Pharmacological management of gastro-oesophageal reflux disease (GORD) in children and young people in primary and secondary care

Introduction:

Following the publication of the NICE guideline on gastro-oesophageal reflux disease in children and young people, it is considered desirable to produce a local treatment guideline to rationalise and optimise its management.

GORD is a common physiological event that can happen at all ages from infancy to old age, often asymptomatic and frequently after feeds/meals. Only a small proportion will need to be clinically managed, in particular for those presenting with symptoms e.g. discomfort or pain, or GORD-associated complications e.g. oesophagitis or pulmonary aspiration.

Key recommendations:

1. For effortless regurgitation of feeds in well infants, advise and reassure parents or carers:
   - Is very common (it affects > 40% of infants)
   - Usually begins before the infant is 8 weeks old
   - May be frequent (5% of those affected have 6 or more episodes each day)
   - Usually becomes less frequent with time (it resolves in 90% of affected infants before they are 1 year old)
   - Does not usually need further investigation and treatment

2. In infants, children and young people with vomiting and regurgitation, look out for the ‘red-flags’ in table 1, which may suggest disorders other than gastro-oesophageal reflux (GOR).

3. Do not offer acid suppressing drugs, e.g. proton pump inhibitors (PPIs) or H2 receptor antagonists (H2RAs), to treat overt regurgitation in infants and children occurring as an isolated symptom.

4. Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking further advice from the General Paediatric Team and taking into account their potential to cause adverse events.

5. Recognise the following as possible complications of GOR in infants, children and young people:
   - Reflux oesophagitis
   - Recurrent aspiration pneumonia
   - Frequent otitis media (e.g. more than 3 episodes in 6 months)
   - Dental erosion in a child or young person with a neurodisability, in particular cerebral palsy

6. Be aware that some symptoms of a non-IgE-mediated cows’ milk protein allergy can be similar to the symptoms of GORD, especially in infants with atopic symptoms, signs and/or a family history. If a non-IgE-mediated cows’ milk protein allergy is suspected, see the NICE guideline on food allergy in children and young people and the Pan Mersey prescribing guidelines for specialist infant formula feeds in lactose intolerance and cows’ milk protein allergy.

This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, St Helens, Warrington, Wirral, and West Lancashire CCGs.
<table>
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<tr>
<th>Symptoms and Signs</th>
<th>Possible Diagnostic Implications</th>
<th>Suggested Actions</th>
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<tr>
<td><strong>Gastrointestinal</strong></td>
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<tr>
<td>Frequent, forceful (projectile) vomiting</td>
<td>May suggest hypertrophic pyloric stenosis in infants up to 2 months old</td>
<td>Paediatric surgery referral</td>
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<tr>
<td>Bile-stained (green or yellow-green) vomit</td>
<td>May suggest intestinal obstruction</td>
<td>Paediatric surgery referral</td>
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<td>Haematemesis (blood in vomit) with the exception of swallowed blood, for example, following a nose bleed or ingested blood from a cracked nipple in some breast-fed infants</td>
<td>May suggest an important and potentially serious bleed from the oesophagus, stomach or upper gut</td>
<td>General Paediatric Rapid Access Clinic referral</td>
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<tr>
<td>Onset of regurgitation and/or vomiting after 6 months old or persisting after 1 year old</td>
<td>Late onset suggests a cause other than reflux, for example a urinary tract infection (also see the Pan Mersey’s Antimicrobial Guide and Management of Common Infections) Persistence suggests an alternative diagnosis</td>
<td>Urine microbiology investigation Consider General Paediatric Team referral</td>
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<tr>
<td>Blood in stool</td>
<td>May suggest a variety of conditions, including bacterial gastroenteritis, infant cows’ milk protein allergy (also see the NICE guideline on food allergy in children and young people) or an acute surgical condition</td>
<td>Stool microbiology investigation General Paediatric Rapid Access referral</td>
</tr>
<tr>
<td>Abdominal tenderness or palpable mass</td>
<td>May suggest intestinal obstruction or another acute surgical condition</td>
<td>Paediatric surgery referral</td>
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<tr>
<td>Chronic diarrhoea</td>
<td>May suggest cows’ milk protein allergy (also see the NICE guideline on food allergy in children and young people and the Pan Mersey prescribing guidelines for specialist infant formula feeds in lactose intolerance and cows’ milk protein allergy)</td>
<td>General Paediatric Rapid Access Clinic referral</td>
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<td><strong>Systemic</strong></td>
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<tr>
<td>Appearing unwell, Fever</td>
<td>May suggest infection (also see the NICE guideline on fever in under 5s and the Pan Mersey’s Antimicrobial Guide and Management of Common Infections)</td>
<td>Clinical assessment and urine microbiology investigation Treat as appropriate</td>
</tr>
<tr>
<td>Dysuria</td>
<td>May suggest urinary tract infection see the Pan Mersey’s Antimicrobial Guide and Management of Common Infections</td>
<td>Clinical assessment and urine microbiology investigation Treat as appropriate</td>
</tr>
<tr>
<td>Bulging fontanelle</td>
<td>May suggest raised intracranial pressure, for example, due to meningitis (also see the Pan Mersey’s Antimicrobial Guide and Management of Common Infections and the NICE guideline on bacterial meningitis and meningococcal septicaemia)</td>
<td>Consider A&amp;E referral if symptoms suggestive of meningitis</td>
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<tr>
<td>Rapidly increasing head circumference (more than 1cm per week)</td>
<td>May suggest raised intracranial pressure, for example, due to hydrocephalus or a brain tumour</td>
<td>General Paediatric Rapid Access Team referral</td>
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<tr>
<td>Persistent morning headache, and vomiting worse in the morning</td>
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<tr>
<td>Altered responsiveness, for example, lethargy or irritability</td>
<td>May suggest an illness such as meningitis (also see the Pan Mersey’s Antimicrobial Guide and Management of Common Infections and the NICE guideline on bacterial meningitis and meningococcal septicaemia)</td>
<td>Seek immediate medical attention, i.e. A&amp;E referral if symptoms suggestive of meningitis</td>
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</table>
Initial Management of GOR and GORD:

1. When reassuring parents and carers about regurgitation, advise them that they should return for review if any of the following occur:
   - the regurgitation becomes persistently projectile
   - there is bile-stained (green or yellow-green) vomiting or haematemesis (blood in vomit)
   - there are new concerns, such as signs of marked distress, feeding difficulties or faltering growth
   - there is persistent, frequent regurgitation beyond the first year of life.

2. In breast-fed infants with frequent regurgitation associated with marked distress

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Breastfeeding assessment (see table 2 for contact details)</th>
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<tbody>
<tr>
<td>Step 2</td>
<td>Offer a trial of thickener (i.e. mixing 'Carobel' with some water, given on a spoon) before / between feeds - follow instructions in pack here. Local CCG policy may advise thickener is purchased “over the counter”</td>
</tr>
<tr>
<td>Step 3</td>
<td>Frequent regurgitation with marked distress despite breastfeeding assessment</td>
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<tr>
<td></td>
<td>Consider a trial of Alginate Therapy (i.e. Gaviscon Infant) for 1 - 2 weeks (mix with boiled &amp; cooled water or with expressed breast milk as per instructions and give part way through each feed or meal using a spoon or feeding bottle).</td>
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<tr>
<td>Step 4</td>
<td>If successful, continue with Alginate but try stopping it at intervals (e.g. every 2 weeks) to see if the infant has recovered. Wean down thickener when symptoms resolve</td>
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Table 2: Breastfeeding Assessment Contact Details

<table>
<thead>
<tr>
<th>Infant feeding helpline</th>
<th>for infants up to 6 weeks old born at Liverpool Women’s Hospital</th>
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<tbody>
<tr>
<td></td>
<td>0151 702 4293</td>
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Peer Breastfeeding Support Team:

- Breast Start (Sefton) – 0151 291 8024
- BAMBIS (Liverpool) – 0151 233 6874
- Bosom Buddies (Knowsley) – 0151 244 3269
- Bosom Buddies (Warrington) – 01942 483056
- Breastfeeding Support Worker (Halton) on 0300 0290029
- Families and Babies (FAB) (West Lancashire) – 01254 772929
- Home Start Breastfeeding Peer Support (Wirral) - 0151 647 8370 or 07780220481

Other breastfeeding support:

- Local community midwife for infants up to 28 days old
- Local health visitors
3. Formula-fed infants with frequent regurgitation associated with marked distress

<table>
<thead>
<tr>
<th>Step 1</th>
<th>• Review feeding history (normal volume 150ml/kg/day)</th>
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</table>
| Step 2 | • Reduce the feed volumes only if excessive for the infant's weight  
• Continue conservative measures - nursing with head slightly up, not to put the baby down immediately after feeds |
| Step 3 | • Offer a trial of smaller, more frequent feeds (while maintaining an appropriate total daily amount of milk)  
• unless the feeds are already small and frequent |
| Step 4 | • Offer a trial of thickened formula or thickener (i.e. mixing *Carobel* to a standard formula) - follow instructions in pack [here](#). Do not use Carobel to thicken formula which is already pre-thickened. Local CCG policy may advise thickener is purchased "over the counter"  
• An effect of a thickened formula should be seen in a few days  
• If successful, continue with thickened formula, but try stopping at intervals to see if the infant has recovered. Wean down thickened formula or thickener when symptoms resolve |
| Step 5 | • Review thickened formula or thickener; if unsuccessful, consider weaning it off*  
• Once thickened formula or thickener has been weaned, consider a trial of Alginate Therapy (i.e. *Gaviscon Infant*) for 1 - 2 weeks |
| Step 6 | • If successful, continue with Alginate but try stopping it at intervals (e.g. every 2 weeks) to see if the infant has recovered. If unsuccessful, consider pharmacologic treatment and/or referral to secondary care |

* Alginate therapy must not be used with thickened formula in combination as this could lead to over-thickening of stomach contents as a result of bezoar formation.  
Alternating thickened formula with Alginate in each feed has been tried with some success.

4. Pharmacological treatment of GORD

Do not offer acid-suppressing drugs, such as H2 receptor antagonists (H2RAs) or proton pump inhibitors (PPIs) to treat overt regurgitation in infants and children occurring as an isolated symptom.

NICE does not endorse use of *metoclopramide, domperidone* or *erythromycin* to treat GOR or GORD without specialist advice. All prokinetics are [Red](#).

NB: ([MHRA/CHM advice](#)) – metoclopramide: risk of neurological adverse effects; domperidone: risk of cardiac side-effects.

Short-term low-dose erythromycin (unlicensed) has been tried although the data are too limited and of insufficient quality to recommend it as an option. It is often associated with GI side effects.
4.1 For infants and children up to 12 years old

GP to consider a 4-week trial of H2RA (Ranitidine 1st line)

**NICE CKS recommends ranitidine oral solution 75mg/5mL for children aged 0 - 2 years.**

For those who are unable to tell you about their symptoms if any one of the following: unexplained feeding difficulties, distress behaviour and faltering growth

In children with persistent heartburn, retrosternal or epigastric pain

Assess the response to the 4-week trial of H2RA and consider referral to the General Paediatrician if the symptoms:

- do not resolve, or
- recur after stopping the treatment

On referral if the child has persistent or significant symptoms that suggest reflux oesophagitis, the General Paediatrician must stop H2RA and recommend a 4-week trial of PPI

(see Appendix 1)

Consider reviewing treatment as necessary

- do not resolve after 4 weeks
- resolves after 4 weeks

**GP consider refer to Gastroenterology Team for further investigation.**

*Consider Domperidone* if appropriate

- For children under 12 years old weighing less than 35kg, use 250microgram/kg TDS
  - Max 10mg TDS

- ECG monitoring as baseline and during treatment (at least annually)
  - Reconsider domperidone need if abnormal ECG found at baseline

- Assess clinical response 4 weeks after treatment initiation

- Interrupt treatment occasionally to assess symptoms recurrence

**Review H2RA or PPI dose**

- Review in 4 weeks
  - Reduce dose or remain on a low dose as maintenance

**Stop and use on-demand**

- Stop treatment when fully resolves

**Safety issues with long term PPI**

- Clostridium Difficile infection
- Increased risk of bone fractures
- Acute interstitial nephritis
- Community acquired pneumonia
- Hypomagnesaemia
- Vitamin B12 deficiency
- Rebound acid hypersecretion

**H2RAs exhibit tachyphylaxis or tolerance. Chronic use is undesirable.**

Ranitidine oral solution 75mg in 5mL contains alcohol (Zantac 8%; Rosemont 7.5%). The amount of alcohol exposed to a child would be considered acceptable at standard doses. However, the effect of cumulative exposure following long term treatment is not known.

**MHRA doesn’t recommend domperidone use for > 1 week but it is recognised that some patients may require longer term treatment with close monitoring. See NPPG positive statement.**
4.2 For young people and adolescents over 12 years old

GP to consider a 4-week trial of **PPI (Omeprazole 1st line)**

| Take into account the patient’s swallowing ability, choice of formulation and costs |
| Assess the response to the 4-week trial of PPI and consider referral to the General Paediatric Team if the symptoms: |
| do not resolve, or | recur after stopping the treatment |
| Refer to Gastroenterology Team for endoscopy or Follow the ‘Red-Flag’ symptoms (table 1) for referral advice |

**NB:** There is limited evidence to recommend using H2RA and PPI in combination. For patients with a particular problem with nocturnal symptoms that do not respond to PPI alone, adding ranitidine at bedtime in the short term can be considered. Prescribing intermittent 2-week courses of H2RA treatment may be a pragmatic approach for both primary and secondary care clinicians. Routine use is not recommended.⁸

**References:**

1. NICE guideline (NG1) – Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people (Jan 2015)
2. **NICE Clinical Knowledge Summaries** – GORD in children (March 2015)
3. Pan Mersey Prescribing guidelines for specialist infant formula feeds in lactose intolerance and cows’ milk protein allergy (Nov 2014)
5. MHRA Drug Safety Update 30th May 2014 – Domperidone: risks of cardiac side effects
6. **Pan Mersey Area Prescribing Committee Safety Statement:** Safety of long term Proton Pump Inhibitors (2016)
8. **NICE Clinical Knowledge Summaries** Dyspepsia – proven GORD (age from 16 onwards) (Nov 2012)
Appendix 1: Oral Proton Pump Inhibitors Recommendation (including methods of administration)

- Regular treatment review is required and formulation choice should be reconsidered at every review.
- The choice of PPI is suggested based on the practicality in drug dosing, administration and dosage recommendation on BNFC
- *Omeprazole liquid 10mg in 5ml* is an unlicensed Special. There is limited evidence of efficacy for omeprazole liquid as bioavailability is unknown. Its use is restricted for children < 7kg with enteral tubes where MUPS tablets are unsuitable. Avoid use in children over 7kg if possible. Theoretically, its efficacy is better when administered via JEJ tube, as the premature degradation in the acidic stomach has been avoided.
- Omeprazole liquid contains sodium. Check with the Special supplier to ascertain the exact sodium contents for the preparation.
- Omeprazole MUPS tablet can be halved; When disperse in water, the granules settle quickly and have a tendency to block fine bore tubes
- For patients with JEJ tube, the dispersed omeprazole granules (either from capsules or MUPS tablets) can be crushed.
- NB: Enteric coating (in the granules) is not required when it is administered directly to the jejunum
- Lansoprazole orodispersible tablet can be halved; dispersed solution is less likely to block feeding tube
- **Refer to Appendix 2 for the manipulation of different dosage formulations**

**Esomeprazole 10mg sachet can be considered for children aged >1 year old, weighing > 10kg as an alternative if the above PPI fails**
Appendix 2: Manipulation of different dosage formulations

If you require a proportion of the tablet e.g. 5mg omeprazole MUPS or 7.5mg lansoprazole orodispersible tablets, halve the tablet before dispersing it.

Dispensing Omeprazole MUPS tablets or Lansoprazole orodispersible tablets for oral administration

- Place the tablet in a medicine pot, add 10ml of water or a small amount of fruit juice
- Allow the tablet to disperse (usually within 5 minutes when agitated)
- Always stir the mixture just before drinking or drawing up using an oral syringe (the mixture will not be clear).
- Then administer the mixture straight away
- Ensure that the medicine pot (and oral syringe if this is used) is rinsed and that this rinsing water is administered also to ensure that the total dose is given.
- Do not use milk or fizzy water.
- Do not chew or crush the small granules in the dispersion

Dispensing Omeprazole MUPS tablets or Lansoprazole orodispersible tablets for NG and PEG tube administration

- Stop the enteral feed
- Flush the enteral feeding tube with the recommended volume of water
- Place the tablet in the barrel of an appropriate size and type of syringe
- Draw water (10ml for lansoprazole; 20ml for omeprazole) into the syringe and allow the tablet to disperse, shaking as required
- Flush the medication dose down the feeding tube.
- Draw another 10 - 20ml of water into the syringe and also flush this via the feeding tube (this will rinse the syringe and ensure that the total dose is administered).
- Finally, flush with the recommended volume of water.
- Re-start the feed, unless a prolonged break is required.

NB: Omeprazole MUPS dispersion contains small granules that settle quickly and have a tendency to block fine-bore feeding tubes (less than 8Fr). Consider Lansoprazole orodispersible tablets as first line where possible.

Dispensing Omeprazole MUPS tablets or capsules for JEJ tube administration

- Place the tablet or the capsule contents in a mortar, add 10 – 20ml of water
- Allow the contents to disperse (usually within 5 minutes when agitated)
- Crush the mixture using a pestle, ensuring that the small granules have completely disappeared
- Draw up the mixture using an appropriate syringe and then administer it straight away
- Ensure that the mortar and pestle is rinsed and that this rinsing water is administered via the same syringe to ensure that the total dose is given.

NB: If the tube becomes blocked, lock the tube using 8.4% sodium bicarbonate to dissolve any enteric coated granules lodged in the tube. This needs to be prescribed.