



NEW JERSEY DRUG UTILIZATION REVIEW BOARD

The Appropriate Use of Proton-Pump Inhibitors and H2 Receptor Antagonists

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Proton pump inhibitors (PPIs) and H2 Receptor Antagonists (H2RAs) are indicated in the management of numerous gastrointestinal conditions including gastroesophageal reflux disease (GERD), duodenal ulcer, gastric ulcer, Helicobacter pylori infection, and to reduce the risk of non-steroidal anti-inflammatory drugs (NSAID)-associated gastric ulcers.

The New Jersey Drug Utilization Review Board (NJDURB) assists the Division of Medical Assistance and Health Services and the Department of Health in the development of criteria and standards to be used in retrospective and prospective drug utilization review, to improve quality of care and reduce unnecessary expenditure. This guide contains information obtained from manufacturer's product package inserts, and is intended to provide healthcare professionals with a review of some of the uses and recommended dosing for PPIs and H2RAs. This information is intended ultimately to help control the pharmacy program prescription costs without affecting the health and welfare of the patients who are prescribed these pharmacological classes of medications.

After reviewing this guide, practitioners should be able to:

- * Understand the use of H2RAs and PPIs in the treatment of GERD, duodenal ulcer, gastric ulcer, and erosive esophagitis
- * Know the doses and duration of the PPIs and H2RAs for their prescribed indication
- * Recommend the optimal administration time for these medications
- * Understand the role of selected PPIs in reducing the risk of NSAID associated gastric ulcer

Table 1: Dosing Regimen of H2RAs and Proton Pump Inhibitors in the Management of Gastroesophageal Reflux Disease

GERD				
Proton Pump Inhibitor or H2 Receptor Antagonist	Short-Term Treatment of Erosive Esophagitis	Treatment of Symptomatic Gastroesophageal Reflux Disease	Maintenance of Healing of Erosive Esophagitis	Cost (First Data Bank)
famotidine¹ (Pepcid, various)	20 mg or 40 mg twice daily for up to 12 weeks	20 mg twice daily for up to 6 weeks		\$
ranitidine¹ (Zantac, GlaxoSmithKline, various)	150 mg four times daily	150 mg twice daily	150 mg twice daily	\$
nizatidine¹ (Axid, various)		150 mg twice daily for 12 weeks		\$
omeprazole² ** (Prilosec, AstraZeneca; various)	20 mg once daily for 4 to 8 weeks	20 mg once daily for 4 wks	20 mg once daily	\$\$
lansoprazole² (Prevacid, TAP)	30 mg once daily for 8 weeks	15 mg once daily for 8 weeks	15 mg once daily	\$\$\$
esomeprazole² (Nexium, AstraZeneca)	20 mg or 40 mg once daily for 4 to 8 wks	20 mg once daily for 4 wks	20 mg once daily	\$\$\$
rabeprazole² (Aciphex, Eisai)	20 mg daily for 4 to 8 wks	20 mg once daily for 4 wks	20 mg once daily	\$\$\$
pantoprazole (Protonix, Wyeth-Ayerst)	40 mg once daily for up to 8 weeks	40 mg once daily for 8 wks	40 mg once daily	\$\$\$

* Duration of therapy for proton pump inhibitor in the treatment of Gastroesophageal Reflux Disease (GERD) ranges from 4 to 8 wks. For patients who do not heal after 4 to 8 wks, an additional 4 to 8 wks of treatment may be considered

* Esophageal healing rates in severe GERD with PPIs: 80% @ 4 weeks, 88% @ 6 weeks, 89% @ 8 wks

* In several studies, healing rates with H2RAs can be summarized: 50% @ 4 weeks, 43 to 58% @ 6 weeks, 67 to 82% @ 12 weeks. Healing rates are faster in patients with less severe GERD

** This product is now covered by Medicaid in its OTC formulation by prescription only. It is generally the least expensive alternative and use is encouraged when appropriate.

H2RAs

PPIs

Footnotes:

1. Dosage adjustments should be made for impaired renal function
2. Dosage adjustments should be made for hepatic insufficiency
3. Dual therapy can be prescribed: omeprazole 40mg once daily with clarithromycin for 14 days
4. Dual therapy can be prescribed: lansoprazole 30mg every 8 hours with amoxicillin for 14 days

Table 2: Dosing Regimen of H2RAs and Proton Pump Inhibitors for Treatment of Peptic Ulcer Disease

PUD				
Proton Pump Inhibitor or H2 Receptor Antagonist	Duodenal Ulcer	Gastric Ulcer	H. pylori eradication	Cost (First Data Bank)
famotidine¹ (Pepcid, various)	20 mg twice a day or 40 mg at bedtime; maintenance 20 mg at bedtime for healed duodenal ulcers.	40 mg at bedtime		\$
ranitidine¹ (Zantac, GlaxoSmithKline, various)	150mg twice daily or 300 mg HS daily; maintenance 150 mg at bedtime for healing duodenal ulcers.	150 mg twice daily; maintenance: 150 mg at bedtime.		\$
nizatidine¹ (Axid, various)	300 mg HS daily; maintenance: 150 mg daily for healed duodenal ulcer.			\$
omeprazole² (Prilosec, AstraZeneca; various)	20 mg once daily for 4 to 8 wks.	40 mg once a day for 4 to 8 weeks	Triple therapy omeprazole 20mg, amoxicillin 1000 mg, clarithromycin 500 mg, all taken BID for 10 days. Patients with ulcer at tx. initiation receive an additional 18 days of omeprazole 20 mg daily. ³	\$\$
lansoprazole (Prevacid, TAP)	15 mg once daily for 4 weeks; maintenance: 15 mg once daily	30 mg once daily for 8 weeks	Triple therapy: lansoprazole 30 mg plus amoxicillin 1000 mg plus clarithromycin 500 mg BID for 10 or 14 days. ⁴	\$\$\$
esomeprazole² (Nexium, AstraZeneca)			Triple therapy: esomeprazole 40 mg once a day with amoxicillin 1000 mg and clarithromycin 500 mg both taken BID, for 10 days	\$\$\$
rabeprazole² (Aciphex, Eisai)	20 mg once daily for 4 weeks		Triple therapy: rabeprazole 20 mg plus amoxicillin 1000 mg plus clarithromycin 500 mg are taken twice a day, for 7 days	\$\$\$
pantoprazole (Protonix, Wyeth-Ayerst)				\$\$\$

* Conventional treatment of active duodenal ulcer with H2RA heals approximately 70% @ 4 weeks, 80% @ 6 weeks, 90% at 8 weeks

Table 3: Optimal administration of Proton pump inhibitors		
Proton pump inhibitor	Dosage forms	Administration Recommendation
omeprazole; Prilosec, AstraZeneca; various	capsule: 10mg; 20 mg; 40 mg	Take one hour before a meal.
		Capsule should not be opened, chewed or crushed and should be swallowed whole.
lansoprazole; Prevacid, TAP	capsule: 15 mg; 30 mg	Take one hour before a meal.
		Capsule should be swallowed whole.
		Capsule can be opened & sprinkle intact granules on one tbs. of apple sauce, cottage cheese or yogurt.
	solutab: 15 mg; 30 mg	Solutab should not be chewed. Place tablet on the tongue and allow it to disintegrate with or without water.
	oral suspension: 15 mg; 30 mg	Suspension should not be given through enteral administration tubes. Packet should be mixed with 2 tablespoons of water only.
esomeprazole; Nexium, AstraZeneca	capsule: 20 mg; 40 mg	Take one hour before eating.
		Capsule should be swallowed whole.
		Capsule can be opened and the pellets inside emptied onto one tablespoon of applesauce.
rabeprazole; Aciphex, Eisai	tablet: 20 mg	Can be taken with or without food.
		Tablet should not be chewed, crushed or split.
pantoprazole; Protonix, Wyeth- Ayerst	tablet: 20 mg; 40 mg	Can be taken with or without food.
		Tablet should be swallowed whole.

* DISCLAIMER-This guide represents a compilation of selected facts taken from the package inserts for the products listed in this guide, and is not intended to be an exhaustive pharmaceutical review. The authors and the NJDURB assume no liability for the use of this review, nor do they warrant or guarantee any of the products. Please consult the Prescribing Information in the manufacturers' product package insert for more complete information or for indications not listed here.

References:

- American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the Management of Rheumatoid Arthritis. Arthritis and Rheumatism. 2002;46(2):328-346.
- Del Valle J, Cohen H, Laine L, et al. Acid Peptic Disorders. In: Yamada T, Aplers DH, Laine L, et al, eds. Textbook of Gastroenterology, 3rd ed. Philadelphia, Lippincott Williams and Wilkins. 1999; 1370-1444.
- Horn, John. The Proton-Pump Inhibitors: Similarities and Differences. Clinical Therapeutics. 2000;22(3):266-80.
- Kastrup EK, et al. editors. Drug Facts and Comparisons. Missouri: Wolters Kluwer Health, Inc.;2005.
- Tutuian R, Castell DO. Management of Gastroesophageal Reflux Disease. The American Journal of the Medical Science. 2003;326(6):309-318.

Table 4: Optimal administration of H2 Receptor Antagonists		
H2RA	Dosage forms	Administration Recommendation
Famotidine (Pepcid)	capsule: 10mg	Famotidine bioavailability may be increased if taken with food. Avoid alcohol
	powder for oral suspension: 40mg/5mL	Oral suspension: shake well before use
	tablet: 10mg [OTC], 20mg, 40mg; chewtab:	Chewtabs contain phenylalanine
	10mg; orally disintegrating tab: 20mg, 40mg	Orally disintegrating tablet: do not break tablet
Ranitidine (Zantac, EFFERdose)	tablets: 150mg, 300mg	May be taken with or without food
	Syrup: 15mg/mL, 25mg/mL	Efferdose should not be chewed, swallowed whole, or dissolved on tongue: dissolve 25mg tablet in at least 5 mL of water; wait until completely dissolved before administering
	Effervescent tab: 25mg, 150mg	Dissolve 150mg efferdose tablet in 6 to 8 ounces of water before drinking. Tablets contains phenylalanine and 1.33mEq sodium per 25mg tablet
Nizatidine (Axid)	capsules: 150mg, 300mg; oral solution: 15mg/mL; tablet: 75mg	Administration with apple juice may decrease absorption

Table 5: Risk Reduction of NSAID-Associated Gastric Ulcer		
Risk	Definition	Suggested management strategies
Low	age < 65 y/o, no aspirin, no prior ulcer or GI complication	<ul style="list-style-type: none"> Non-selective NSAID alone
Moderate and High	One or two risk factors (e.g., age > 65 y/o, high dose NSAIDs, low dose-aspirin)	<ul style="list-style-type: none"> Non-pharmacologic therapy Partially selective NSAID plus PPI or misoprostol Cox-2 inhibitor (avoid in individual with high risk of cardiovascular events)
* Risk factors for NSAID-associated gastroduodenal ulcer include advanced age, history of ulcer, concomitant use of corticosteroids or anticoagulants, higher dosages of NSAIDs or a serious underlying disease.		
* Currently, esomeprazole (Nexium™) is FDA approved for this indication. Prevacid NapraPac™ 375 or 500 mg, a combination package containing lansoprazole 15 mg and naproxen 375 mg or 500 mg, is also approved for risk reduction of NSAID-associated gastric ulcers		
* The recommended dose is 20 mg or 40 mg of esomeprazole (Nexium™) once daily for up to 6 months		