

g=Generic/TRADE/Pregnancy Category	Comments / Drug Interactions (DI) / Side Effects (SE)	Dose (Adult) <sup>5,6</sup> , Use, ~Duration	\$ / 30d
<b>H2-Receptor Antagonists (H2RA's):</b> nocturnal acid suppression (may dose at HS with a daytime PPI, but tachyphalaxis may develop ≥ 7d; limited efficacy in GERD) <sup>22</sup>			
Uninvestigated GERD: PPI somewhat more effective than H2RA (pantoprazole 20mg od vs ranitidine 150mg bid); complete Sx control: <b>77 vs 59%</b> at 12 month <b>NNT=6</b> Talley 2002 n=307, 12month (early 4wk results favored PPI)			
<b>Cimetidine</b> USA approved 1977 200*▼, 300, 400, 600, 800*▼mg tab; 60mg/ml soln	<b>TAGAMET</b> ,g •useful: dyspepsia esp maintenance, GERD esp mild, prn for dietary indiscretion; Not NSAID prophylaxis •few significant differences between H2RA's: <b>ranitidine</b> may be preferred H2RA's due to comparable safety, efficacy & lower cost - may avoid cimetidine in patients who are elderly or at ↑risk of <b>DIs</b> • <b>DI:</b> Cimetidine ☞ inhibit CYP <sub>450</sub> 1A2, 2C19, 2D6 eg. warfarin, phenytoin, theophylline... (CYP <sub>450</sub> : ranitidine minor effect; nizatidine/famotidine little or no effect on). - space <b>antacid</b> administration 30-60 minutes apart from H2RA's	<b>800mg po HS</b> - GU acute <sup>x 8wk</sup> , DU acute <sup>x 4-8wk</sup> <b>600mg po BID</b> - GERD	<b>15</b> 17
<b>Famotidine</b> 20, 40mg tab {20mg, 40mg Vial}	<b>PEPCID</b> ,g • <b>DI:</b> Cimetidine ☞ inhibit CYP <sub>450</sub> 1A2, 2C19, 2D6 eg. warfarin, phenytoin, theophylline... (CYP <sub>450</sub> : ranitidine minor effect; nizatidine/famotidine little or no effect on). - space <b>antacid</b> administration 30-60 minutes apart from H2RA's • <b>SE:</b> Uncommon: diarrhea, constipation, headache, fatigue, confusion (risk ↑ in elderly and in patients with ↓renal function). Rare: thrombocytopenia <b>SE: Cimetidine</b> ☞ slightly higher side effect risk seen with higher doses for a prolonged time; reversible gynecomastia (< 1%); weak antiandrogenic effect; may cause <b>transient</b> ↑ in SCr & LFTs	<b>40mg po HS</b> - GU acute <sup>x 8wk</sup> , DU acute <sup>x 4-8wk</sup> <b>20mg po HS</b> - PUD maint.☞ <b>20mg po BID</b> - GERD <b>20mg IV q12h</b>	<b>34</b> 24 38 200
<b>Nizatidine</b> 150, 300mg cap	<b>AXID</b> ,g • <b>SE:</b> Uncommon: diarrhea, constipation, headache, fatigue, confusion (risk ↑ in elderly and in patients with ↓renal function). Rare: thrombocytopenia <b>SE: Cimetidine</b> ☞ slightly higher side effect risk seen with higher doses for a prolonged time; reversible gynecomastia (< 1%); weak antiandrogenic effect; may cause <b>transient</b> ↑ in SCr & LFTs	<b>300mg po HS</b> - GU acute <sup>x 8wk</sup> , DU acute <sup>x 4-8wk</sup> <b>150mg po HS</b> - PUD maint.☞ <b>150mg po BID</b> - GERD	<b>41</b> 26 45
<b>Ranitidine</b> USA approved 1983 150, 300mg tab; 15mg/ml oral solution {50mg Vial}	<b>ZANTAC</b> ,g • <b>SE:</b> Uncommon: diarrhea, constipation, headache, fatigue, confusion (risk ↑ in elderly and in patients with ↓renal function). Rare: thrombocytopenia <b>SE: Cimetidine</b> ☞ slightly higher side effect risk seen with higher doses for a prolonged time; reversible gynecomastia (< 1%); weak antiandrogenic effect; may cause <b>transient</b> ↑ in SCr & LFTs •↓ dosage in patients with ↓ renal function, ↓ hepatic function, or elderly •higher dosages may be suitable for some patients/conditions	<b>150mg po bid or 300mg HS</b> - GU acute <sup>x 8wk</sup> , DU acute <sup>x 4-8wk</sup> <b>150mg po HS</b> - PUD maint.☞ <b>150mg po BID</b> - GERD; <b>50mg IV q12h or 150mg oral solution BID</b>	<b>27 or 26</b> 17 27 100

**Proton Pump Inhibitors-PPI:** Superior efficacy vs H2RAs incl. double dose esp for daytime/meal related acid secretion give 30min before meals.<sup>22</sup> GERD: BID dose if severe persistent sx. (Reassess dose q2-3months)<sup>6,22</sup>  
**Peptic ulcer bleeding:** PPI ↓rebleed risk NNT=12, need for surgery NNT=20, but NO mortality benefit.<sup>21</sup> Liver failure: ↓dose. **DI:** levels ↓ for meds dependent on low pH for absorption → [Ca<sup>++</sup> carb, dase & erlo-tinib, keto & itra -conazole, Fe<sup>++</sup>, P1's<sup>HIV</sup> & thyroxine]; can give with antacids; some CYP450 metab. **Long term:** ↓ B12 serum levels esp. in elderly, ? ↓ Mg<sup>++</sup> level; may ↑ pneumonia, C. difficile & hip fracture<sup>7,8</sup>. Rare: interstitial nephritis, rash & allergy.  
 PPI's have equivalent clinical efficacy at standard doses.<sup>9</sup> Pt variation in response to one PPI vs another may be seen. Reassess double dose & need for ongoing tx regularly, esp. after being inpatient. Consider PPI if on dual antiplatelet tx.  
**Erosive esophagitis:** standard doses of PPI's recommended; relapse rates ↑ with step down therapy.<sup>9</sup> **Rebound hypersecretion** is common when H2RA or PPIs are stopped after a few months of continuous use.

<b>Esomeprazole</b> 20, 40mg long football shaped tab Delayed Release; 10mg* x sachet	<b>NEXIUM</b> B • <b>S-isomer of omeprazole:</b> ↑ bioavailability; 20mg/day=standard dose but 40mg/day common; Similar DI's/SE's <sup>10</sup> ; Clarithromycin ↑s levels. ZES 40-80mg BID. <b>NG tube</b> with water	<b>40mg po OD ac</b> - GERD acute <sup>x 2-8wk</sup> <b>20mg po OD ac</b> - GERD maint. <sup>22</sup>	<b>82</b> <b>82</b>
<b>Lansoprazole</b> 15, 30mg Delay Release cap (15*, 30*mg FasTab & IV*) can mix in applesauce for swallowing difficulties	<b>PREVACID</b> B • <b>DI:</b> ↓ theophylline levels 10%; some CYP 2D6 & 2C19 inhibition; tacrolimus ↑?, mycophenolate ↓? • <b>SE:</b> diarrhea 4.1%, HA 2.9%, nausea 2.6%, rash •effective in hypersecretory conditions e.g. ZES: dose range 30-90mg po BID •may give contents via <b>NG tube</b> in apple juice or water; or use FasTab <sup>\$79</sup>	<b>30mg po OD ac</b> - GU acute <sup>x 4-8wk</sup> <b>30mg po OD ac</b> - DU acute <sup>x 2-4wk</sup> <b>30mg po OD ac</b> - PUD refract x 8-12wk, GERD acute <sup>x 2-8wk</sup> ≥15mg po OD ac - GERD maint.	<b>79</b> 79 79 79
<b>Omeprazole LOSEC, Apo Ratio</b> 10, 20mg Delayed Release tab; OTC in USA; USA approved 1989 Losec MUPS (micropellets): available "hospital only"	<b>LOSEC</b> C • <b>DI:</b> inhibit CYP <sup>2C19</sup> ; ↑ level of diazepam, dig, mycophenolate?, phenytoin?, Tegretol, triazolam & warf. • <b>SE:</b> HA 2.4%; diarrhea 1.9%; nausea 0.9%; rash, sweating •long-term safety good: approved 1988 •effective in hypersecretory conditions e.g. ZES: dose range: 60mg OD-120mg TID • <b>NG tube:</b> use MUPS or Susp compounded or mix tab with sodium bicarbonate •On NIHB	<b>20mg po OD ac</b> - GU acute <sup>x 4-8wk</sup> <b>20mg po OD ac</b> - DU acute <sup>x 2-4wk</sup> <b>40mg po OD ac</b> - PUD refractory <sup>x 8-12wk</sup> ≥10mg po OD ac - GERD maint.	<b>46</b> Losec cap <b>86</b> APO <b>86</b> APO, 165 54g, 70
<b>Pantoprazole</b> 40mg Enteric tab, 20mg* tab; 40mg Vial.g (suspension manufactured by some pharmacies)	<b>PANTOLOC</b> ,g B •rapid onset / similar outcomes vs omeprazole <b>SE:</b> HA; diarrhea; nausea; pruritus • <b>less DI's</b> less CYP450 effect <sup>2C19</sup> ; ↑dig? • <b>IV</b> 40mg IV od or GI bleed 80mg bolus: 8mg/hr x72hr •✓ hypersecretory conditions e.g. ZES: Dose range 40-120mg po BID; 80mg IV BID-TID	<b>40mg po OD ac</b> -GU acute <sup>x 4-8wk</sup> , DU acute <sup>x 2-4wk</sup> , GERD acute <sup>x 2-8wk</sup> ≥20mg po OD ac - GERD maint.	<b>56g, 75</b> 50
<b>Rabeprazole</b> 10, 20mg Enteric coated tab (USA name=Aciphex)	<b>PARIET</b> ,g B • <b>SE:</b> HA 2.4%, rash, diarrhea. ZES: 30-60mg po BID •On NIHB formulary • <b>less DI's</b> as less CYP450 effect & non-enzymatic metabolism; ↑dig.	<b>20mg po OD ac</b> - GU & DU acute, GERD <sup>x 4-8wk</sup> ≥10mg po OD ac - GERD maint.	<b>41g, 54*</b> <b>24g, 30</b>

↓ = ↓dose for renal dysfx Cost = total cost in Sask.; Considerations of cost should be given to the potential for shorter duration of therapy & ↑ efficacy of PPIs vs H2RAs. ▼ = covered by NIHB ☉ = not covered by NIHB  
 ☞ = Max. allowable cost ☞ = Exception Drug Status SK. ✕ = non-formulary SK. ☞ = prior approval required for NIHB ac=before meals CYP = cytochrome P450 enzymes DI = drug interaction dig=digoxin DU=duodenal ulcer GERD = gastroesophageal reflux disease GI=gastrointestinal GU=gastric ulcer HA=headache Hx=history LFTs=liver function tests PUD=peptic ulcer disease SCR= creatinine serum SE=side effect SX=symptoms ZES=Zollinger-Ellison Syndrome  
 ☞ = H. pylori eradication preferable to long-term acid suppression in PUD; **PREVENT NSAID induced ulcers** in high-GI risk: **standard dose PPI**<sup>18</sup> or misoprostol ☞ 200ug TID \$38 (range BID-QID)

OTC H2-Receptor Antagonists		
Famotidine* <b>PEPCID AC</b> coated /chewtab	10-20mg Tab	x30/ ≥ \$12
Ranitidine <b>ZANTAC-75-150</b>	75-150mg Tab	x30/ ≥ \$12
Generic versions of famotidine/ranitidine available; cost of 30 tablets/ <\$10		
* Pepcid Complete = (famotidine/calcium carb./magnesium hydroxide; 10 tabs ≡ \$9)		

Special Considerations <sup>11,10</sup>
☞=may use if benefit outweighs risk ☞=avoid if possible
• <b>Pregnancy:</b> H2RAs ☞-all B; ranitidine preferred. <sup>12</sup> PPIs ☞: lansoprazole & pantoprazole B; omeprazole most experience C
• <b>Lactation:</b> H2RAs ☞-famotidine may be preferred. PPIs ☞- avoid due to lack of data & potential adverse effects
• <b>Pediatrics:</b> H2RAs -limited trials in kids <12 yrs; PPIs -caution, not well established; omeprazole, esomeprazole & lansoprazole ☞ <sup>13</sup>

**NSAID Ulcer Complication Risk Factors:** (x= ↑ in O.R.) Hx of ulcer complications x13.5, Multiple NSAIDs x9, High dose NSAIDs x7, Concomitant anticoagulant use x6.4, Age ≥70 x5.6, Age ≥60 x3.1, Concomitant steroids x2.2, Hx of CVD x1.8  
**Red Flags:** age >50, or VBAD: V=persistent vomiting >7day, B=bleeding (anemia, melena), A=abdominal mass/weight loss (eg. 3kg/10% body weight), D=dysphagia: jaundice, family hx of gastric cancer or prior ulcer dx; then immediate endoscopy.  
 • Lifestyle changes for DIET (minimize foods that worsen Sx, eat lighter meals & chew well), AVOID (lying down for >2hr after eating & tight clothing), ELEVATE head of bed, EXERCISE, moderate alcohol use & stop SMOKING!  
**Meds ↑GERD:** anticholinergic, B-blocker, barbiturate, benzos, caffeine, digoxin, CCB diltiazem, erythromycin, estrogen, ethanol, narcotic, nicotine, NTG, orlistat, progesterone & theophylline. ↑irritation: ASA, bisphosphonate, iron, KCL, NSAIDs & quinidine.  
**Dyspepsia:** chronic peptic ulcer dx <15% (H. pylori causes up to 90% of duodenal & up to 70% of the gastric ulcers, or caused by the use of NSAIDs), GERD +/ - esophagitis ~25%, malignancy ~2% & functional or nonulcer dyspepsia ~60%. PUD complications: Perforation <10%, Obstruction ~2%, Bleed ~15%.

# Acid Suppression - Comparison Chart Supplement

## RxFiles

## References

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- <sup>2</sup> [http://www.oregonrx.org/OrgrxPDF/PPI%20review/PPI%20FINAL%20EPC%20report/PPI%20Final%20Report11\\_221.pdf](http://www.oregonrx.org/OrgrxPDF/PPI%20review/PPI%20FINAL%20EPC%20report/PPI%20Final%20Report11_221.pdf)
- <sup>3</sup> <http://www.oregonrx.org/OrgrxPDF/PPI%20review/PPI%20EPC%20UPDATE/Update%20Report%20PPIs.pdf>
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- <sup>5</sup> AHFS 2008; Micromedex 2008
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- <sup>7</sup> Laheij RJ, Sturkenboom MC, Hassing RJ, Dieleman J, Stricker BH, Jansen JB. Risk of community-acquired **pneumonia** and use of gastric acid-suppressive drugs. *JAMA.* 2004 Oct 27;292(16):1955-60. (Dial S, Delaney JA, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired **Clostridium difficile**-associated disease. *JAMA.* 2005 Dec 21;294(23):2989-95. Dial S, Delaney JA, Schneider V, Suissa S. Proton pump inhibitor use and risk of community-acquired **Clostridium difficile**-associated disease defined by prescription for oral vancomycin therapy. *CMAJ.* 2006 Sep 26;175(7):745-8. ) (Lowe DO, Mamdani MM, Kopp A, Low DE, Juurlink DN. Proton pump inhibitors and hospitalization for **Clostridium difficile**-associated disease: a population-based study. *Clin Infect Dis.* 2006 Nov 15;43(10):1272-6. Epub 2006 Oct 13. Among community-dwelling older patients, PPI use is not a risk factor for hospitalization with CDAD.) [CAG Clinical Affairs Committee. Community-acquired **pneumonia** and acid-suppressive drugs: position statement. *Can J Gastroenterol.* 2006 Feb;20(2):119-21, 123-5.] (Gulmez SE, Holm A, Frederiksen H, et al. Use of proton pump inhibitors and the risk of community-acquired **pneumonia**: a population-based case-control study. *Arch Intern Med.* 2007 May 14;167(9):950-5. The use of PPIs, especially when recently begun, is associated with an increased risk of community-acquired pneumonia.)
- <sup>8</sup> Pham C, Sadowski-Hayes L, Regal R. Prevalent Prescribing of Proton Pump Inhibitors: Prudent or Pernicious. *P&T* 2006;31(3):159-165. (Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of **hip fracture**. *JAMA.* 2006 Dec 27;296(24):2947-53. Long-term PPI therapy, particularly at high doses, is associated with an increased risk of hip fracture. InfoPOEMs: Long-term use (greater than one year) of proton pump inhibitors (PPIs) is associated with an increased risk of hip fracture in adults over age 50 years. Risk is also higher among individuals taking higher doses of PPIs and increases with duration of use. Appropriate use, dose, and duration of therapy should be carefully assessed on an individual basis. (LOE = 3b)) (Vestergaard P, Rejnmark L, Mosekilde L. Proton pump inhibitors, histamine H2 receptor antagonists, and other antacid medications and the risk of fracture. *Calcif Tissue Int.* 2006 Aug;79(2):76-83. Epub 2006 Aug 15.] (Targownik, L. E. MD MSHS, Lix, L. M. PhD, Metge, C. J. PhD, Prior, H., J. MSc, Leung, S. MSc, Leslie, W. D. MD. Use of proton pump inhibitors and risk of osteoporosis-related fractures. *Can Med Assoc J* 2008 179: p. 319-326)
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- <sup>18</sup> **Treatment Guidelines:** *Drugs for Peptic Ulcers & GERD. The Medical Letter:* February, 2004; 2(18) pp. 9-12. (**New & Updated August 2008**)
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- this data becomes available. Losec (omeprazole) After a thorough analysis, based on the data available to us at this time, we are unable to definitively conclude if there is a potential for increased cardiovascular risk associated with the long-term use of omeprazole. We will continue to evaluate should more conclusive data become available, and will advise Canadians if any further regulatory actions are required.)
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- Wilkerson PM, et al. A poor response to proton pump inhibition is not a contraindication for laparoscopic **antireflux surgery** for gastro esophageal reflux disease. *Surg Endosc*. 2005 Sep;19(9):1272-7. Epub 2005 Jul 14.
- Wang WH, Huang JQ, Zheng GF, et al. Is proton pump inhibitor testing an effective approach to diagnose gastroesophageal reflux disease in patients with noncardiac chest pain?: a meta-analysis. *Arch Intern Med*. 2005 Jun 13;165(11):1222-8. CONCLUSION: The use of PPI treatment as a diagnostic test for detecting GERD in patients with NCCP has an acceptable sensitivity and specificity and could be used as an initial approach by primary care physicians to detect GERD in selected patients with NCCP. (InfoPOEMs: In patients with chest pain known NOT to be cardiac in origin, response to treatment with an stomach-acid reducing proton pump inhibitor will identify most patients with gastroesophageal reflux (GERD) and can be the first step in explaining the chest pain. [\(LOE = 1b\)](#))
- Zacny J, Zamakhshary M, Sketris I, et al. Systematic review: the efficacy of intermittent and on-demand therapy with histamine H2-receptor antagonists or proton pump inhibitors for gastro-oesophageal reflux disease patients. *Aliment Pharmacol Ther*. 2005 Jun 1;21(11):1299-312. CONCLUSIONS: Intermittent proton pump inhibitor or H2-receptor antagonist therapy is not effective in maintaining control in oesophagitis patients. H2-receptor antagonists are effective for relief of heartburn episodes. On-demand proton pump inhibitor therapy may work in a proportion of non-erosive gastro-oesophageal reflux disease patients excluded. The benefit did not persist through the next 5 months when patients could use medications as needed rather than in a scheduled manner. Ranitidine was more cost-effective than omeprazole. It still makes sense to try ranitidine first for these patients, then stepping up to omeprazole if their symptoms are not improved adequately, particularly since this is a benign, self-limited condition. [\(LOE = 1b\)](#))