



# THERAPEUTICS INITIATIVE

Evidence Based Drug Therapy

## Treatment of Gastroesophageal Reflux Disease (GERD)

Symptoms due to esophageal reflux are common; intermittent mild symptoms of heartburn occur in more than one third of healthy individuals at least once a month. The spectrum of disease associated with reflux spans from mild symptoms, not requiring treatment to severe erosive reflux esophagitis requiring intensive aggressive investigation and treatment. This article focuses on the management of this problem in adults in the primary care setting.

### What non-pharmacologic techniques are helpful in GERD?

Elimination of agents that increase acid, such as coffee; cause ulceration, such as NSAIDs; delay gastric emptying, such as narcotics or fatty foods; or decrease lower esophageal sphincter pressure, such as cigarettes, alcohol and many drugs. Weight loss and elevation of the head of the bed on 15 cm blocks can be helpful.

### What drugs decrease lower esophageal sphincter pressure and worsen GERD?

Anticholinergic drugs, antispasmodic drugs, many anti-histamine and antiemetic drugs, tricyclic antidepressants, phenothiazine neuroleptics, nitrates and calcium channel blockers. If possible these should be reduced in dose or discontinued.



### How should one manage the patient with symptoms of heartburn?

(see algorithm)

Most patients with heartburn do not seek medical attention, and the vast majority of those who do, respond to intermittent courses of antacid therapy. For those patients with persistent symptoms, suppression of acid secretion with cimetidine or other H<sub>2</sub>-blocker for a 6 week trial is effective in controlling the symptoms in 60 to 70 percent of patients with mild to moderate esophagitis.<sup>1</sup> For patients who do not respond to an H<sub>2</sub>-blocker a prokinetic drug can be tried (see Table).

Table: Drugs proven effective in management of GERD

Drug	Trade Names	Mechanism of Action	Dose	Daily Cost
antacids	Many liquid and tablet forms	Neutralization of acid	30 ml QID	\$1.08
alginic acid compound	Gaviscon Maxeran, Reglan	Neutralization of acid and protective barrier	10 ml QID 2 tab QID	\$0.60 \$0.80
H <sub>2</sub> -blockers	Letter 1	Reduction of gastric acid secretion by competitive antagonism of H <sub>2</sub> receptors	Letter 1	\$0.27 to \$1.71 Letter 1
cisapride metoclopramide	Prepulsid	Prokinetic, increased rate of gastric emptying, increased lower esophageal sphincter pressure	10 mg QID 20 mg BID 10 mg QID	\$2.48 \$0.26
omeprazole	Losec	Irreversible inhibitor of gastric H <sup>+</sup> K <sup>+</sup> ATP ase (the proton pump) Inhibits both basal and stimulated acid secretion	20 mg daily	\$2.30



# therapeutics letter

## Are prokinetic agents useful?

The prokinetic agents metoclopramide and cisapride are of similar effectiveness to H<sub>2</sub>-blockers. A prokinetic drug plus an H<sub>2</sub>-blocker improves the response but the combination is not as effective as omeprazole. Because of their cost and/or safety profile prokinetic agents are seldom indicated for maintenance therapy.

## What is the treatment of choice in the patient with severe erosive esophagitis?

H<sub>2</sub>-blockers are only effective in about 30% of patients with severe erosive esophagitis, demonstrated by endoscopy. Omeprazole 20 to 40 mg per day for eight weeks provides the potent acid suppression necessary to achieve a healing rate of over 80% of these difficult patients.<sup>2</sup> Omeprazole is not licensed for use in children; dosage and safety have not been established. A dosage and safety study in children is in progress at B.C. Children's Hospital.

## What should be done in the refractory patient and in the patients who relapse?

A small number of refractory patients require higher doses of omeprazole for up to 12 weeks to achieve healing.

Those who relapse off medication frequently require long-term omeprazole maintenance therapy under the supervision of an endoscopist.<sup>3</sup>

## What are the concerns about long-term omeprazole therapy?

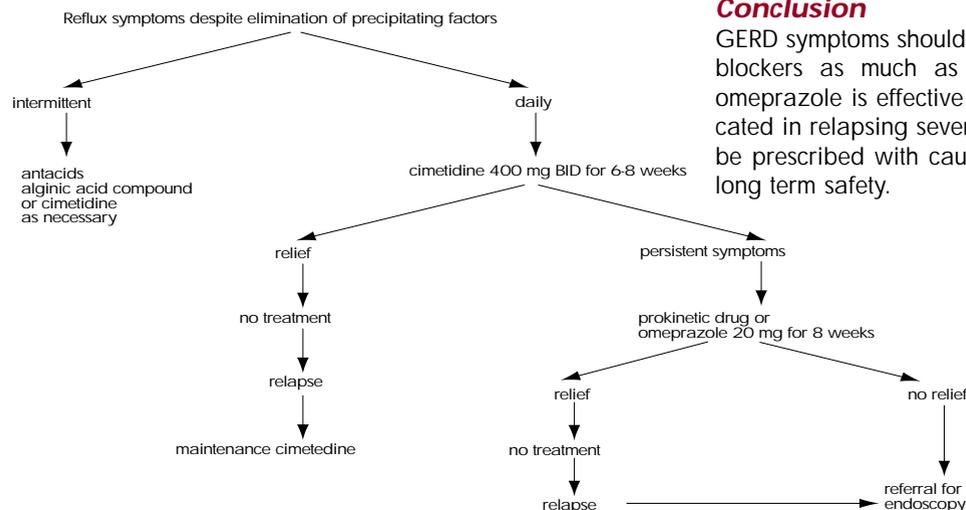
Daily omeprazole dosing causes chronic hypochlorhydria with the following potential complications: gastric bacterial overgrowth with the risk of gram negative aspiration pneumonia, decreased vitamin B<sub>12</sub> absorption,<sup>4</sup> benign gastric polyps and other gastric pathology<sup>5</sup>. The patients most likely at risk of complications are those who have a genetic deficiency of the active enzyme (CYP 2C19) responsible for metabolizing omeprazole (about 5% of Caucasians and 20% of Orientals).<sup>6</sup> These individuals, who can only be identified in a research setting, are exposed to plasma concentrations of omeprazole which are >10 times higher than other patients taking omeprazole.<sup>7</sup>

Because of these concerns the patient must be involved in any decision concerning long-term omeprazole maintenance therapy, and the maintenance dose should be reduced to the minimum dose that will prevent relapses.

## Conclusion

GERD symptoms should be treated with antacids or H<sub>2</sub>-blockers as much as possible. In refractory cases omeprazole is effective. Long term omeprazole is indicated in relapsing severe erosive esophagitis, but must be prescribed with caution until more is known about long term safety.

Algorithm:



## References

1. Johnson DA: *Medical therapy for gastroesophageal reflux disease*. Am J Med 92 (suppl 5A):88S-97S; 1992.
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7. Andersson T, Cederberg C, Edvardsson G, Heggelund A, Lundborg P: *Effect of omeprazole treatment on diazepam plasma levels in slow versus normal rapid metabolizers of omeprazole*. Clin Pharmacol Ther 47:79-85; 1990.

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