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 presented 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 infant 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 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 cow’s 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 cow’s 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 cow’s milk protein allergy.
Table 1: ‘Red flag’ symptoms suggesting disorders other than GOR:

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Possible Diagnostic Implications</th>
<th>Suggested Actions</th>
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<tbody>
<tr>
<td><strong>Gastrointestinal</strong></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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<tr>
<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 Ambulatory referral</td>
</tr>
<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 cow’s 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 Ambulatory 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>
</tr>
<tr>
<td>Chronic diarrhoea</td>
<td>May suggest cow’s 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 cow’s milk protein allergy.)</td>
<td>General Paediatric Team referral</td>
</tr>
<tr>
<td><strong>Systemic</strong></td>
<td></td>
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<tr>
<td>Appearing unwell, Fever</td>
<td>May suggest infection (also see the NICE guideline on feverish illness in children and the Pan Mersey’s Antimicrobial Guide and Management of Common Infections)</td>
<td>Clinical assessment and urine microbiology investigation General Paediatric Team referral</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 General Paediatric Team referral</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>General Paediatric Team referral</td>
</tr>
<tr>
<td>Rapidly increasing head circumference (more than 1cm per week) Persistent morning headache, and vomiting worse in the morning</td>
<td>May suggest raised intracranial pressure, for example, due to hydrocephalus or a brain tumour</td>
<td>General Paediatric Ambulatory Team referral</td>
</tr>
<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>Urgent referral to the Seniors</td>
</tr>
</tbody>
</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
   - Breastfeeding assessment (see table 2 for contact details)
   - Frequent regurgitation with marked distress despite breastfeeding assessment
   - Consider a trial of Alginate Therapy (i.e. Gaviscon Infant) for 1 - 2 weeks
   - If successful, continue with Alginate but try stopping it at intervals (e.g. every 2 weeks) to see if the infant has recovered

Table 2: Breastfeeding Assessment Contact Details

<table>
<thead>
<tr>
<th>Infant feeding helpline</th>
<th>Description</th>
<th>Contact Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>– 0151 702 4293</td>
<td>for infants up to 6 weeks old born at Liverpool Women’s Hospital</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
- Bridge Water Community Healthcare (St Helen) – 0300 300 0103
- Families and Babies (FAB) (West Lancashire) – 01254 772929
- Halton breastfeeding peer support service – 0151 495 5450

**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</th>
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<tbody>
<tr>
<td>1</td>
<td>Review feeding history (normal volume 150ml/kg/day)</td>
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<tr>
<td>2</td>
<td>Reduce the feed volumes only if excessive for the infant's weight</td>
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</tbody>
</table>
| 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 |
| 4    | Offer a trial of thickened standard formula (i.e. mixing ‘Thick & Easy’ or ‘Carobel’ or ‘Resource Thickened Up Clear Oral Powder’ to a standard formula)  
  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 thickener when symptoms resolves |
| 5    | Review thickened standard formula if unsuccessful, consider wean off thickener *  
  Consider a trial of Alginate Therapy (i.e. Gaviscon Infant) for 1 - 2 weeks |
| 6    | If successful, continue with Alginate but try stopping it at intervals (e.g. every 2 weeks) to see if the infant has recovered |

* 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

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.²
4.1 For infants and children up to 12 years old

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 Paediatric Ambulatory Clinic if the symptoms:

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

If the child develops persistent or significant symptoms that suggest reflux oesophagitis, the General Paediatrician must stop H2RA and offer a 4-week trial of PPI (see Appendix 1)

Consider reviewing treatment as necessary (Specialist)

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

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 (Specialist)

- Review in 4 weeks
- Transfer the prescribing to GP if low dose maintenance treatment is deemed necessary

Stop and use on-demand (Specialist)

- Stop treatment when fully resolves

Consider PRN use to manage occasional symptoms.
Transfer the prescribing of PRN treatment to the GP.

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

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.

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.
4.2 For young people and adolescents over 12 years old

Reference:

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 cow’s milk protein allergy (Nov 2014)
5. MHRA Drug Safety Update 30th May 2014 – Domperidone: risks of cardiac side effects
8. NICE Clinical Knowledge Summaries Dyspepsia – proven GORD (age from 16 onwards) (Nov 2012)

NB: There is limited evidence to recommend using H2RA and PPI in combination. For patient 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
Appendix 1: Oral Proton Pump Inhibitors Recommendation

- 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**

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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.

Dispersing 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

Dispersing 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.

Dispersing 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.