Gastroesophageal Reflux Disease (GERD) in Children (1 of 14)

1. Child presents with symptoms suggestive of gastroesophageal reflux (GER) disease

2. ASSESSMENT
   Are warning signs present?
   - Yes
     - Nonpharmacological therapy
   - No
     - Uncomplicated GER

3. EVALUATION
   Is GERD highly likely?
   - Yes
     - Alternative diagnosis
     - Evaluation
   - No

A. Nonpharmacological therapy

B. Pharmacological therapy
   Empiric therapy
   - Proton pump inhibitors (PPIs)
   - Histamine₂-receptor antagonists (H₂RAs)

B. Pharmacological therapy
   Maintenance therapy
   - Maintain on lowest effective dose or
   - Consider on-demand or intermittent therapy

B. Pharmacological therapy
   Trial of step-up therapy until good response
   - If on H₂RA, switch to PPI
   - Consider other therapeutic options for PPI-resistant GERD
   - Refer patient to pediatric gastroenterologist if w/ disease persistence, recurrence or progression

C. Surgery

Not all products are available or approved for above use in all countries. Specific prescribing information may be found in the latest MIMS.
Gastroesophageal Reflux Disease in Children (2 of 14)

1 GASTROESOPHAGEAL REFLUX DISEASE

- Gastroesophageal reflux (GER) is the normal physiologic passage of gastric contents into the esophagus
  - Frequency of physiologic regurgitation decreases as a child reaches the 1st year of life, & eventually resolves by 12-18 months of age
- Gastroesophageal reflux is categorized as a disease [gastroesophageal reflux disease (GERD)] when reflux is associated with warning signs &/or complications, & requires further evaluation
- More common in formula-fed infants than in purely breastfed infants
- Increased incidence in infants 4 months of age

Etiology
- Produced by various mechanisms such as frequent occurrence of transient relaxation of the lower esophageal sphincter (LES), pressure abnormalities in the LES
  - Other factors in the pathology of GERD include poor esophageal clearance, delayed gastric emptying time, hiatal hernia
- Genetic predisposition has been associated w/ the diagnosis of GERD

Risk Factors
- Neurological impairment
- Obesity
- History of esophageal atresia repair
- Hiatal hernia
- Achalasia
- Chronic respiratory disease (idiopathic interstitial fibrosis, cystic fibrosis, bronchopulmonary dysplasia)
- Lung transplantation
- Preterm infants
- Certain genetic disorders

2 ASSESSMENT

- Since GERD occurs w/ few, if any, abnormal physical findings, a well-taken history is essential in establishing the diagnosis of GERD
- There is no gold standard for the diagnosis of GERD
  - Diagnostic tests are used to document pathologic reflux & presence of complications

History & Physical Examination

Signs & Symptoms
- Infants <12 months of age:
  - Refusal to eat
  - Recurrent vomiting
  - Poor weight gain
  - Irritability
  - Sleep disturbance
- Children ≥1 year of age & adolescents:
  - Abdominal pain/heartburn
  - Recurrent vomiting
  - Dysphagia
  - Asthma
  - Recurrent pneumonia
- Respiratory symptoms (coughing, wheezing, choking)
- Upper airway symptoms (prolonged/chronic cough, hoarseness)

Warning Signs
- Gastrointestinal tract bleeding (hematemesis, hematochezia)
- Abdominal tenderness/distension, palpable abdominal mass
- Bilious vomiting
- Projectile vomiting
- Fever
- Lethargy, irritability
- Hepatosplenomegaly
- Seizures
- Bulging fontanelle
- Positive for genetic/metabolic syndrome

Laboratory Tests

Esophageal pH Monitoring
- Used to quantify the frequency & duration of esophageal acid exposure per episode
  - Does not correlate w/ the severity of acid reflux in GER & GERD
- Depends on the total number of reflux episodes, number of episodes w/ duration lasting >5 minutes, duration of longest reflux episode, & the reflux index (RI: percentage of the total duration w/ recorded esophageal pH of <4.0)
- Not recommended for routine use but may be considered in patients suffering from unexplained apnea/non-epileptic seizure-like episodes/upper airway inflammation, atypical asthma, recurrent pneumonia, frequent otitis media, & dental erosion
### Laboratory Tests (Cont’d)

#### Multichannel Intraluminal Impedance (MII) Monitoring
- Measures electrical impedance between multiple electrodes placed throughout the esophageal lining
- Detects changes caused by fluid, gas, solid, & mixed boluses, & can detect even small bolus volumes
- Usually combined w/ esophageal pH monitoring to be able to monitor whether refluxed material is acidic, non-acidic, or weakly acidic

#### Biopsy
- Required examination after obtaining histologic material during endoscopy
- Histologic abnormalities characteristic of GERD include intraepithelial eosinophilia, basal hyperplasia, spongiosis, & epithelial extensions (rete pegs)

#### Imaging

##### Upper Gastrointestinal Tract Contrast Radiography
- Involves administration of contrast medium to obtain a series of images up to the ligament of Treitz to fully visualize the upper GI tract
- 31-86% sensitivity; 21-83% specificity for GERD
- Not recommended for routine use but may be useful in differentiating GERD from anatomic abnormalities such as antral web, pyloric stenosis, or intestinal malrotation

##### Endoscopy
- Indicated for patients w/ heartburn, hematemesis, melena, epigastric abdominal pain, dysphagia
- Has high specificity (95%) but low sensitivity (<50%) for GERD
  - Since PPI therapy is usually started prior to any test, the sensitivity of endoscopy as a diagnostic test for GERD is poor
- 60% of patients w/ GERD may have non-erosive reflux disease (NERD)
- The first diagnostic test to consider in the presence of alarm symptoms or risk factors for Barrett’s esophagus, in evaluating symptom response to twice-daily PPI therapy, & prior to antireflux surgery
- Routine endoscopy in the general population is not recommended

##### Esophageal Manometry
- Measures upper & lower sphincter pressures, esophageal peristalsis, & motility of the esophageal mucosa during swallowing
- Not recommended in diagnosing GERD but can be used to study the mechanisms causing GERD in a patients, & to rule out other causes of motility problems in the esophagus (eg achalasia, neurologic disorders)

##### Gastroesophageal Scintigraphy (Milk Scan)
- Utilizes $^{99m}$Tc-labeled material to scan the gastroesophageal tract in order to evaluate postprandial reflux & gastric emptying
- Helps identify patients w/ delayed gastric emptying &/or aspiration of refluxed material
- Not recommended for routine use because of low sensitivity (15-59%) & specificity (83-100%) for GERD

##### Ultrasonography
- Esophageal or gastric ultrasound may be considered when barium contrast study is not available
- May help detect the presence of fluid in the gastroesophageal junction, length & position of the LES, & gastro-esophageal angle of His measurement

#### Possible Complications
- Reflux esophagitis
- Aspiration pneumonia
- Otitis media
- Dental erosion
EVALUATION

Clinical Diagnosis Based on Symptomatology

- This classification allows symptoms to define the disease

Eosophageal GERD

- Characterized by the constellation of symptoms that may or may not be defined by further diagnostic tests
  - Includes vomiting, poor weight gain, dysphagia, abdominal pain, substernal/retrosternal pain, esophagitis

Eosophageal Symptomatic Syndromes refer to uninvestigated patients w/ esophageal symptoms but without evidence of esophageal injury

- Include the typical reflux syndrome defined by the presence of troublesome heartburn &/or regurgitation which are characteristic symptoms of GERD
  - Typical reflux syndrome can often be diagnosed without diagnostic testing; however, alarm symptoms should be excluded first

Eosophageal Syndromes w/ esophageal injury include patients w/ demonstrable esophageal injury (eg reflux esophagitis, stricture, Barrett’s esophagus, adenocarcinoma)

Extraesophageal GERD w/ Established Associations

- Defined by conditions w/ an established association w/ GERD based on population-based studies
  - Eg reflux cough syndrome, reflux asthma syndrome, reflux laryngitis syndrome, reflux dental erosion syndrome
  - It is rare for extraesophageal syndromes to occur alone without a concomitant manifestation of typical esophageal syndrome
  - These syndromes are usually multifactorial, w/ GERD as only one of the many other potential aggravating factors

Extraesophageal GERD w/ Proposed Associations

- Defined by conditions whose causal associations w/ GERD are unclear or lacking in evidence
  - Eg sinusitis, pharyngitis, recurrent otitis media, pulmonary fibrosis

Clinical Diagnosis Based on Endoscopic Findings

Erosive Reflux Disease (ERD)

- Defined by presence of esophageal mucosal damage
  - Eg erosive esophagitis, Barrett’s esophagus

Non-erosive Reflux Disease (NERD)

- Defined by absence of esophageal mucosal damage (endoscopy-negative reflux disease)
  - More common in Asia

Endoscopic Classification Criteria

- Classification criteria frequently used for pediatric GERD include Hetzel-Dent, Savary-Miller, & Los Angeles

<table>
<thead>
<tr>
<th>Classification Criteria</th>
<th>Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Los Angeles A</td>
<td>≥1 isolated mucosal breaks, each ≤5 mm long</td>
<td></td>
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<tr>
<td>Los Angeles B</td>
<td>≥1 isolated mucosal break &gt;5 mm long, not continuous w/ top of adjacent mucosal folds</td>
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<tr>
<td>Los Angeles C</td>
<td>≥1 mucosal breaks bridging the top of adjacent mucosal folds, involving &lt;75% of luminal circumference</td>
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<tr>
<td>Los Angeles D</td>
<td>&gt;75% of the luminal circumference w/ ≥1 mucosal breaks bridging the top of folds</td>
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</tr>
<tr>
<td>Hetzel-Dent 0</td>
<td>No mucosal abnormalities</td>
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<tr>
<td>Hetzel-Dent 1</td>
<td>Erythema, hyperemia, mucosal friability present; macroscopic erosions absent</td>
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<tr>
<td>Hetzel-Dent 2</td>
<td>Superficial erosions involving &lt;10% of the mucosal surface of the distal 5 cm of squamous epithelium</td>
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<tr>
<td>Hetzel-Dent 3</td>
<td>Ulcerations/erosions involving 10-50% of the mucosal surface of the distal 5 cm of squamous epithelium</td>
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<tr>
<td>Hetzel-Dent 4</td>
<td>Esophageal mucosa w/ deep ulceration present, or confluent erosion involving more than 50% of the mucosal surface of the distal 5 cm of squamous epithelium</td>
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<tr>
<td>Savary-Miller I</td>
<td>≥1 supravestibular, nonconfluent reddish spots w/ or without exudates</td>
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<tr>
<td>Savary-Miller II</td>
<td>Confluent, noncircumferential erosive &amp; exudative lesions in the distal esophagus present</td>
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<tr>
<td>Savary-Miller III</td>
<td>Circumferential erosions in the distal esophagus, covered by hemorrhagic &amp; pseudomembranous exudates</td>
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<tr>
<td>Savary-Miller IV</td>
<td>Chronic complications (eg deep ulcers, stenosis, scarring w/ Barrett’s metaplasia) present</td>
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</tbody>
</table>
A NON-PHARMACOLOGICAL THERAPY

Dietary Changes
- May consider switching to milk formula that contains extensively hydrolyzed protein or amino acid-based formula instead of regular formulas
- Maternal diet modification is encouraged for mothers of breastfeeding infants
  - Avoidance of egg & milk intake may be considered
- Thickeners (thickening agent, rice cereals) may be considered in healthy formula-fed infants but should be used w/ caution especially in preterm infants at increased risk for necrotizing enterocolitis
- May try small, frequent feedings instead of one big meal while ensuring appropriate total daily amount of nutrition
- Eating before bedtime should be avoided
- Food that may trigger symptoms in adolescents (eg caffeine, carbonated drinks, chocolate, mint-containing food, spicy food) should be avoided

Patient/Parent/Guardian Education

Positional Modifications
- Infants should be kept in an upright position during feeding
- Infants & children should be fully awake when ingesting food
- Semi-supine positioning for at least 2 hours after food ingestion may help reduce reflux-related respiratory events
- Supine positioning during sleep is recommended

Obesity
- Weight loss should be considered in older obese children
- Studies have shown improvement in pH profiles in children who lost weight

Smoking & Alcohol
- Smoking cessation & avoidance of alcohol intake are strongly encouraged adolescents
- Exposure to secondhand smoke also increases irritability in infants & should be avoided

PRINCIPLES OF THERAPY

- Conservative therapy is always the initial management scheme for pediatric patients w/ GERD
- 3 steps involved in the management of GERD include lifestyle modification, acid-suppressive medications, & administration of gastric lining protectants (prokinetic agents) to improve transit of stomach contents
- Following PPI therapy, histological exams is recommended to be able to characterize Barrett's esophagus & to rule out presence of dysplasia

Treatment Goals
- Relief of symptoms
- Healing of esophagitis
- Prevention of recurrence & complications
### Empiric Therapy
- Appropriate initial management for uncomplicated symptomatic GERD in older children & adolescents
  - Not recommended for infants & young children w/ uncomplicated GER
  - May be considered in infants whose GER is accompanied by complications & in cases where nonpharmacologic therapies have been deemed ineffective
- A 4-week trial period is recommended

### Histamine-2 Receptor Antagonists (H2RAs)
- Eg Cimetidine, Famotidine, Nizatidine, Ranitidine
  - Inhibits gastric acid secretion by blocking histamine 2 receptors in the parietal cells
  - Effectively reduces gastric pH by up to 90% when given 3 times daily
  - Also possesses therapeutic properties against erosive esophagitis
  - Use is limited due to tachyphylaxis or tolerance w/ chronic use

### Proton Pump Inhibitors (PPIs)
- Eg Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole
  - Demonstrates superior efficacy compared to other acid suppressants for older children & adolescents
    - Maintains intragastric pH at or above 4 longer & inhibits food-induced acid secretion
    - Reduces symptoms & possesses therapeutic properties against erosive esophagitis
    - Inhibits gastric acid secretion by blocking the Na⁺-K⁺ ATPase enzyme activity in parietal cells
    - Efficacy remains unchanged even w/ chronic use compared to H2RAs

### Maintenance Therapy
- Goal is to have a symptom-free patient without esophagitis
- Use the lowest dose & least potent medication that can obtain a complete & sustained symptomatic response
- The need for maintenance therapy is determined by the impact of the residual symptoms on the patient’s quality of life
- Recommended duration of therapy for moderate to severe heartburn is 2-4 weeks, 4-8 weeks for diagnosed esophagitis, & 3-6 months for severe erosive esophagitis (followed by repeat endoscopy)

### Options for Chronic Acid Suppression:
- **Step-up therapy** involves starting treatment w/ the less potent agents & moving up for treatment response
  - If patient does not respond to an H₂RA within 2 weeks, switch to PPI
  - If patient does not respond to this regimen but some improvement in symptoms are seen, dose of PPI may be increased
  - Consider other therapeutic options in PPI-resistant GERD including switching to a different PPI, changing medication time, or adding a prokinetic agent or an H₂RA at night
  - If patient still does not respond to above regimens, patient’s symptoms are likely not secondary to reflux & warrant diagnostic testing & referral to pediatric gastroenterologist
- **Step-down therapy** makes use initially of a potent acid suppressant, then decreasing dose or switching to less-potent agents
  - PPI dose should be tapered for at least 4 weeks, then weaning from PPIs using H₂RA to control rebound may be considered
  - This is followed by stepping down further to on-demand use of antacids if patient was asymptomatic while taking an H₂RA

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Adjunctive Pharmacotherapy

Antacids
- Eg Aluminum hydroxide, Bismuth salicylate, Calcium carbonate, Magnesium hydroxide, Sodium bicarbonate
- Neutralizes gastric secretions in the gastrointestinal tract
- Long-term antacid therapy for pediatric patients is not recommended

Prokinetic Agents
- Eg Baclofen, Bethanecol, Cisapride, Domperidone, Erythromycin, Metoclopramide
- Alternative treatment & are not for routine use in patients w/ GERD
- Cisapride increases gastric emptying & helps improve esophageal/intestinal peristalsis
  - Significantly reduces the RI but efficacy for symptom control is not established
  - The need for Cisapride therapy should be weighed against its adverse effects (eg QT-interval prolongation, ventricular tachycardia, ventricular fibrillation) before initiating therapy
- Antidopaminergic agents (eg Domperidone, Metoclopramide) help facilitate gastric emptying & RI, reducing symptoms in infants w/ reflux
  - Baclofen, a γ-amino-butyric-acid receptor agonist, possesses functions that reduce the time for gastric emptying
  - Studies have shown that Baclofen may also decrease emesis frequency
  - Erythromycin is another treatment option that may be considered to reduce the time for gastric emptying
  - Further studies are needed to prove the efficacy of prokinetic agents for the treatment of GERD in children

Surface Protective Agents
- Eg Alginate, Sucralfate
- Treatment option against mucosal erosion; should not be used as monotherapy for GERD
  - Alginate may be used for formula-fed infants to help thicken liquid preparations during feeding

Management Based on Symptomatology

- There is no gold standard for the diagnosis of GERD
- Duration of treatment w/ PPIs or H2RAs depend on patient’s symptoms

Regurgitation & Vomiting
- Thorough history & physical examination may be sufficient to distinguish uncomplicated from complicated GER in infants & children w/ recurrent regurgitation
- Infants w/ recurrent regurgitation but w/ poor weight gain should undergo thorough history & physical exam w/ lab exams (CBC, serum electrolytes, BUN, serum creatinine) to rule out other possible etiologies of the symptoms
  - Dietary modifications (extensively hydrolyzed formula, amino acid-based formula) to test for cow’s milk allergy may also be considered
- Infants in unexplained state of distress w/ constant crying bouts should be investigated for diseases other than GERD, as reflux is not a common cause for these symptoms

Heartburn
- Conservative therapies (lifestyle changes, avoidance of trigger factors) are encouraged prior to initiation of drug treatments
- PPIs may be given for 2-4 weeks to test for responsiveness to this treatment & for patients w/ moderate to severe heartburn
  - Gradual discontinuation of PPI & continuation of conservative therapies are recommended after positive results w/ PPIs
- As needed use of PPIs, antacids, & H2RAs may also be considered for symptomatic relief

Reflux Esophagitis
- 3 months of PPI therapy is recommended as initial therapy in patients w/ erosive esophagitis
  - Dose may be increased if patient is unresponsive after 4 weeks
- Endoscopic monitoring may be used to assess for treatment response in patients w/ atypical signs & symptoms, persistent symptoms despite appropriate therapy, or those w/ esophageal stricture or moderate-severe esophagitis
- Long-term PPI therapy or surgery may be considered for chronic or relapsing reflux esophagitis

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**MANAGEMENT BASED ON SYMPTOMATOLOGY (CONT’D)**

**Dysphagia, Odynophagia, & Food Refusal**
- Odynophagia & dysphagia have been associated with the presence of esophagitis
- Feeding refusal may be related to GER/GERD but further studies are needed to establish this association
  - Some studies incorporated abnormal pH probe findings in infants & children with feeding difficulty, except in infants with excessive regurgitation
- May suggest upper GI barium contrast radiography in infants with feeding refusal &/or feeding difficulty, & for older children with dysphagia
- Pharmacological therapy may only be considered in patients with symptoms highly suggestive of GERD

**Apnea**
- Presence of prolonged apnea has been associated with acid reflux in premature infants
  - Combined esophageal pH monitoring & MII may help establish the relationship between the presence of apnea & regurgitation in a patient
- Infants with regurgitation complicated by apparent life-threatening events (ALTEs) may benefit from milk mixed w/ thickeners
- Symptoms are most likely to resolve as the child ages, therefore pharmacological therapies are not recommended

**Reactive Airways Disease**
- Studies have shown that GER may produce airway hyperresponsiveness & airflow obstruction leading to asthma exacerbation in asthmatic patients
- Asthma may in turn be a factor in the development of GERD due to reduced resting LES pressure
- Studies have shown that 60-80% of children with asthma have abnormal pH or MII/pH findings
- PPI therapy may be considered in asthmatic patients with persistent heartburn or regurgitation

**Recurrent Pneumonia**
- Reflux of gastric contents has been associated with recurrent pneumonia & interstitial lung disease
- Pharmacological therapy (PPIs, H₂RAs, prokinetic agents) may be considered in patients with minimal lung disease associated with GERD, & should be advised about the importance of prompt follow-up
- Antireflux surgery should be considered in patients with severely impaired lung function to prevent further pulmonary damage

**Upper Airway Symptoms**
- Upper respiratory tract manifestations such as chronic cough, hoarseness, sinusitis, otitis media, & laryngoscopic features such as edema, erythema, & nodularity have been linked to the presence of GERD
- Other etiologies should be taken into consideration prior to starting therapy for GERD
  - Children may undergo laryngoscopy to rule out possible functional or anatomical abnormalities

**Dental Erosions**
- Several studies found the association of GERD with dental erosions secondary to acidic pH exposure
- Referral to a pediatric dentist is recommended

**Sandifer Syndrome**
- A rare disorder associated with GERD characterized by spasmodic torsional dystonia with arching of the neck, head, eyes & trunk
- Antireflux medications & specialist referral are recommended

**Barrett’s Esophagus**
- Diagnosis for Barrett’s esophagus should be established prior to initiation of therapy
- Following PPI therapy, histological examination is recommended to be able to characterize Barrett’s esophagus & rule out presence of dysplasia

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SURGERY

Indications for Antireflux Surgery
• Failed medical management
• Noncompliance w/ therapy, medication side effects, inadequate symptom control, refractory GERD (persistence of GERD symptoms in compliant patients despite standard treatment or twice-daily dosing of PPI for at least 8 weeks)
• Severe erosive GERD or severe GERD complications (eg peptic stricture, Barrett’s esophagus)
• Extraesophageal conditions (eg pulmonary aspiration, asthma, recurrent aspiration related to GERD)
• Long-term management required
• Patient/parent/guardian preference
  - Despite success w/ medications, may opt for surgery due to cost of medications or life-long need to take acid-suppressive agents
  - However, should be advised against surgery if symptoms are well controlled on medical therapy

Antireflux Surgery
• Has evolved from open type to a laparoscopic procedure & in recent years, to transoral incisionless fundoplication
• Surgical success is highest in patients presenting w/ typical GERD symptoms & demonstrating good response to treatment w/ PPI
  - In considering antireflux surgery, inform patients regarding the risk of long-term PPI therapy after surgery
• Esophageal manometry & ambulatory reflux studies should be done before surgery to rule out other disorders, eg achalasia, non-reflux-induced esophageal spasm, scleroderma

Fundoplication
• Involves either a partial (Toupet or Thal) or a complete (Nissen/360 degrees) wrap of the LES w/ a section of the stomach, thus, increasing LES pressure
  - Nissen fundoplication is more commonly performed in children
  - Partial fundoplication is preferred in patients w/ more severe disease accompanied by motor abnormalities
• No statistically significant difference was observed in normal children when studies compared Nissen, Toupet, & Thal fundoplication; recurrence rate was lower however for children w/ neurological disorders who underwent Nissen fundoplication
• Laparoscopic Nissen technique is preferred over open Nissen fundoplication due to lower morbidity rates, shorter hospital stay, & fewer perioperative complications
• Complications include inability to belch & vomit, persistent dysphagia, postprandial pain, epigastric fullness, bloating, temporary swallowing discomfort, intense flatus

Total Esophagogastric Dissociation (TEGD; Bianchi’s procedure)
• Surgical alternative for patients w/ failed attempts at fundoplication or those w/ severe neurologic diseases
• Completely eliminates risk of GERD recurrence
• Involves the complete transection of the esophagus from the stomach & creation of esophagojejunal anastomosis

Endoscopic Procedures
• Further studies are needed to prove the efficacy of endoscopic procedures as an alternative surgical treatment for GERD in children

Endoluminal Endoscopic Gastroplication
• An endoscopic treatment option for GERD involving the creation of numerous folds or plicae in the gastric mucosa below the LES
• Recent procedures, eg titanium beads implantation & full-thickness plication, intend to reduce acid reflux episodes or transient lower esophageal sphincter relaxations & increase LES basal pressure
• Studies have shown successful outcomes in patients who have been symptom-free at 1 year post-op, & w/ recurrence rates as low as 25% at 3rd year post-op

Stretta Procedure
• A procedure involving the application of radiofrequency energy around the gastroesophageal junction, w/ the goal of reducing reflux by creating scars along the lower esophagus
• The scarring created serves as high pressure zones & areas where vagal afferent fibers are interrupted

Enteral Tube Feeding
• Involves placement of a nasojejunal or gastrojejunal tube, allowing bypass of the stomach during feeding
• Indications include infants, children & young people who will benefit from decreased intragastric feeding causing regurgitation, or reflux-related pulmonary aspiration; infants w/ poor weight gain & faltering growth associated w/ GERD; neurologically-impaired children at increased risk for complications post-op
• Clinical decision & planning should include an individualized nutrition plan, strategies to reduce duration of enteral tube placement, & anticipation of removal
## Dosage Guidelines

### ANTACIDS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Available Strength</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum hydroxide [Al(OH)₃]</td>
<td>600 mg/tab</td>
<td>1-2 tab PO 6 hrly (May be taken w/ or without food)</td>
<td>Adverse Reactions: Constipation; phosphate depletion may occur w/ prolonged use or in large doses</td>
</tr>
<tr>
<td>Magnesium hydroxide [Mg(OH)₂]</td>
<td>400 mg/5 mL susp</td>
<td>15 mL PO at bedtime (May be taken w/ or without food)</td>
<td>Adverse Reactions: GI effects (diarrhea, abdominal cramps); hypermagnesemia in patients w/ renal impairment</td>
</tr>
<tr>
<td>Magnesium oxide</td>
<td>84.5 mg/cap</td>
<td>400 mg/day PO (Should be taken on an empty stomach)</td>
<td>Adverse Reactions: GI effects (cramping, diarrhea, vomiting, upset stomach, paralytic ileus); Other effects (rashes, hives, itching, hypermagnesemia)</td>
</tr>
<tr>
<td>Bismuth salicylate (Bismuth subsalicylate)</td>
<td>262 mg/15 mL susp; 262 mg/tab; 524 mg tab</td>
<td>524 mg PO every ½-1 hr Max dose: 8 doses/day</td>
<td>Adverse Reactions: Darkening of stool &amp; tongue, hypersensitivity reactions</td>
</tr>
</tbody>
</table>

Special Instructions:
- Aluminum hydroxide is often given w/ magnesium-containing antacid (eg Magnesium hydroxide, Magnesium oxide)

### Intestinal Adsorbent

<table>
<thead>
<tr>
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<tr>
<td>Bismuth salicylate (Bismuth subsalicylate)</td>
<td>262 mg/15 mL susp; 262 mg/tab; 524 mg tab</td>
<td>524 mg PO every ½-1 hr Max dose: 8 doses/day</td>
<td>Adverse Reactions: Darkening of stool &amp; tongue, hypersensitivity reactions</td>
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</table>

Special Instructions:
- Use w/ caution in patients w/ renal impairment
- Avoid in patients w/ salicylate or Aspirin sensitivity, history of severe GI bleeding & coagulopathy

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All dosage recommendations are for children w/ normal renal & hepatic function unless otherwise stated.

Not all products are available or approved for above use in all countries.

Products listed above may not be mentioned in the disease management chart but have been placed here based on indications listed in regional manufacturers’ product information.

Specific prescribing information may be found in the latest MIMS.
## Dosage Guidelines

### ANTI DIARRHEAL

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<th>Drug</th>
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<th>Remarks</th>
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<tbody>
<tr>
<td>Dioctahedral smectite</td>
<td>&lt;1 yr: 3 g/day PO in 2-3 divided doses</td>
<td>Adverse Reactions:</td>
</tr>
<tr>
<td></td>
<td>1-2 yr: 3-6 g/day PO in 2-3 divided doses</td>
<td>• May aggravate constipation</td>
</tr>
<tr>
<td></td>
<td>&gt;2 yr: 6-9 g/day PO in 2-3 divided doses</td>
<td>Special Instructions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May be diluted to or taken w/ water, milk,</td>
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<td>tea, food</td>
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<td>• Should not be used in patients w/</td>
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<td>renal or hepatic impairment, fructose</td>
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<tr>
<td></td>
<td></td>
<td>isomaltase deficiency, acute</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dysentery w/ bloody stool &amp; high fever,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>diarrhea associated w/ broad-spectrum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>antibiotic</td>
</tr>
</tbody>
</table>

### ANTIEMETIC

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alizapride</td>
<td>5 mg/kg/day PO in divided doses</td>
<td>Adverse Reactions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CNS effects (drowsiness, dizziness,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>headache, extrapyramidal symptoms or EPS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Endocrine effects (amenorrhea, galactorrhea)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GI effect (diarrhea)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special Instructions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Contraindicated in Parkinson’s disease,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GI perforation, pheochromocytoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use w/ caution in renal impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May impair ability to drive or operate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>machineries</td>
</tr>
</tbody>
</table>

### HISTAMINE\textsubscript{2}-RECEPTOR ANTAGONISTS (H\textsubscript{2}RAs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>&gt;1 yr: 25-30 mg/kg/day PO in divided doses</td>
<td>Adverse Reactions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CNS effects (headache, dizziness,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>somnolence, insomnia, agitation); GI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>effects (diarrhea, N/V); Other effects (</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rashes, myalgia, arthralgia)</td>
</tr>
<tr>
<td>Famotidine</td>
<td>Initial therapy: 20-40 mg PO 12 hrly x 6-12 wk</td>
<td>• Altered LFTs, reversible confusion in the</td>
</tr>
<tr>
<td></td>
<td>Maintenance therapy: 20 mg PO 12 hrly</td>
<td>elderly &amp; those w/ renal failure have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>occasionally occurred</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rarely reported effects: Hepatotoxicity,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hypersensitivity reactions, CV effects (</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tachycardia, bradycardia, hypotension)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hematologic effects (leucopenia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>thrombocytopenia, agranulocytosis), acute</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pancreatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cimetidine has weak anti-androgenic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>effects; impotence &amp; gynecomastia have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>occurred &amp; are usually reversible</td>
</tr>
<tr>
<td>Nizatidine</td>
<td>≥12 yr: 150 mg PO 12 hrly for up to 8 wk</td>
<td>Special Instructions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Famotidine &amp; Nizatidine may be taken w/ or w/ food</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• All doses of Cimetidine should be taken w/ food</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Intravenous injections should be given</td>
</tr>
<tr>
<td></td>
<td></td>
<td>slowly; intravenous infusion is preferred</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(esp for high doses &amp; in patients w/ CV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>impairment)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use w/ caution in patients w/ hepatic &amp;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>renal impairment; dose adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cimetidine may reduce hepatic metabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of some drugs through inhibition of cytochrome F450 isoenzymes; closely monitor those on oral anticoagulants, Lidocaine, Phenytoin or Theophylline; dose reduction may be necessary</td>
</tr>
</tbody>
</table>

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Specific prescribing information may be found in the latest MIMS.
Gastroesophageal Reflux Disease in Children (12 of 14)

Dosage Guidelines

### HISTAMINE₂-RECEPTOR ANTAGONISTS (H₂RAs) (CONT'D)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranitidine</td>
<td>150 mg PO 12 hrly or 300 mg PO at bedtime for up to 8 wk or 50 mg IM or slow IV for 1-2 min 6-8 hrly or intermittent IV infusion at 25 mg/hr for 2 hr repeated 6-8 hrly <strong>Severe cases:</strong> 150 mg PO 6 hrly x 12 wk</td>
<td><strong>Adverse Reactions</strong>&lt;br&gt;• CNS effects (headache, dizziness, somnolence, insomnia, agitation); GI effects (diarrhea, N/V); Other effects (rashes, myalgia, arthralgia)&lt;br&gt;• Altered LFTs, reversible confusion in the elderly &amp; those w/ renal failure have occasionally occurred&lt;br&gt;• Rarely reported effects: Hepatotoxicity, hypersensitivity reactions, CV effects (tachycardia, bradycardia, hypotension), hematologic effects (leucopenia, thrombocytopenia, agranulocytosis), acute pancreatitis&lt;br&gt;<strong>Special Instructions</strong>&lt;br&gt;• Intravenous injections should be given slowly; intravenous infusion is preferred (esp for high doses &amp; in patients w/ CV impairment)&lt;br&gt;• Use w/ caution in patients w/ hepatic &amp; renal impairment; dose adjustment recommended</td>
</tr>
</tbody>
</table>

### OTHER DRUGS USED IN THE TREATMENT OF GERD¹

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alginic acid/Al(OH)₃/ Mg carbonate</td>
<td>1-2 tab PO 12 hrly [per tab: Alginic acid 200 mg/Al(OH)₃ 30 mg/Mg carbonate 40 mg] <strong>Max dose:</strong> 3 g of Al(OH)₃, 2g of Mg carbonate in a 24-hr period for &lt;2 wk</td>
<td><strong>Adverse Reactions</strong>&lt;br&gt;• GI effects (diarrhea or constipation, abdominal distention, hiccups)&lt;br&gt;<strong>Special Instructions</strong>&lt;br&gt;• Use w/ caution in patients w/ Na-restricted diet</td>
</tr>
<tr>
<td>Al(OH)₃-Mg carbonate/Attapulgite (activated)</td>
<td>1 sachet daily into a half glass of water after meals [per sachet: Al(OH)₃-Mg carbonate 0.5 g/Attapulgite (activated) 2.5 g]</td>
<td><strong>Adverse Reactions</strong>&lt;br&gt;• Related to Aluminium: Phosphorus depletion during prolonged use or at high dosages&lt;br&gt;<strong>Special Instructions</strong>&lt;br&gt;• Use w/ caution in patients bedridden or w/ megacolon (risk of scatoma)&lt;br&gt;• Take into account the dose of aluminium in case of renal insufficiency &amp; chronic dialysis (risk of encephalopathy)&lt;br&gt;• Avoid in patients w/ severe renal insufficiency &amp; digestive tract stenosis</td>
</tr>
<tr>
<td>Na alginate/K bicarbonate</td>
<td>&gt;12 yr: 500-1000 mg (Na alginate) PO Doses taken w/ food (after meals &amp; at bedtime)</td>
<td><strong>Adverse Reactions</strong>&lt;br&gt;• Skin rashes have been reported&lt;br&gt;<strong>Special Instructions</strong>&lt;br&gt;• Use w/ caution in patients on Na- &amp; Ca-restricted diet, in heart failure &amp; renal dysfunction&lt;br&gt;• May be used during pregnancy &amp; lactation</td>
</tr>
<tr>
<td>Na alginate/Na bicarbonate/Ca carbonate</td>
<td>6-12 yr: 250-500 mg (Na alginate) PO &gt;12 yr: 500-1000 mg (Na alginate) PO Doses taken w/ food (after meals &amp; at bedtime)</td>
<td><strong>Adverse Reactions</strong>&lt;br&gt;• GI effect (abdominal distension)&lt;br&gt;<strong>Special Instructions</strong>&lt;br&gt;• Use w/ caution in patients w/ Na- &amp; Ca-restricted diet, in heart failure &amp; renal dysfunction&lt;br&gt;• May be used during pregnancy &amp; lactation</td>
</tr>
</tbody>
</table>

¹Various combinations are available. Please see the latest MIMS for available formulations.

All dosage recommendations are for children w/ normal renal & hepatic function unless otherwise stated.

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# Gastroesophageal Reflux Disease in Children (13 of 14)

## Dosage Guidelines

### PROPULSIVES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosage</th>
<th>Max Dose</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisapride</td>
<td>Initial therapy: 0.2-0.8 mg/kg PO 6-8 hrly</td>
<td>Max dose: 20 mg/day</td>
<td>Doses to be taken 15 min before meals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doses to be taken 15 min before meals &amp; at bedtime</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adverse Reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• CNS effects (dizziness, depression); CV effect (chest pain); GI effects (nausea, abdominal cramps, borborygmi, diarrhea); Other effects (fatigue, lower back pain, rash, pruritus, angioedema, bronchospasm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Special Instructions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindicated in GI hemorrhage, obstruction &amp; perforation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Use with caution in arrhythmias, ventricular tachycardia, ventricular fibrillation, history of heart disease, CHF, renal impairment, hypocalcemia, hypomagnesemia, respiratory disorders</td>
</tr>
<tr>
<td>Domperidone</td>
<td>0.25-0.5 mg/kg body wt PO 6-8 hrly</td>
<td>Doses to be taken 15-30 min before meals &amp; at bedtime</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adverse Reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• GI effects (abdominal cramps, abnormal liver function tests, dry mouth); Endocrine effects (elevated prolactin levels, galactorrhea, gynecomastia); Dermatologic effects (urticaria, rash); CNS effects (extrapyramidal reactions, drowsiness, headache)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Associated with increased risk of ventricular arrhythmia or sudden cardiac death, particularly with doses &gt;30 mg/day</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Special Instructions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Use the lowest effective dose for the shortest duration necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Avoid in patients with GI hemorrhage, obstruction or perforation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Avoid in patients with prolactinoma, GI perforation, hemorrhage or obstruction, moderate or severe hepatic impairment, significant electrolyte disturbances, known existing prolongation of cardiac conduction intervals (particularly QTc), underlying cardiac disease, concomitant use of QT-prolonging drugs or CYP3A4 inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>&lt;1 yr: 0.1 mg/kg PO 12 hrly</td>
<td>1-6 yr: 0.1 mg/kg PO 8-12 hrly</td>
<td>&gt;6 yr: Max of 0.5 mg/kg/day in 2 divided doses</td>
</tr>
<tr>
<td></td>
<td>Doses should be taken at least 15 min before meals</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adverse Reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CNS effects (restlessness, drowsiness, headache, extrapyramidal reactions &amp; dystonic reactions have been reported e.g. tardive dyskinesia &amp; parkinsonian symptoms); Endocrine effects (increased prolactin resulting in galactorrhea or gynecomastia); GI effect (diarrhea)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Special Instructions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Avoid in patients whose stimulation of muscular contractions may adversely affect GI conditions (e.g. GI hemorrhage, obstruction, perforation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Should be avoided in patients with pheochromocytoma, epilepsy, Parkinson’s disease, history of depression &amp; in patients taking drugs that can also cause extrapyramidal symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Use with caution in patients with renal or hepatic impairment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Combination w/ Pantoprazole is available. Specific prescribing information may be found in the latest MIMS.

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## Dosage Guidelines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROTON PUMP INHIBITORS (PPIs)</strong></td>
<td></td>
<td>Adverse Reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Generally well tolerated; most commonly reported: Headache, diarrhea, rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Less common: GI effects (constipation, flatulence, abdominal pain, N/V, dry mouth); Dermatologic effects (pruritus, urticaria); Musculoskeletal effects (arthralgia, myalgia); Other effects (dizziness, fatigue, insomnia, cough, upper resp tract infection)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypersensitivity reactions, elevated liver enzymes, &amp; isolated cases of photosensitivity &amp; hepatotoxicity have been reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special Instructions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use w/ caution in patients w/ hepatic impairment; dose adjustment recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Concomitant use w/ Atazanavir or Nelfinavir is not recommended (PPIs reduce exposure to these drugs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Exclude possibility of gastric malignancy prior to treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bone fracture: Several published observational studies suggest that PPI therapy may be associated w/ an increased risk for osteoporosis-related fractures of the hip, wrist or spine. Patients should use the lowest dose &amp; shortest duration of PPI therapy appropriate to the condition being treated</td>
</tr>
</tbody>
</table>

### Dexlansoprazole
- **>12 yr:** 30 mg PO 24 hrly x 4 wk

### Esomeprazole
- **1-11 yr w/ <20 kg body wt:** 10 mg PO/IV 24 hrly x 8 wk
- **1-11 yr w/ ≥20 kg body wt:** 10-20 mg PO/IV 24 hrly x 8 wk
- **≥12 yr:** 20 mg PO/IV 24 hrly

### Lansoprazole
- **1-11 yr w/ >30 kg body wt:**
  - 30 mg PO 24 hrly x up to 12 wk
  - Initial therapy: 30 mg PO 24 hrly x 4-8 wk
  - Maintenance therapy: 15 mg PO 24 hrly
- **1-11 yr w/ <30 kg body wt:**
  - 15 mg PO 24 hrly x up to 12 wk
- **≥12 yr:**
  - Initial therapy: 30 mg PO 24 hrly x 4-8 wk
  - Maintenance therapy: 15 mg PO 24 hrly

### Omeprazole
- **≥1 yr w/ 5-10 kg body wt:** 5 mg PO 24 hrly x 2-4 wk
- **≥1 yr w/ 10-20 kg body wt:** 10 mg PO 24 hrly x 2-4 wk
- **≥1 yr w/ >20 kg body wt:** 20 mg PO 24 hrly x 2-4 wk

### Pantoprazole
- **≥12 yr:**
  - Initial therapy: 20 mg PO 24 hrly
  - Maintenance therapy: 20 mg PO 24 hrly
  - May increase to 40 mg/day for relapse; reduce dose to 20 mg/day once relapse resolves

### Rabeprazole
- **>12 yr:**
  - Initial therapy: 20 mg PO 24 hrly
  - Maintenance therapy: 20 mg PO 24 hrly
  - Reduce to 10 mg PO 24 hrly in the morning x 8 wk

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1 Combination w/ Sodium bicarbonate is available. Specific prescribing information may be found in the latest MIMS.
2 Combination w/ Domperidone is available. Specific prescribing information may be found in the latest MIMS.

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Please see the end of this section for the reference list.