

Proton Pump Inhibitors (PPIs):

Use and Risks in Pediatrics

To help reduce the occurrence of PPIs being prescribed excessively, outside indication, age and duration of treatment per approved indication for pediatrics, please review all information below.

General Use

PPIs should be used for the treatment of Gastroesophageal Reflux Disease (GERD) and Erosive Esophagitis (EE) when indicated.

Risks

Recent studies have shown that long-term use of PPIs are associated with increased risks for the following serious side effects:

- Clostridioides difficile-associated disease
- Community acquired pneumonia
- Nutritional deficiencies (e.g. vitamin B₁₂, hypomagnesemia)
- Elevation of gastric pH (e.g. delayed gastric-emptying changes)
- Risk of adverse drug interactions (i.e. Metabolized via CYT p450)

Safety and Efficacy

Although PPIs have shown a remarkable tolerability profile, the clinical use of these agents in children is based on adult data. In recent years, several studies have shown that PPIs are associated with an increased risk of infectious complications (pneumonia, *Clostridioides difficile* infection, small bowel bacterial overgrowth) and nutritional deficiencies (vitamin B₁₂ deficiency, osteoporosis). Also, elevation of the gastric pH related to PPI usage may have deleterious effects on the gastrointestinal tract, including delayed gastric emptying, increased intestinal bacterial translocation, decreased gastric mucus viscosity, changes in the normal microbial flora and possible impaired neutrophil function *in vitro*. Despite their tolerability short-term, there are concerns regarding the long-term use of these agents.⁵

A study conducted at Texas Tech University HSC El Paso Department of Pediatrics determined PPI exposure for more than six weeks was associated with Non-Specific Gastric Inflammation (NSGI), with the highest risk among patients using higher doses for longer periods of time. They hypothesized that NSGI is related to a disruption in the normal gastric pH caused by PPI use. The study questioned the benefit of continuing PPIs use beyond six weeks.⁵

Provider Tips

When prescribing PPIs, providers should ensure that they:

- Evaluate all pediatric patients on PPIs for continued need and appropriate dosing.
- Provide parents and or caregivers with information on potential risks of long term PPI therapy.
- Prescribe PPIs in 30-day increments for up to 8 weeks, if the PPI is determined necessary (recommended).
- Consider a cost-saving generic PPI if the medication must be used.
- Re-assess pediatric patients prior to continued PPI use or refer to a Gastrointestinal (GI) specialist.

Products Available

The Medicaid available products currently on the Texas Vendor Drug Program Preferred Drug List include:

- Omeprazole, Pantoprazole, Protonix (pantoprazole) suspension and Nexium (esomeprazole).

When prescribing PPIs, age, indication, weight, dose and duration need to be considered. Please reference the information in the table below when prescribing the preferred agents:

Comparing the Preferred Agents - Omeprazole, Pantoprazole and Nexium					
Drug Name	Age	Indications	Weight	Dose	Duration
Omeprazole	1 mo to < 1yr	EE	3 - 5 kg	2.5mg/day	6 weeks
	1 mo to < 1yr	EE	5 - 10 kg	5mg/day	6 weeks
	1 mo to < 1yr	EE	≥ 10 kg	10mg/day	6 weeks
	1 yr - 16 yr	GERD	5 - 10 kg	5mg/day	4 weeks
	1 yr - 16 yr	GERD	10 - 20 kg	10mg/day	4 weeks
	1 yr - 16 yr	GERD	≥ 20kg	20mg/day	4 weeks
	1 yr - 16 yr	EE	5 - 10 kg	5mg/day	Treatment: up to 8 weeks, maintenance up to 1 year
	1 yr - 16 yr	EE	10 - 20 kg	10mg/day	Treatment: up to 8 weeks, maintenance up to 1 year
Pantoprazole	5 yr - 18 yr	EE	15 - 40 kg	20 mg/day	8 weeks
	5 yr - 18 yr	EE	≥ 40 kg	40 mg/day	8 weeks
Nexium	1 mo to < 11 mo	EE	3 – 5 kg	2.5mg/day	6 weeks
	1 mo to < 11 mo	EE	> 5 – 7.5 kg	5mg/day	6 weeks
	1 mo to < 11 mo	EE	> 7.5 – 12kg	10mg/day	6 weeks
	1 yr - 11 yr	EE	< 20kg	10mg/day	8 weeks
	1 yr - 11 yr	EE	≥ 20kg	10 – 20mg/day	8 weeks
	1 yr - 11 yr	GERD		10mg/day	8 weeks
	12 yr - 17 yr	EE		20 – 40mg/day	8 weeks
	12 yr - 17 yr	GERD		20mg/day	4 weeks

References

1. Prilosec package insert. AstraZenica Pharmaceuticals. <http://www.azpicentral.com/prilosec/prilosec.pdf>. Website accessed April 13, 2016
2. Protonix package insert. Pfizer Inc. <http://labeling.pfizer.com/ShowLabeling.aspx?id=135>. Website accessed April 13, 2016
3. Nexium package insert. AstraZenica Pharmaceuticals. <http://www.azpicentral.com/nexium/nexium.pdf>. Website accessed April 13, 2016
4. Elsevier/Gold Standard. Clinical Pharmacology PPI Drug Class Overview. <http://clinicalpharmacology-ip.com/Forms/Resources/overviews.aspx?oStructureId=1217047>. Website accessed April 13, 2016.
5. US National library of Medicine/National Institutes of Health; Non-Specific Gastric Inflammation in Children Associated with Proton Pump Inhibitor Treatment for More than 6 Weeks; Website accessed April 13, 2016. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3895915/>
6. Centers for Medicare and Medicaid Fact Sheet; Proton Pump Inhibitors: Use in Pediatrics; Website accessed April 13, 2016.
7. <https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ppi-pediatric-factsheet11-14.pdf>

Please direct any questions to the Superior Pharmacy department at 1-800-218-7453, ext. 22080 or 22272.