted to Secondary care only.** **Duration of treatment – usually 7-14 days, then review**

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events in transplant patients/acute transplant rejection on systemic steroids	As per "Prophylaxis of gastrointestinal adverse events with oral corticosteroids"	**First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **Duration of treatment – for the duration of oral corticosteroids**
Prophylaxis of gastrointestinal adverse events in autoimmune hepatitis or alcoholic hepatitis responsive to steroids	As per "Prophylaxis of gastrointestinal adverse events with oral corticosteroids"	**First-line** Omeprazole capsules 20mg once daily **Second-line (or if taking concomitant clopidogrel)** Lansoprazole capsules 15mg once daily **Duration of treatment – for the duration of oral corticosteroids**
Treatment of dyspepsia in pregnancy[11,12]	• The first measure for patients is recommendation of lifestyle advice. • Antacid and alginates products are recommended as first-line products (alginate products may be particularly useful if GORD symptoms are dominant). • Patients can be asked to continue ongoing antacid treatment by purchasing from their local pharmacy (unless they meet a general exception that requires the treatment to be prescribed by a GP, such as symptoms that suggest the condition is not minor). • For severe symptoms or symptoms persisting with an antacid or alginate, use a PPI.	**First-line** Peptac® or equivalent – 10-20mL four times daily (after food and before bed). **Second-line (following optimisation of first-line)** Omeprazole capsules 20mg once daily **Duration of treatment – for the duration of symptoms in pregnancy**

Indication	Recommendations	Choice of medication and duration of treatment
Hyperemesis Gravidarum[11]	• The use of a H_2-antagonist or PPI in hyperemesis gravidarum is intended to treat the associated epigastric pain. • For this reason, please refer to "Dyspepsia in pregnancy".	**First-line** Peptac® or equivalent – 10-20mL four times daily (after food and before bed). **Second-line (following optimisation of first-line)** Omeprazole capsules 20mg once daily **<u>Duration of treatment – for the duration of symptoms in pregnancy</u>**
Symptom management of oesophageal disorders whilst taking a Multikinase inhibitor (including Tyrosine Kinase inhibitors)	• There is a risk of reduced absorption of certain multikinase inhibitors when given with acid suppressive agent, and should be avoided if possible. • If acid suppression is absolutely necessary due to adverse effects, the multikinase inhibitor needs to be given at a separate time from the acid suppressive agent. • Antacids are short-acting acid suppressive agents and are hence preferred for symptom management. • Antacids should be taken at least 4 hours before or 2 hours after a multikinase inhibitor. • Patients who remain symptomatic despite having trialled antacids titrated up to the maximum daily dose should be assessed prior to offering another line of therapy. This would consider: o The risk of reduced absorption of the respective multikinase inhibitor by the acid suppressive therapy; o The risk of interaction with other regular medication (& the possibility of these causing an increase in gastric acid production); o The severity of the symptoms; o Counselling on lifestyle measures to reduce gastric acid production; • The current availability of any unaffected batches of H_2-antagonists	**First-line** Peptac® or equivalent – 10-20mL four times daily (after food and before bed). **The dose of antacid must be taken either 2 hours before or 4 hours after the multikinase inhibitor.** **Second-line** **The patient must be reviewed to determine the need for further acid suppressive therapy;** **if further treatment is needed, the choice of agent must be made based on availability, safety, risk of interaction with the multikinase inhibitor and other regular medication.**

Indication	Recommendations	Choice of medication and duration of treatment
Enteral tube administration of PPIs in adults[13–16]	**Lansoprazole dispersible tablets** can be used for enteral tubes larger than 8Fr. • The dispersible tablet is placed into a barrel of an enteral syringe. • Draw 10mL into the syringe. • Invert the syringe and draw an additional 1mL of air into it. • Shake the syringe gently for 10-20 seconds until the tablet has dispersed. • After the tablet has dispersed, administer via enteral tube. • Refill the syringe with approximately 5mL water, shake gently, and flush the enteral tube. An **omeprazole unlicensed specials suspension** is also available. The suspension has a short expiry and is not cost-effective compared to the lansoprazole dispersible tablets. It can be administered without further dilution via an enteral tube. After administration, draw up an equal volume of water into the syringe used for omeprazole and flush via the enteral tube to ensure the whole dose is given.	**First-line** Lansoprazole dispersible tablets (dispersed in water) **Second-line** (if fine bore tube <8Fr or if issues in compliance) Omeprazole unlicensed special suspension [Δ] [Δ] Omeprazole unlicensed specials suspension has a very short expiry and is not cost-effective; it should be reserved for those patients who require gastroprotection via enteral tube and there are compliance issues with the preparation & administration of a lansoprazole dispersible tablet, or if their tube becomes blocked when using lansoprazole dispersible tablets, or where the tube is fine bore (<8 Fr).

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events with oral corticosteroids in **paediatrics**[2]	• Consider a PPI when gastroprotection is required in patients receiving oral corticosteroids who are at high risk of gastrointestinal bleeding or dyspepsia. • The risk factors for gastrointestinal adverse effects include: o History of gastroduodenal ulcer, gastrointestinal bleeding, or gastroduodenal perforation; o Concomitant use of drugs that are known to increase the risk of gastrointestinal bleeding, such as NSAIDs and anticoagulants; o Serious comorbidity, such as advanced cancer.	Lansoprazole dispersible tablets*† <u>For children up to 30kg</u>: 0.5-1mg/kg (max 15mg) every morning <u>For children 30kg and over</u>: 15mg every morning **<u>Duration of treatment – for the duration of corticosteroid treatment</u>** *Please note that the SPC for lansoprazole dispersible tablets cannot recommend the use of the medication in children due to limited data; however, it is a recommended treatment option used by Specialist teams at Great Ormond Street Hospital. †If dispersing the tablet in water, consider dose rounding to the nearest quarter tablet into water and using the whole of the resultant solution.

Indication	Recommendations	Choice of medication and duration of treatment

Treatment of Gastro-Oesophageal Reflux (GOR) and Gastro-Oesophageal Reflux Disease (GORD) in **children and young people** who can tolerate oral feeding.[17]	• In breast fed infants with frequent regurgitation associated with marked distress despite a breastfeeding assessment and advice, consider alginate therapy for a trial period of 1-2 weeks.
	• In formula-fed infants, if the stepped approach of feeding is unsuccessful as per Section 1.2.3 of NICE Guidance, stop the thickened formula and offer alginate therapy for a trial period of 1-2 weeks.
	• Alginate therapy can be continued if successful, but try stopping at intervals to see if the infant has recovered.
	• Acid-suppressing drugs should not be offered to treat over regurgitation in infants and children occurring as an isolated symptom.
	• Consider a 4-week trial of a PPI for those who are unable to tell you about their symptoms who have overt regurgitation and one or more of the following:
	  ○ Unexplained feeding difficulties (e.g. refusing feeds, gagging or choking).
	  ○ Distressed behaviour
	  ○ Faltering growth
	  • Consider a 4-week trial of a PPI for children and young people with persistent heartburn, retrosternal or epigastric pain.
	  • Assess the response to the 4-week trial and refer to specialist if symptoms do not resolve or recur after stopping treatment.
	• Offer PPI treatment to infants, children and young people with endoscopy-proven reflux oesophagitis, and consider repeat endoscopic examinations as necessary to guide subsequent treatment.
	• Please note that some Specialists may recommend higher doses in the most severe cases of GORD (on Consultant approval only).
		Alginate therapy
		Gaviscon infant® powder sachets
		Neonate (body weight up to 4.5kg)
		1 dose as required; maximum 6 doses per day
		Neonate (body weight 4.5kg or above)
		2 doses as required; maximum 12 doses per day
		Child aged 1-23 months (body weight up to 4.5kg)
		1 dose as required; maximum 6 doses per day
		Child aged 1-23 months (body weight 4.5kg or above)
		2 doses as required; maximum 12 doses per day
		
		PPI therapy
		Lansoprazole dispersible tablets*†
		For children up to 30kg:
		0.5-1mg/kg (max 15mg) every morning
		For children 30kg and over:
		15mg every morning
		Duration of treatment – 4 weeks, then review
		
		*Please note that the SPC for lansoprazole dispersible tablets cannot recommend the use of the medication in children due to limited data; however, it is a recommended treatment option used by Specialist teams at Great Ormond Street Hospital.
		†If dispersing the tablet in water, consider dose rounding to the nearest quarter tablet into water and using the whole of the resultant solution.

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of Gastro-Oesophageal Reflux (GOR), treatment of Gastro-Oesophageal Reflux Disease (GORD) or prophylaxis of gastrointestinal adverse events with oral corticosteroids in **children and young people who are fed by enteral tubes**.[15–17]	• As per "Treatment of Gastro-Oesophageal Reflux (GOR) and Gastro-Oesophageal Reflux Disease (GORD) in children and young people who can tolerate oral feeding" or "Prophylaxis of gastrointestinal adverse events with oral corticosteroids in paediatrics" sections. • Please note that some Specialists may recommend higher doses of PPI in the most severe cases of GORD (on Consultant approval only).	**For enteral tubes 8 Fr or greater** Lansoprazole dispersible tablets For children up to 30kg: 0.5-1mg/kg (max 15mg) every morning For children 30kg and over: 15mg every morning **For fine bore tubes (<8 Fr) or compliance issues** Omeprazole suspension (unlicensed specials product)[Δ] For Neonate 700 micrograms/kg once daily for 7–14 days, then increased if necessary to 1.4–2.8 mg/kg once daily. For Child 1 month–1 year 700 micrograms/kg once daily, increased if necessary to 3 mg/kg once daily (max. per dose 20 mg). For Child 2–17 years (body-weight 10–19 kg) 10 mg once daily, increased if necessary to 20 mg once daily, in severe ulcerating reflux oesophagitis, maximum 12 weeks at higher dose. For Child 2–17 years (body-weight 20 kg and above) 20 mg once daily, increased if necessary to 40 mg once daily, in severe ulcerating reflux oesophagitis, maximum 12 weeks at higher dose. [Δ] Omeprazole unlicensed specials suspension has a very short expiry and is not cost-effective; it should be reserved for those patients who require gastroprotection via enteral tube and there are compliance issues with the preparation & administration of a lansoprazole dispersible tablet, or if their tube becomes blocked when using lansoprazole dispersible tablets, or where the tube is fine bore (<8 Fr).

References

1. National Institute of Clinical Excellence. NSAIDs - prescribing issues - NICE CKS. https://cks.nice.org.uk/nsaids-prescribing-issues#!scenario. Published August 2019. Accessed October 22, 2019.

2. National Institute of Clinical Excellence. Corticosteroids - oral - NICE CKS. https://cks.nice.org.uk/corticosteroids-oral#!scenario. Published November 2017. Accessed October 22, 2019.

3. National Institute of Clinical Excellence. Antiplatelet treatment - NICE CKS. https://cks.nice.org.uk/antiplatelet-treatment#!scenarioClarification. Published September 2018. Accessed October 22, 2019.

4. Drebes A, Gates C. DOAC Prescribing Support for NCL: AF and VTE. April 2018. https://www.ncl-mon.nhs.uk/wp-content/uploads/Guidelines/9_DOAC_prescribing_support.pdf.

5. Drebes A, Gates C. Direct Oral Anticoagulant (DOAC) Interactions. August 2018. https://www.ncl-mon.nhs.uk/wp-content/uploads/Guidelines/9_DOAC_interactions_guide.pdf.

6. National Institute of Clinical Excellence. Recommendations | Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. https://www.nice.org.uk/guidance/cg184/chapter/1-Recommendations. Published October 2019. Accessed October 25, 2019.

7. National Institute of Clinical Excellence. Appendix A: Dosage information on proton pump inhibitors | Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. https://www.nice.org.uk/guidance/cg184/chapter/Appendix-A-Dosage-information-on-proton-pump-inhibitors. Published October 2019. Accessed October 25, 2019.

8. National Institute of Clinical Excellence. Peptic ulceration (British National Formulary). https://bnf.nice.org.uk/treatment-summary/peptic-ulceration.html. Published September 2019. Accessed October 25, 2019.

9. Crowe S. Treatment regimens for Helicobacter pylori - UpToDate. https://www.uptodate.com/contents/treatment-regimens-for-helicobacter-pylori. Published September 2019. Accessed October 25, 2019.

10. North Central London Joint Formulary Committee. Minutes from the NCL JFC meeting April 2019. April 2019. https://www.ncl-mon.nhs.uk/wp-content/uploads/JFC/Minutes/1904_NCL_JFC_Minutes_April2019.pdf.

11. National Institute of Clinical Excellence. Dyspepsia - pregnancy-associated - NICE CKS. https://cks.nice.org.uk/dyspepsia-pregnancy-associated#!scenario. Published April 2017. Accessed October 25, 2019.

12. NHS England. Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs. https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-guidance-for-ccgs.pdf. Published March 29, 2018. Accessed October 30, 2019.

13. Lupin Healthcare. Lansoprazole 15mg Orodispersible Tablets - Summary of Product Characteristics. https://www.medicines.org.uk/emc/product/7182/smpc. Published January 2019. Accessed October 25, 2019.

14. Lupin Healthcare. Lansoprazole 30mg Orodispersible Tablets - Summary of Product Characteristics. https://www.medicines.org.uk/emc/product/7183/smpc#USEHANDLING. Published January 2019. Accessed October 29, 2019.

15. White R, Bradnam V. Handbook of Drug Administration via Enteral Feeding Tubes > Drug: Omeprazole. https://www.medicinescomplete.com/#/content/tubes/c282?hspl=omeprazole. Published February 15, 2018. Accessed October 28, 2019.

16. White R, Bradnam V. Handbook of Drug Administration via Enteral Feeding Tubes > Drug: Lansoprazole. http://www.medicinescomplete.com/#/content/tubes/c211?hspl=lansoprazole. Published February 15, 2018. Accessed October 28, 2019.

17. National Institute of Clinical Excellence. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. https://www.nice.org.uk/guidance/ng1/chapter/1-Recommendations. Published October 2019. Accessed October 29, 2019.

Groups / Individuals who have overseen the development of this guidance:	NCL Joint Formulary Committee Support Pharmacists
Groups which were consulted and have given approval:	Trust version was approved by NCL Consultants, Specialist Pharmacists and Formulary Pharmacists. Abbreviated version was approved by NCL CCGs
File name:	Supply disruption of oral ranitidine – Primary Care communication
Version number:	V2.0
Available on:	https://www.ncl-mon.nhs.uk/
Disseminated to:	All Trusts and CCGs in NCL
Equality impact assessment:	No impact identified
NCL Joint Formulary Committee Approval date:	23/12/2019
Review date:	20/01/2019

Document control

Date	Version	Amendments
07/11/2019	V1.0	First version
19/11/2019	V1.1	'Review date' updated
23/12/2019	V2.0	Indications for acid suppressions with multikinase inhibitors added DOAC monograph updated Added an additional scenario when unlicensed omeprazole suspension may be suitable Section 3 updated