Drug Use Research & Management Program
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Month/Year of Review: March 2014
PDL Classes: Proton Pump Inhibitors

Date of Last Review: November 2012
Source Document: OSU College of Pharmacy

Current Status of PDL Class:

- Preferred Agents: OMEPRAZOLE CAPSULE DR, PANTOPRAZOLE SODIUM TABLET DR
- Non-preferred Agents: LANSOPRAZOLE, DEXLANSOPRAZOLE (DEXILANT®), RABEPRAZOLE (ACIPHEX®), ESOMEPRAZOLE (NEXIUM®), OMEPRAZOLE/SODIUM BICARBONATE (ZEGRID®)

Previous Conclusions Recommendations:

- Patients should be re-evaluated for benefits and risks while on long term PPI therapy for potential adverse events.
- There is no consistent difference in efficacy or safety between agents to justify selection of any PPI as clinically superior to the other drugs in the class.
- No evidence supports differences in efficacy or adverse effects in subpopulations by race and ethnicity, age, gender, or co-morbidities.

PA Criteria: Prior Authorization (PA) criteria is in place for PPIs to promote PDL options, restrict chronic use to patients who failed H2-Antagonists, preferred PPIs or who have severe disease and restricts BID use to patients with severe disease, H. pylori, or pediatric patients (Appendix 1).

Research Questions:

- Is there any new comparative evidence of different PPIs?
- Is there any new comparative safety data of PPIs?
- Are there subpopulations of patients for which one medication or formulation is more effective or associated with fewer adverse effects?

Methods:

The DERP Scan was used to identify any new comparative research that has emerged since the last P&T review.[1]

Conclusions and Recommendations:

- No further review or research needed at this time; update PA criteria.
- Evaluate comparative costs in executive session.

References:

1. Thakurta S. Drug Effectiveness Review Project. Drug Class Review: Proton Pump Inhibitors. Preliminary Scan Report. December 2013.

Appendix 1: PA Criteria:

Appendix A

Proton Pump Inhibitors (PPIs)

Goal(s):

- Promote PDL options.
- Restrict chronic use (greater than eight weeks) to patients who failed H2-antagonist, preferred PPIs or who have severe disease, e.g. Barrett's, or Zollinger Ellison syndrome.
- Restrict BID use to patients with severe disease, H.pylori or pediatric patients.

Notes:

- This is a "global" PA.
- If an active PA for a PPI already exists, then any PPI will pay.
- A new PA is required if the dosing schedule changes, e.g., an active PA for once daily dosing restricts the PPI to once a day.
- BID dosing requires a new PA, however, the strength of the dose could be increased without an additional PA, e.g., a change from 20mg daily could be increased to 40 mg ONCE a day without an additional PA.

Length of Authorization: 2 weeks to lifetime (criteria specific)

Requires PA:

- Non-preferred drugs

Covered Alternatives

- Preferred alternatives listed at www.orpdl.org
- Individual components for treatment of H.pylori that are preferred products.

ROUTE	HICL	BRAND	GENERIC	FORMULATIONS
ORAL	021607	Nexium	esomeprazole	Capsules, delayed-release: 20, 40mg Suspension, delayed-release pkts: 10, 20, 40mg
ORAL	008993	Prevacid	lansoprazole	Capsules, delayed-release: 15, 30 mg Enteric coated granules for oral suspension, delayed release: 15, 30mg
ORAL	025742	Prevacid NapraPAC	lansoprazole + naproxen	Delayed release capsules + naproxen tablets kit - 15 – 375, 15 -500
ORAL	004673	Zegerid	omeprazole	Packet for solution: 20, 40mg Capsules: 20, 40mg
ORAL	36085	Kapdex	Dexlansoprazole	Capsules, delayed-release: 30, 60mg
ORAL	011590, 022008	Protonix	pantoprazole	Tablets, delayed-release: 20 mg, 40 mg Suspension, delayed-release: 40mg
ORAL	011590	pantoprazole	pantoprazole	Tablets, delayed-release: 20 mg, 40 mg
ORAL	018847	Aciphex	rabeprazole	Tablets, delayed-release: 20 mg

Approval Criteria		
1. What is the diagnosis being treated?	Record ICD9 code	
2. Is drug requested preferred?	**Yes: Go to 4**	**No: Go to 3**
3. . Will the prescriber consider a change to a preferred product?	**Yes: Inform provider of covered alternatives in class.**	**No: Go to 4**
4. Is diagnosis a) Zollinger-Ellison (251.5)? b) Barrett's esophagus (530.85)? c) Multiple Endocrine Adenoma (237.4)? d) Malignant Mastoma (202.6)? e) MEN Type I (258.01)?	Yes: Approve for a life time; BID dosing OK.	No: Go to 5
5. Is the diagnosis dyspepsia (536.8)?	Yes: Pass to RPH, DENY (OHP coverage) Diagnosis is below the line; preferred agents are available without PA.	No: Go to 6
6. Has patient tried and failed a preferred PPI for a 8 week trial (2 weeks for H. Pylori)	Yes: Go to #7	No: Go to #12
7. Is diagnosis H.Pylori?	Yes: Approve for 2 weeks – BID dosing OK	No: Go to #8
8. Is diagnosis active GI bleed? (531.0-531.2, 532.0-532.2, 533.0-533.2, 534.0-534.2)	Yes: Approve for 8 weeks - BID dosing OK	No: Go to # 9
9. Is diagnosis Gastric or Duodenal Ulcer (531.3-531.9, 531.3-532.9, 533.3-533.9, 534.3-534.9) and/or does patient have 2 or more of the following risk factors: - > 65 years - requires > 3 mths of NSAIDs, aspirin or steroids - on anticoagulation (warfarin, enoxapirin, etc.) - History of GI Bleed or Ulcer?	Yes: Approve QD for 1 year, if previously failed an 8 week QD trial at highest dose approve BID for 1 year. May approve BID dosing for pediatrics <12 years old	No: Go to #10
10. Is the diagnosis symptomatic GERD (530.81, 530.10 – 530.19)	Yes: Approve QD dosing for 1 year; if previously failed an 8 week QD trial at highest dose approve BID for 1 year. May approve BID dosing for pediatrics<12 years old	No: Go to #11
11. Is diagnosis a) Ulcer of esophagus (530.2x) b) Stricture & stenosis of esophagus (530.3) c) Perforation of esophagus (530.4)	Yes: Approve up to BID for 1 year.	No: Go to #13
12. Is the request for tube administration?	Yes: Approve QD dosing for 1 year. May approve BID dosing for pediatrics <12 years old.	No: Pass to RPH. Deny and recommend omeprazole 20 mg QD or BID.
13. All other diagnoses will need to be evaluated by a pharmacist for appropriateness and OHP line coverage.	• Diagnoses above the line and where PPI is appropriate can be covered. • Diagnoses below the line and where PPI is appropriate should be denied as not covered. • Diagnoses above the line but where PPIs are not appropriate should be denied and not medically appropriate.	

Date: March 2014

Clinical Notes:

FDA safety alerts:

Medication	FDA Alert
Clostridium difficile-associated diarrhea[10]	PPIs may be associated with an increased risk of *Clostridium difficile*–associated diarrhea (CDAD). A diagnosis of CDAD should be considered for patients taking PPIs who develop diarrhea that does not improve.
Low magnesium level associated with long-term PPI use[11]	Prescription PPIs may cause low serum magnesium levels (hypomagnesemia) if taken for prolonged periods of time (in most cases, longer than one year). In approximately one-quarter of the cases reviewed, magnesium supplementation alone did not improve low serum magnesium levels and the PPI had to be discontinued.
Avoid concomitant use of Plavix® and omeprazole[12]	FDA issued a reminder that it **continues to warn against the concomitant use of Plavix (clopidogrel) and omeprazole** because the co-administration can result in significant reductions in clopidogrel's active metabolite levels and antiplatelet activity. This information was added to the drug label of Plavix in November 2009, and has been the source of continued discussion in the medical literature. Patients at risk of heart attacks or strokes, who are given Plavix to prevent blood clots, will not get the full anti-clotting effect if they also take omeprazole. Omeprazole is found in prescription products (Prilosec, Zegerid, and generic products) and over-the-counter products (Prilosec OTC, Zegerid OTC, and generic products).FDA wishes to emphasize additional facts that may be a source of confusion among healthcare professionals: • With regard to the proton pump inhibitor (PPI) drug class, this recommendation **applies only to omeprazole** and not to all PPIs. Not all PPIs have the same inhibitory effect on the enzyme (CYP 2C19) that is crucial for conversion of Plavix into its active form. • Pantoprazole (Protonix) may be an alternative PPI for consideration. It is a weak inhibitor of CYP2C19 and has less effect on the pharmacological activity of Plavix than omeprazole.