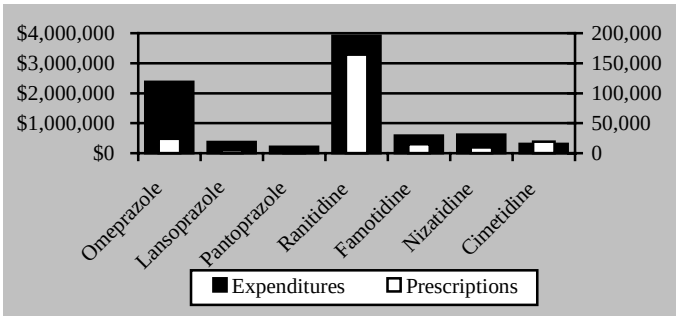
Acid Suppression
Comparison Chart Supplement

May, 1999

Omeprazole (*Losec*®) and ranitidine (*Zantac*®) are the most frequently prescribed proton pump inhibitor (PPI) and histamine$_2$ receptor antagonist (H2RA), respectively. Together they accounted for $6.2 million of 1998 drug expenditures in Saskatchewan.

1998 Acid Suppression Utilization (SK)



The **Comparison Chart** on page 2 lists the available proton pump inhibitors (**PPIs**) and histamine-2 receptor antagonists (**H2RAs**). PPIs are generally superior but more costly than H2RAs in treating acid related diseases.[1,2,3]

PPIs: There are few significant differences between the available PPIs.[1] Omeprazole (Losec®) and lansoprazole (Prevacid®) have shown excellent safety and efficacy in both short and long-term use.[1,4,5,6] Although lansoprazole has been associated with more rapid symptom resolution and healing, overall healing rates are similar to omeprazole.[7,8,9] Pantoprazole (Pantoloc®) appears to have similar efficacy and less potential for drug interactions than other PPIs; however, less is known about its long-term safety.[1,10]

Tips for optimal use of PPIs:
- PPIs are most effective if given just before (up to 30 minutes prior to) meals.[11,22]
- In cases where higher PPI dosages are needed, dividing doses is somewhat more effective than giving single doses.[11]
- Lansoprazole capsules may be opened and the granules given with applesauce or with apple juice via a feeding tube.[10]
- Omeprazole and pantoprazole should be swallowed whole.
- Omeprazole is the only PPI studied showing effectiveness in the prevention of NSAID induced ulcers.[12,13]
- Pantoprazole and lansoprazole are currently less costly than omeprazole at usual doses; however, low-dose omeprazole (10mg) is less costly than low-dose lansoprazole (15mg).

H2RAs: All H2RAs are well tolerated and side effects are infrequent. Cimetidine has a higher risk of CYP_{450} related drug interactions and certain side effects such as confusion and increased prolactin levels (see comparison chart).[14]

Tips for Optimal use of H2RAs:
- In *H. pylori* positive patients with PUD, eradication therapy is preferable to long-term maintenance therapy.[15]
- Usual doses of H2RAs are not effective in preventing NSAID induced gastric ulcers.[16]
- If patients are also using antacids, spacing administration by two hours will prevent a reduction in H2RA bioavailability.[17]
- Reduce dosage in patients with decreased renal function.
- Ranitidine and cimetidine are less costly than famotidine and nizatidine. Ranitidine (or famotidine) may be preferred in elderly patients or those at risk of drug interactions.

Acid Suppression in GERD

Although lifestyle changes are useful in controlling GERD, many patients will require drug treatment. Mild, infrequent heartburn may be managed with the intermittent use of antacids and nonprescription H2RAs. PPIs or higher-dose H2RAs are indicated in patients with more severe symptoms, poor response to previous therapy, or erosive esophagitis.

There has been a recent debate over whether a *step-up* or *step-down* approach should be used in the treatment of GERD. *Step-down* therapy uses a short (~2-4 week) course of therapy with a PPI followed by patient reassessment.[18] If patient has not improved, a double-dose of the PPI may be tried for 4 weeks. Once improved, therapy may continue with full or lower-dose PPI, an H2RA, or simple lifestyle modification when there is no history of recurrence. The traditional *step-up* approach favors an initial trial of less-costly, full-dose H2RAs before considering PPIs.[19] A majority at the 1996 Second Canadian Consensus Conference favored *a step-up* approach although debate has continued over this issue.[1,18,19,20]

GERD Maintenance Therapy: Patients with erosive esophagitis and more severe GERD require maintenance therapy with PPIs.[19] H2RAs may be adequate for patients with non-erosive esophagitis who are symptomatically controlled. For patients requiring maintenance therapy with PPIs, the long-term efficacy and safety of omeprazole and lansoprazole is now fairly well established. While full-doses of H2RAs will usually be required, lower-doses of PPIs (e.g. omeprazole 10mg po od) may be adequate in some patients.[21] The use of an H2RA (e.g. ranitidine) at HS in addition to a daytime PPI may provide more complete nocturnal acid suppression than a PPI-only regimen in certain patients with chronic GERD.[22]

References available on request

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Comparison Chart - Oral Acid Suppression Pharmacotherapy

Prepared by: Loren Regier - ***www.sdh.sk.ca/RxFiles*** **-AUG, 2000**

	Comments	Use	Usual Adult Dosage[1,23]	Approx. Duration	$ per Month
H2-Receptor Antagonists (H2RA's)					
Cimetidine TAGAMET 200,300,400,600mg tab; 60mg/ml solution	•few significant differences between H2RA's: ranitidine or cimetidine may be preferred H2RA's due to comparable safety, efficacy and lower cost - may avoid cimetidine in patients who are elderly or at risk of DI's •**DI's**: **Cimetidine** ☞ inhibition of CYP_{450} system e.g. warfarin, phenytoin, theophylline, etc. (Ranitidine has minor effect on the CYP_{450} system); - space antacid administration at least 2 hours apart from H2RAs •**SE's** - uncommon: diarrhea, constipation, headache, fatigue, confusion (risk increased in elderly and in patients with decreased renal function); **SE's - Cimetidine** ☞ slightly higher side effect risk seen with higher doses for a prolonged time; reversible gynecomastia (< 1%); weak antiandrogenic effect; may cause transient ↑ in SCr & LFTs •**↓ dosage** in patients with **↓ renal fx, ↓hepatic fx, or elderly** •higher dosages may be suitable for some patients/conditions --- •**Pylorid®** = **ranitidine bismuth citrate** 400mg; ✍; indicated for H. pylori eradication when combined with antibiotics	GU-acute DU-acute PUD-maint.† GERD	800mg po HS **800mg po HS** 400mg po HS 400mg po QID	x8 wks x4-8wks	13.00 **13.00** 10.00 18.00
Famotidine PEPCID 20, 40mg tab		GU-acute DU-acute PUD-maint.† GERD	40mg po HS **40mg po HS** 20mg po HS 20mg po BID	x8 wks x4-8 wks	28.00 **28.00** 20.00 31.00
Nizatidine AXID 150, 300mg cap		GU-acute DU-acute PUD-maint.† GERD	300mg po HS **300mg po HS** 150mg po HS 150mg po BID	x8 wks x4-8 wks	41.00 **41.00** 26.00 45.00
Ranitidine ZANTAC 150, 300mg tab; 15mg/ml solution		GU-acute DU-acute PUD-maint.† GERD	150mg po BID **300mg po HS** 150mg po HS 150mg po BID	x8 wks x4-8 wks	15.00 **16.00** 12.00 15.00
Proton Pump Inhibitors (PPI's)					
Lansoprazole PREVACID 15, 30mg Delayed Release cap ✍	•**DI's**: ↓ theophylline levels by 10%; also some inhibition of CYP 2D6 •**SE's**: diarrhea 4.1%, HA 2.9%, nausea 2.6%. Long-term safety established •effective in hypersecretory conditions e.g. ZE: dosage range 60-180mg/d; - doses >90mg/day should be given BID •may provide more rapid symptom relief (compared to omeprazole) but healing rates similar •may give contents via **NG tube** in apple juice	GU-acute DU-acute refractory-PUD GERD-acute GERD-maint.	30mg po OD ac **30mg po OD ac** 30mg po OD ac 30mg po OD ac **≥**15mg po OD ac	x4-8 wks x2-4 wks x8-12 wks x2-8 wks N/A	79.00 **79.00** 79.00 79.00 79.00
Omeprazole LOSEC **magnesium** 10, 20mg Delayed Release tab ✍	•**DI's**: inhibition of CYP 2C9 (↑ levels of phenytoin, diazepam, warfarin) •**SE's**: HA 2.4%; diarrhea 1.9%; nausea 0.9%. Long-term safety established •effective in hypersecretory conditions e.g. ZE: dosage range: 60-360mg/d; doses >60mg/day should be given BID or TID • effective for treatment & prevention of NSAID induced ulcers (20mg/day)	GU-acute DU-acute refractory-PUD GERD-acute GERD-maint.	40mg po OD ac **20mg po OD ac** 40mg po OD ac 20mg po OD **≥**10mg po OD	x4-8 wks x2-4 wks x8-12 wks x2-8 wks N/A	165.00 **86.00** 165.00 86.00 70.00
Pantoprazole PANTOLOC 40mg Enteric tab ✍	•shortest history of use; long-term safety not yet established •theoretically fewer DI's than other PPIs due to less effect on CYP 450 •IV formulation recently approved in Canada	GU-acute DU-acute GERD-acute	40mg po OD am **40mg po OD am** 40mg po OD am	x4-8 wks x2-4 wks x2-8 wks	75.00 **75.00** 75.00

$ Cost = retail cost to consumer in SK (includes markup and dispensing fee); In comparing costs, consideration should be given to the potential for shorter duration of therapy and increased efficacy of PPIs versus H2RAs; ✍ = exception drug status (EDS) in SK; **DI** = drug interactions; **SE** = side effects; **CYP** = cytochrome P_{450} enzymes; **GU** = gastric ulcer; **DU** = duodenal ulcer; **PUD** = peptic ulcer disease; **GERD** = gastroesophageal reflux disease; **HA** = headache; **SCr** = serum creatinine; **LFTs** = liver function tests; **ZE** = Zollinger-Ellison syndrome; **†** = *H. pylori* eradication preferable to long-term maintenance acid suppression in PUD; H2RAs not useful in preventing **NSAID induced ulcers** (misoprostol 200µg bid or omeprazole 20mg od)

OTC H2-Receptor Antagonists			
•Cimetidine	*GAVISCON PREVENT®*	100mg Tab	12tab/ $8
•Famotidine	*PEPCID AC®*	10mg Tab	12tab/ $**6**
•Ranitidine	*ZANTAC®–75*	75mg Tab	12tab/ $6

Special Considerations[22,24]

- **Pregnancy**: H2RAs ✔-all $Risk_F$ B; ranitidine preferred.[25] PPIs ✘-omeprazole $Risk_F$ C; lansoprazole $Risk_F$ B
- **Lactation**: H2RAs ✔-famotidine may be preferred. PPIs ✘- avoid due to lack of data & potential adverse effects
- **Pediatrics**: H2RAs -caution in children <12 years; PPIs -caution, not well established; omeprazole ✔(1 study)[26]

✔=may use if benefit outweighs risk; ✘ =avoid if possible

$Risk_F$ B = Risk Factor B: no evidence of risk (in animal studies or uncontrolled human studies); **$Risk_F$ C** = Risk Factor C: possible risk to fetus (evident in animal studies)

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The Rx Files - May, 1999 - L.D. Regier

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