DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people

- This guidance is based on NICE NG1 January 2015 Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people

- Gastro-oesophageal reflux (GOR) is a common and normal asymptomatic occurrence seen in infants noticeable by the effortless regurgitation of feeds in young babies. **It does not usually need further investigation or treatment.**
    - it affects at least 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**)
    - regurgitation of feeds can be managed by advising and reassuring parents and carers

- Only a small proportion will need to be clinically managed as GORD (reflux that causes symptoms (for example, discomfort or pain) severe enough to merit medical treatment, or to gastro oesophageal reflux-associated complications (such as oesophagitis or pulmonary aspiration)

- In infants, children and young people with vomiting or regurgitation, look out for the 'red flags' that may require referral (see table 2), which may suggest disorders other than GOR.

- Do not routinely investigate or treat for GOR if an infant or child without overt regurgitation presents with only 1 of the following:
    - unexplained feeding difficulties (for example, refusing to feed, gagging or choking)
    - distressed behavior
    - faltering growth
    - chronic cough hoarseness
    - a single episode of pneumonia

- Do not offer metoclopramide, domperidone or erythromycin to treat GOR(D) unless all of the following conditions are met:
    - the potential benefits outweigh the risk of adverse events
    - other interventions have been tried
    - there is specialist paediatric healthcare professional agreement for its use.

  See domperidone position statement

- Be aware that some symptoms of a non-IgE-mediated cows' milk allergy (CMA) 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 JAPC infant feeding guidelines and the NICE guideline on food allergy in children and young people . Consider referral to access a paediatric dietician.

Initial management of GOR and GORD

When reassuring parents and carers about regurgitation, advise them that they should return for review if any of the following occur:

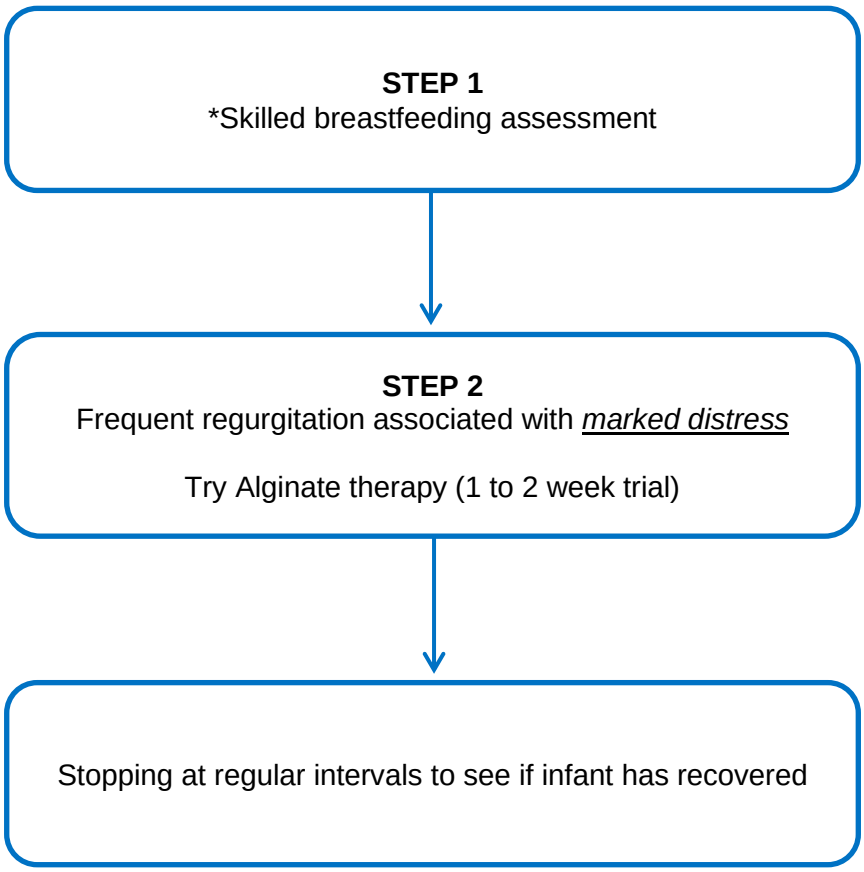
- The regurgitation becomes persistently projectile
- There is bile-stained (green or yellow-green) vomiting or haematemesis (blood in vomit)
- There are new concerns, such as signs of marked distress, feeding difficulties or faltering growth
- There is persistent, frequent regurgitation beyond the first year of life.

Advise patients NOT to use positional management to treat GOR in sleeping infants. Infants should be placed on their back when sleeping.

Gastro-oesophageal reflux (GOR) is the passage of gastric contents into the oesophagus. It is a common physiological event that can happen at all ages from infancy to old age, and is often asymptomatic. It occurs more frequently after feeds/meals. In many infants, GOR is associated with a tendency to 'overt regurgitation' – the visible regurgitation of feeds.

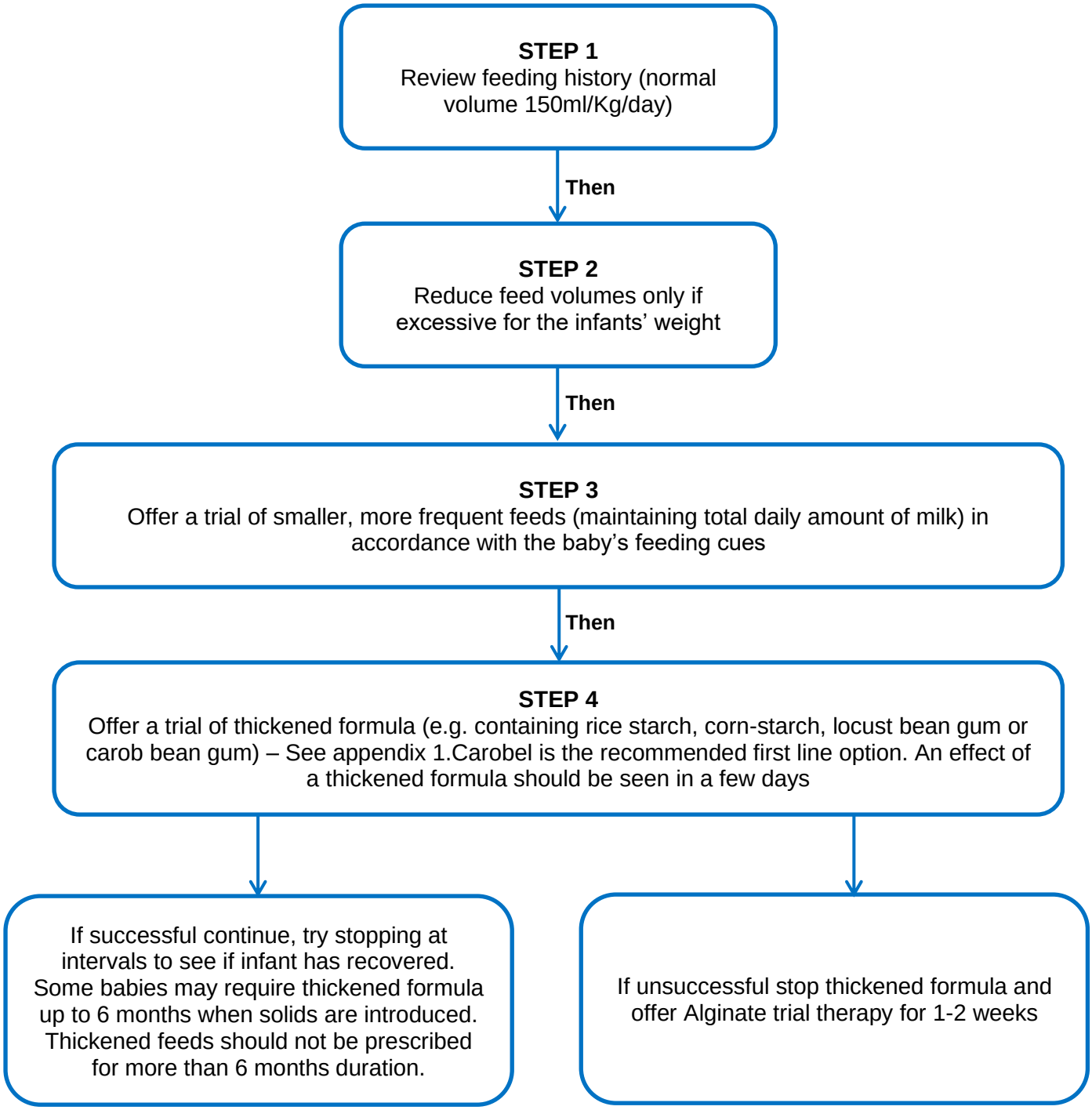
Gastro-oesophageal reflux disease (GORD) refers to gastro-oesophageal reflux that causes symptoms (for example, discomfort or pain) severe enough to merit medical treatment, or to gastro oesophageal reflux-associated complications (such as oesophagitis or pulmonary aspiration). In adults, the term GORD is often used more narrowly, referring specifically to reflux oesophagitis.

1. Breast fed infants with frequent regurgitation



* This could include Derbyshire community services from a health visitor or specialist breastfeeding support from the breastfeeding support team.

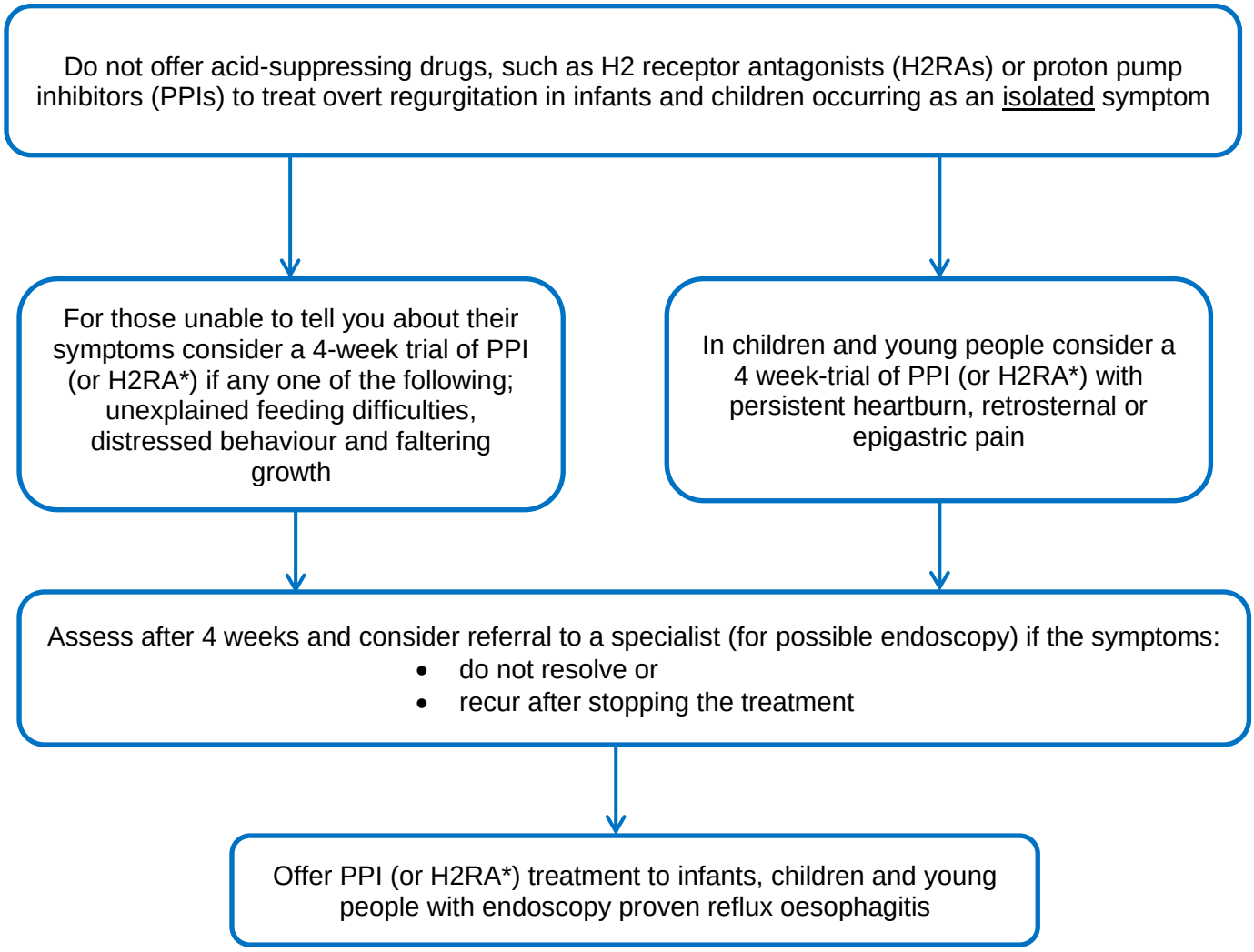
2. Formula-fed infants with frequent regurgitation associated <u>with marked distress</u>



Note: Do not offer acid suppressing drugs to treat overt regurgitation in infants and children occurring as an isolated symptom.

3. Pharmacological treatment of GORD

In a small proportion of infants, GOR may be associated with signs of distress or may lead to certain recognised complications that need clinical management. This is known as gastro oesophageal reflux disease (GORD).



* EMA has issued a recommendation of suspension of ranitidine medicines in the EU. See appendix 2 for further information on alternative H2RA.

Table 1 Detailed prescribing information

Age/weight	Dosing	Notes
Alginates		
GAVISCON INFANT		
Neonate body-weight <4.5kg **or** Child 1-23 month and <4.5kg	1 sachet mixed with feeds (or water, for breast fed infants) when required	Max 6 sachets in 24 hours
Neonate body-weight >4.5kg **or** Child 1-23 month and >4.5kg	2 sachets mixed with feeds (or water, for breast fed infants) when required	Max 12 sachets in 24 hours
PEPTAC (sodium alginate + sodium bicarbonate & calcium carbonate)		
Child 6-11 years	5-10mls after meals and at bedtime	Suspension
Child 12-17 years	10-20mls after meals and at bedtime	
ACIDEX ADVANCE (sodium alginate + potassium hydrogen carbonate)		
Child 2-11 years (under medical advice only)	2.5- 5mls after meals and at bedtime	Suspension
Child 12 -17 years	5-10mls after meals and at bedtime	
Proton pump inhibitors 'Special' suspensions are usually more expensive, have a short half-life and questionable stability when compared to licensed medicines		
LANSOPRAZOLE • Available as capsules and orodispersible tablets (fast-tabs); Should be taken at least 30 minutes before food • Not licensed for use in children*; licensed for administration via NG tube • Dose rounded to the nearest half or quarter of tablet **before** dispersing in water for oral liquid administration due to lack of uniformity once dispersed in water. • FasTabs (either whole or a proportion) can be placed on the tongue and allowed to disperse before swallowing * lansoprazole SPC states 'Treatment of small children below one year of age should be avoided as available data have not shown beneficial effects in the treatment of gastro-oesophageal reflux disease'.		
Child body weight under 30kg	0.5mg-1mg/kg (max 15mg) once daily in the morning (Round dose to the nearest quarter tab)	Not licensed for use in children*
neonate	-	*Consider omeprazole*
2.5-5kg	*Starting dose 3.75mg once daily*	*Quarter of a 15mg fast tab*
5-10kg	*Starting dose 7.5mg once daily*	*Half of a 15mg fast tab*
10-30kg	*Starting dose 15mg once daily*	
Child body weight > 30kg	15-30mg once daily in the morning	
OMEPRAZOLE • Available as capsules or dispersible MUPS tablets. Caps and tabs not licensed for use in children except for severe ulcerating reflux oesophagitis in children over 1 year • **Dispersible gastro-resistant tablets (MUPS)**: Doses can be rounded to the nearest quarter tablet e.g. 2.5mg. The tablet (½ , ¼ or ¾) can be mixed in water, fruit juice, apple sauce or yoghurt on a spoon. Do NOT use milk or carbonated water. The division must be done **before** mixing the tablet as the omeprazole granules do not produce a uniform mixture when dispersed in a liquid. MUPs should not be dispersed in water to draw off a proportion. Try to avoid use of an oral syringe where granules will remain deposited. The enteric coated pellets must not be chewed. • **Capsules**: for children who can drink or swallow semi-solid food- open the capsule and swallow the contents with half a glass of water or after mixing the contents in a slightly acidic fluid e.g. fruit juice or applesauce, or in non-carbonated water. The enteric coated pellets must not be chewed. • Licensed omeprazole **oral suspension** is GREY- to be used only when dispersible MUP tablets have been tried and not tolerated or in cases where doses cannot be safely rounded to the nearest quarter tablet.		
Neonate	700microg/kg once daily for 7-14 days, then increased if necessary to 1.4mg-2.8mg/kg once daily	
Children 1 months-2 years	700microg/kg once daily, increased if necessary to 3mg/kg (max. 20mg) once daily	
<2.5kg	*Starting dose 2.5mg once daily*	*Quarter of a 10mg MUPS tab*
2.5-7kg	*Starting dose 2.5-5mg once daily*	*Quarter or half of 10mg MUPS*
7-10kg	*Starting dose 5mg once daily*	*Half of a 10mg MUPS tab*
Children 2-17 years (body weight 10-19kg)	10mg once daily increased if necessary to 20mg once daily (severe ulcerating reflux oesophagitis)	Max. 12weeks at higher dose.
Children 2-17 years (body weight ≥20kg)	20mg once daily increased if necessary to 40mg once daily (severe ulcerating reflux oesophagitis)	Max. 12weeks at higher dose.

Source BNF for children accessed online [16/2/2022]

Table 2 Red flag symptoms suggesting disorders other than GOR(D)

Symptoms and signs	Possible diagnostic implications	Suggested actions
Gastrointestinal		
Frequent, forceful (projectile) vomiting	May suggest hypertrophic pyloric stenosis in infants up to 2 months old	Refer for same day assessment if clinically unwell, otherwise to rapid access clinic
Bile-stained (green or yellow-green) vomit	May suggest intestinal obstruction	Refer for urgent same day assessment
Haematemesis (blood in vomit) with the exception of swallowed blood, for example, following a nosebleed or ingested blood from a cracked nipple in some breast-fed infants	May suggest an important and potentially serious bleed from the oesophagus, stomach or upper gut	Refer for same day assessment if clinically unwell otherwise to rapid access clinic
Onset of regurgitation and/or vomiting after 6 months old or persisting after 1 year old	Late onset suggests a cause other than reflux, for example a urinary tract infection (also see the NICE Urinary tract infection in under 16s . Persistence suggests an alternative diagnosis	Urine culture investigation and specialist referral as per NICE
Blood in stool	May suggest a variety of conditions, including bacterial gastroenteritis, infant cows' milk protein allergy (also see the NICE guideline on food allergy in under 19s) or an acute surgical condition	Stool microbiology investigation. Refer same day for assessment if clinically unwell, otherwise to rapid access clinic
Abdominal distension, tenderness or palpable mass	May suggest intestinal obstruction or another acute surgical condition	Refer for same day assessment
Chronic diarrhea	May suggest cows' milk (protein) allergy (also see the NICE guideline on food allergy in under 19s)	See JAPC infant feeding guidance. Refer as per guidance
Systemic		
Appearing unwell Fever	May suggest infection (see NICE guideline on Fever in under 5s)	Refer for assessment as per NICE guideline depending on features
Dysuria	May suggest urinary tract infection (also see the NICE guideline on urinary tract infection in under 16s)	Clinical assessment and urine culture investigation. Specialist referral depending on NICE UTI guidelines
Bulging fontanelle	May suggest raised intracranial pressure, for example, due to meningitis (also see the NICE guideline on bacterial meningitis and meningococcal septicaemia in under 16s	Refer for urgent assessment same day assessment. Consider calling 999 ambulance
Rapidly increasing head circumference (more than 1 cm per week) Persistent morning headache, and vomiting worse in the morning	May suggest raised intracranial pressure, for example, due to hydrocephalus or a brain tumour	Refer for urgent same day assessment if clinically unwell, otherwise to rapid access clinic
Altered responsiveness, for example, lethargy or irritability	May suggest an illness such as meningitis (also see the NICE guideline on bacterial meningitis and meningococcal septicaemia in under 16s)	Refer for urgent same day assessment. Consider calling 999 ambulance
Infants and children with, or at high risk of atopy	May suggest cows' milk protein allergy (also see the NICE guideline food allergy in under 19s)	See JAPC infant feeding guidance. Referring as per guidance

Investigations and referrals
Arrange a specialist hospital assessment for infants, children and young people for possible upper GI endoscopy with biopsies if there is:

- haematemesis not caused by swallowed blood (assessment to take place on the same day if clinically indicated; also see table 2)
- melaena; (assessment to take place on the same day if clinically indicated; also see table 2)
- dysphagia (assessment to take place on the same day if clinically indicated)
- no improvement in regurgitation after 1 year old
- persistent, faltering growth associated with overt regurgitation
- unexplained distress in children and young people with communication difficulties
- retrosternal, epigastric or upper abdominal pain that needs ongoing medical therapy or is refractory to medical therapy
- feeding aversion and a history of regurgitation
- unexplained iron-deficiency anaemia
- a suspected diagnosis of Sandifer's syndrome

When deciding whether to investigate or treat, take into account that the following are associated with an increased prevalence of GORD:

- Premature birth
- Parental history of heartburn or acid regurgitation
- Obesity
- Hiatus hernia
- History of congenital diaphragmatic hernia (repaired)
- History of congenital oesophageal atresia (repaired)
- A neurodisability

Other definitions
Marked distress there is very limited evidence, and no objective or widely accepted clinical definition, for what constitutes 'marked distress' in infants and children who are unable to adequately communicate (expressively) their sensory emotions. In this guideline, 'marked distress' refers to an outward demonstration of pain or unhappiness that is outside what is considered to be the normal range by an appropriately trained, competent healthcare professional, based on a thorough assessment. This assessment should include a careful analysis of the description offered by the parents or carers in the clinical context of the individual child

Overt regurgitation refers to the voluntary or involuntary movement of part or all of the stomach contents up the oesophagus at least to the mouth, and often emerging from the mouth.
Regurgitation is in principle clinically observable, so is an overt phenomenon, although lesser degrees of regurgitation into the mouth might be overlooked.

Useful resources
Breast Feeding Network http://www.breastfeedingnetwork.org.uk/ - resources for clinicians and mothers

References
NICE (NG1) Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people [assessed 15/02/2022]
NICE (QS112) Gastro-oesophageal reflux in children and young people. https://www.nice.org.uk/guidance/qs112 [assessed 01/03/2022]

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Appendix 1

Carobel (first line)

The preferred option to commercial anti-regurgitation formulas is the addition of a thickening agent to formula milk. These thicken in the bottle, so need to be given with a wide or variflow teat. If prescribed, feed thickeners must be endorsed ACBS.

Carobel is the first line recommended product for thickened feeds, it is significantly more cost effective than proprietary thickened feeds and enables easy reassessment on ongoing needs as it can be omitted from periodic feeds.

Brand Name	Teat Size Required	Thickening Agent	Preparations	Cost
Instant Carobel	Wide/ variable flow (split)	Carob seed flour	135g carton with 1.7g scoop	£3.04 for 135g pack

Price as per MIMs Feb 2022

Other thickening agents available contain significant calories and are only ACBS approved in infants <1yr with faltering growth – seek advice from a paediatrician or paediatric dietitian.

Instructions for using Carobel to thicken bottle feeds

- add ½ scoop to 90mls hand-warm feed. Shake well and leave to thicken for 3-4 minutes. Shake again and feed.
- thickness can be increased by using 1 scoop in 60mls
- wide/variflow teat will be required

Powdered 'anti-regurgitation' formulas (second line option)

Parents should be encouraged to buy over the counter powdered 'anti-regurgitation' formulas (containing carob seed flour or corn starch), which thicken on mixing or on contact with stomach acid. SMA Staydown is ACBS approved for significant GOR (not to be used for a period >6 months, not to be used in conjunction with any other feed thickener or antacid products). It has special instructions for preparation – advise parents to follow the packet instructions exactly. If prescribed, pre-thickened formulas must be endorsed ACBS.

Brand Name	Teat Size Required	Thickening Agent	Preparations
SMA Anti-reflux	Standard (silicone)	Corn Starch	900g tin

Other over the counter powdered anti-regurgitation formulas are available. Examples include Aptamil Anti-reflux or Cow&Gate anti-reflux, which can be purchased from pharmacies or supermarkets.

Reviewing thickened formula use

- when starting a thickened formula or thickening agent, review efficacy after two weeks. If successful, continue for 3 months or until weaning
- do not prescribe a thickened formula for longer than 6 months in total
- do not prescribe Gaviscon concurrently with a thickened feed or thickening agent

Appendix 2

Alternative H2RA for gastro-oesophageal reflux disease in children

Consider PPI (see p.5) ahead of H2RA

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

Table taken from DHSC Supply Disruption Alert SDA/2019/005(U2) Issued 20 December 2019

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

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

Document update	**Date**