North Central London
Joint Formulary Committee

Recommendations on use of gastro-protective agents: PPIs and H2-Receptor Antagonists

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. Since then, all preparations of ranitidine have been out of stock and the MHRA have suspended licenses for all ranitidine products.

In response to this, NCL have previously outlined the indications (in Table 1) for patients that require long-term or life-long gastroprotective treatment to be safely switched to a recommended proton pump inhibitor (PPI). Clinical teams are advised to:

1. **Actively assess for the need of gastroprotection; patients who do not require gastroprotection should be weaned off therapy (with an oral antacid or alginate for symptom cover).**
2. **Review treatment durations for all gastroprotective agents as indicated in Table 1. Patients undergoing treatment with gastroprotective agents beyond these durations should undergo a clinical review.**
3. **Patients that require long-term or life-long gastroprotective treatment can be safely initiated on a recommended proton pump inhibitor (PPI) in line with Table 1.**
4. **Patients may be initiated on a H2-receptor antagonist (with the lowest acquisition cost in primary care) if they match the initiation criteria outlined in section 3 in the event that i) proton pump inhibitors are contraindicated/not tolerated or ii) dual therapy with a proton pump inhibitor + H2-receptor antagonist (H2RA) is required following an insufficient response to proton pump inhibitors alone.**
5. **Other indications not listed in this document will require further input from specialists in NCL.**

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] In the subsequent weeks, manufacturers recalled their ranitidine products and the MHRA suspended all UK marketing authorisations for ranitidine containing products for human use. The Department of Health and Social Care (DHSC) released a supply disruption alert[3], informing healthcare professionals to switch patients on oral ranitidine to an alternative treatment. JFC published guidance to support this (see Table 1).

In July 2024, the JFC agreed that NCL criteria to determine the appropriate use of alternative H2-receptor antagonists would also be beneficial to reduce variation in practice. The NCL initiation criteria for H2RA (see section 3) recommend initiation in the event that i) PPIs are contraindicated/not tolerated, or ii) dual therapy with a PPI and a H2RA is required following an insufficient response to PPIs alone.

2. Indications where a switch toward PPI use is recommended

The indications in Table 1 are those where it has been agreed that an initiation of a PPI is appropriate, or a switch from H2RAs 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). H2RAs and PPIs have different risk/benefit profiles; 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 in a first-line setting e.g. no protection or antacid.

The ranitidine recall has led to 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.

Quick reference list

Adults

Prophylactic indications

- Stress ulcer prophylaxis (SUP)
- 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
- Prophylaxis of gastrointestinal adverse events in adult haematology or oncology patients

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
- Pre-operative acid reduction in patients at risk of aspiration, or for the prophylaxis of aspiration pneumonitis in patients undergoing a caesarean section (also known as prevention of Mendelson's syndrome)
- 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 indications

Prophylactic indications

- Prophylaxis of gastrointestinal adverse events in paediatric haematology or oncology patients
- 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 - PENDING

Table 1 – Indications which has been agreed that it is appropriate to initiate or switch to a PPI

Indication	Recommendations	Choice of medication and duration of treatment
Stress ulcer prophylaxis in adults (SUP)[4]	• Patients should be clinically assessed for the clinical need of SUP. • Patients at low risk for a gastrointestinal bleed (e.g. patients ventilated <48 hours, few morbidities, no coagulopathy or no history of GI bleed) should be reviewed for clinical need of SUP medication on a case-by-case basis. • If SUP is required, IV ranitidine can be used in critically ill patients who cannot receive enteral medications. • In patients who are established on enteral feed and absorbing (or eating and drinking) the clinical need for SUP should be reviewed. • In patients who are able to receive enteral medications and who require SUP a dispersible PPI should be prescribed. • If ranitidine IV becomes unavailable in the future, IV PPIs may be used.	**If SUP is indicated and medication can be administered orally:** Lansoprazole capsules 30mg once daily **If SUP is indicated and medication can be administered via NG tube:** Lansoprazole dispersible tablets 30mg once daily (dispersed in water)‡ **If SUP is indicated and the patient is nil by mouth, has no enteral access and ranitidine IV is not available:** Intravenous omeprazole 40mg once daily* **Duration of treatment – until the patient is eating and drinking for ≥24 hours and clinically assessed as low ongoing risk of GI bleed.** **‡ Please see the section below for more information on the administration of PPIs via enteral tubes** ***Intravenous PPI of choice may differ at some Trusts in NCL due to formulary status. Trusts that do not use omeprazole should consider an equivalent dose of their formulary intravenous PPI.**

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events with NSAIDs[5]	• 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 **<u>Duration of treatment – for the duration of NSAIDs</u>**
Prophylaxis of gastrointestinal adverse events with oral corticosteroids[6]	• 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 **<u>Duration of treatment – for the duration of oral corticosteroids</u>**

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events with anti-platelets[7]	• 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 (75mg daily), 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)[8,9]	• 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. • Gastroprotection could be considered in high risk patients requiring VTE thromboprophylaxis (although not routinely required)	**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)[8]	• 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)[10,11]	• 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[10,11]	• 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 patient's 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[10,11]	• 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[10–12]	• 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**

Treatment of Gastric/duodenal ulcer (not NSAID induced)[10–12]	• 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**

Indication	Recommendations	Choice of medication and duration of treatment
Eradication of *Helicobacter pylori*[12–14]	• Use standard first-line combination therapy using a PPI and associated antibiotics • In patients that fail first-line eradication therapy, a salvage regimen of bismuth quadruple therapy can be considered (PPI + tetracycline + metronidazole + tripotassium dicitratopbismuthate) • Pepto Bismol® was ratified onto the NCL Joint Formulary in April 2019 by the JFC as a treatment option (as part of combination therapy) for patients with resistant *H pylori* after first-line treatment and previous exposure to levofloxacin (restricted to Secondary care only).	**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**
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**

Indication	Recommendations	Choice of medication and duration of treatment
Treatment of dyspepsia in pregnancy[15,16]	• 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**
Hyperemesis Gravidarum[16]	• 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 **Duration of treatment – for the duration of symptoms in pregnancy**

Indication	Recommendations	Choice of medication and duration of treatment
Pre-operative acid reduction in patients at high risk of aspiration/ prophylaxis of aspiration pneumonitis (including patients undergoing a caesarean section) - also known as prevention of Mendelson's syndrome[17–19]	• There are several treatment options to prevent aspiration; these are similar between pregnant and non-pregnant populations. • The aims of treatment is to increase the gastric pH >2.5 and/or reduce gastric volume. • There are suggestions of alternative treatment options in text for caesarean section patients. However, the studies used to determine the possible treatment options were generally of poor quality. • Oral ranitidine was formerly supplied to patients via a PGD. The production of a new PGD to suit the needs of the local population should be considered. • Trusts in NCL should have further discussions locally and come to a decision as to the treatment protocol to adopt in their respective patient cohorts.	**Alternative options in the absence of oral ranitidine formulations:** • A non-particulate antacid (e.g. **30mL sodium citrate**) administered immediately prior to surgery. • **Oral metoclopramide 10mg administered for two doses** (e.g. the night before and morning of surgery) • **Acid suppressive medication** ○ **Intravenous ranitidine** can be administered immediately prior to induction for emergency surgery **OR** ○ Consider **omeprazole 20-40mg** for two doses administered orally for elective surgery (e.g. the night before and morning of surgery) • **A combination of these medications can be considered for acid suppression and gastric volume reduction.**

Indication	Recommendations	Choice of medication and duration of treatment

Prophylaxis of gastrointestinal adverse events in adult haematology or oncology patients	• Each patient should be assessed for their risk of developing gastrointestinal adverse events prior to initiating chemotherapy.
	• Risk factors include:
	  ○ History of gastroduodenal ulcer, gastrointestinal bleeding, or gastroduodenal perforation;
	  ○ Older age
	  ○ Concomitant use of drugs that are known to increase the risk of gastrointestinal bleeding (e.g. anticoagulants, NSAIDs, corticosteroids etc).
	  ○ Low platelet levels (<50 x 10^9/L)
	• Patients who require gastroprotection should be offered a PPI in the first instance.
	• Trusts should consider whether each chemotherapy protocol used locally require an amendment, or whether a local arrangement can be made to substitute H_2-antagonists with recommended PPIs
		First-line
		Lansoprazole capsules 15-30mg once daily
		<u>Duration of treatment – for the duration of chemotherapy</u>

Indication	Recommendations	Choice of medication and duration of treatment
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; o 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[20–23]	**Lansoprazole dispersible tablets** can be used for enteral tubes 8Fr or larger. • 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. **Lansoprazole capsules** can be used for enteral tubes of all sizes. • Open the contents of a capsule into a medicine pot. • Add 15mL sodium bicarbonate 8.4%. • Stir to dissolve the granules. • Draw the resulting solution into a syringe and administer via the enteral tube. • Add a further 15mL water into the medicine pot; stir to ensure any remaining drug remaining in the pot is mixed with water. • Draw up this dispersion and flush down the tube to ensure the whole dose is given. • Flush the tube with water. If the tube becomes blocked, lock the tube using sodium bicarbonate 8.4% to dissolve any enteric coated granules lodged in the tube. Omeprazole powder for oral suspension is licensed for use in NG and PEG tubes (not tubes terminating in the jejunum): • The powder for oral suspension should be reconstituted by Pharmacy. • Shake the bottle of suspension for 20 seconds. • Draw up the required dose into an enteral syringe. • Administer the medication through the enteral feeding tube. • Draw up 10mL of water and flush the feeding tube	**First-line** Lansoprazole dispersible tablets (dispersed in water) **OR** (if fine bore tube <8Fr) Lansoprazole capsules (opened and dispersed in sodium bicarbonate 8.4%) **Second-line** Omeprazole powder for oral suspension [Δ] OR Omeprazole oral solution [Δ] Please note once constituted, omeprazole powder for oral suspension has a shelf-life of 28 days subject to being kept in an environment between 2-8 degrees Celsius.

Indication	Recommendations	Choice of medication and duration of treatment
Prophylaxis of gastrointestinal adverse events in paediatric haematology or oncology patients[24]	• Each patient should be assessed for their risk of developing gastrointestinal adverse events prior to initiating chemotherapy. • The risk of developing dyspepsia or epigastric pain is compounded by several factors, such as concomitant corticosteroids, stress, chemotherapy, low platelets, nausea and vomiting. • Patients who require gastroprotection should be offered a PPI in the first instance. • Trusts should consider whether each chemotherapy protocol used locally require an amendment, or whether a local arrangement can be made to substitute H_2-antagonists with recommended PPIs	Lansoprazole dispersible tablets* For children up to 30kg: 0.5-1mg/kg (max 15mg) every morning For children 30kg and over: 15mg every morning **<u>Duration of treatment – for the duration of chemotherapy</u>** *Please note that the SPC for lansoprazole dispersible tablets cannot recommend the use of the medication in children due to limited data[20]; however, it is a recommended treatment due to the lower risk of interactions with chemotherapy compared to omeprazole.
Prophylaxis of gastrointestinal adverse events with oral corticosteroids in paediatrics[6]	• 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.[25]	• 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**.[22,23,25]	• 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).	UNDER REVIEW – PENDING Contact your trust specialist pharmacist or NCL Medicines Optimisation Team for advice

For indications not listed in this document, the most appropriate treatment protocol to be used has not yet been agreed between the Joint Formulary Committee and Specialists. Patients should be reviewed for the need of gastroprotection, and an appropriate agent 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).

3. H_2-receptor antagonist use

In general, PPIs are more effective at providing gastroprotection and are lower cost compared to H2RAs and therefore remain the preferred option (in line with the JFC July 2024 review). Prescribing of H2RAs is restricted in NCL in line with the criteria below. The NCL JFC recommend that due to equivalent efficacy and safety across H2RAs (within drug class), the choice of H2RA in NCL should be based on lowest drug acquisition cost in primary care.

H2RA initiation criteria are as follows:

- Approved for gastroprotection in patients on high-dose steroids for immune checkpoint inhibitor toxicities (JFC July 2024)
- Not approved for management of long COVID (UMC June 2022)

Consider switching patients from proton pump inhibitors (PPI) to H2-receptor antagonist for indications listed in Table 1 in the following circumstances:

- PPI contraindicated and continuation of gastroprotection required;
- PPI not tolerated or patient has a perceived allergy and continuation of gastroprotection required:
    - First consider switching to an alternative PPI.
    - If intolerance persists, switch to a H2-receptor antagonist.
- Hypomagnesaemia – this is a class effect with PPIs but has been suggested to be dose dependent. Consideration should be given to reducing the dose of PPI in the first instance if clinically appropriate.
- Acute interstitial nephritis whilst receiving PPI - seek nephrology advice. Consider holding while under investigation.

Consider adding a H2-receptor antagonist to a PPI (dual therapy) if there is an insufficient response with a PPI alone in the following circumstances:

- Scleroderma – patients with GI involvement may require dual treatment of PPI + H2-receptor antagonist with disease progression
- Barrett's disease - may require dual treatment of PPI + H2-receptor antagonist with disease progression
- Uncontrolled disease on monotherapy PPI - may require dual treatment of PPI + H2-receptor antagonist

Patients requiring further consideration before switching from a PPI to H2-receptor antagonist:

- Hyponatraemia is usually seen within the first 3 months of initiating PPI therapy. If a patient is experiencing hyponatraemia less than 90 days since initiation of a PPI:
    - Clinicians should consider other causes of hyponatraemia and address these if clinically appropriate.
    - Consider switching to lansoprazole as it is associated with the lowest risk of hyponatraemia (lansoprazole has the lowest risk of PPI associated hyponatraemia. The SPC for lansoprazole lists hyponatraemia as a very rare (< 1/10,000) adverse effect of lansoprazole compared to the incidence in omeprazole, which is ≥ 1/10,000 to < 1/1,000).
    - If the above steps do not work, consider switching to a H2-receptor antagonist
- Patients with *C. difficile* that require gastric protection – H2-receptor antagonists are still associated with increased risk therefore consider risk-benefit profile.

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Document control

Date	Version	Amendments
31/10/2019	V1.0	First version
01/11/2019	V1.1	Minor amendment to enteral feeding tubes (fine-bore defined as <8 Fr) Additional sentence added to encourage clinicians to evaluate risk versus benefit of using PPIs in certain patient populations
01/11/2019	V1.2	Additional line for consideration in thromboprophylaxis
19/11/2019	V1.3	'Review date' updated
11/12/2019	V2.0	Indications for acid suppressions with multikinase inhibitors added DOAC monograph updated Section 3 updated
19/08/2024	V3.0	Document and title updated to provide recommendations on use of gastroprotective agents in NCL: PPIs and H2RAs. Initial summary, section 1 and section 2 made more concise and amended to include JFC July 2024 decision. Section 3 amended to incorporate previous JFC and UMC decisions regarding H2RAs (including removal of 2 previously approved JFC decisions from meetings in July 2021 and Nov 2020). JFC July 2024 H2RA initiation criteria included in section 3.
30/05/2025	V4.0	Document updated to include licensed omeprazole liquids in adult enteral feeding section; paediatric enteral feeding section still subject to review.
15/07/2025	V4.0	Wording updated on Point 4 of first page and page 21, enabling prescribers choice to select a H2RA with the lowest acquisition cost, where appropriate.
05/08/2025	V4.0	Updated advice for acute interstitial nephritis whilst receiving PPI – page 21