

Prepared by the British Columbia Drug and Poison Information Centre

Rabeprazole

Rabeprazole (Pariet®) was launched in the summer of 2002, becoming the fifth proton-pump inhibitor (PPI) available in Canada. Other PPIs include omeprazole (Losec®), pantoprazole (Pantoloc®, Panto® IV), lansoprazole (Prevacid®), and esomeprazole (Nexium®). Rabeprazole was marketed in the United States in 1999 and has been available since 1998 in the United Kingdom, the European Union, and Japan. Licensed indications differ by country. Like other PPIs, rabeprazole blocks the final step in gastric acid secretion by inhibiting parietal cell H⁺/K⁺ ATPase activity. All PPIs are administered as enteric-coated preparations which are absorbed in the small bowel. Once absorbed, PPIs become activated via protonation in the acidic canaliculi of gastric parietal cells. They then covalently bind to the H⁺/K⁺ ATPase enzyme producing sustained inhibition of basal and stimulated gastric acid secretion. Pharmacokinetic comparisons are given in Table I.

Efficacy

The available PPIs appear to be of similar efficacy, having little therapeutic advantage between them with respect to clinical endpoints.¹⁻⁴ Data from controlled trials demonstrate that rabeprazole is as safe and effective as omeprazole in the treatment of **gastroesophageal reflux disease (GERD)**, long-term prevention of **GERD relapse**, and as monotherapy treatment of **gastric or duodenal ulcers**.⁵ Rabeprazole was found to be effective in the **Zollinger-Ellison syndrome** in an uncontrolled 12-month trial.⁵ It has been suggested that rabeprazole may have a more rapid onset of action than other available PPIs but the clinical relevance of this has not been determined.^{2,6} Doses for those indications approved in Canada are provided in Table II.

In several trials for *Helicobacter pylori* eradication rabeprazole has been found safe and effective as part of a triple therapy regimen and of comparable efficacy to omeprazole and lansoprazole.^{5,7-9} The most recent Canadian guidelines for *H. pylori* eradication¹⁰ were published prior to the availability of rabeprazole in Canada. In British Columbia, rabeprazole is included as an option in triple therapy regimens at a recommended dose of 20 mg twice daily.¹¹ No published trials involving rabeprazole in the treatment or prevention of NSAID-induced gastric or duodenal ulcers are currently available.

Safety

Direct comparison of ADR profiles between the PPIs is difficult as trials comparing the various agents generally enroll insufficient numbers of patients to yield reliable conclusions.¹

Adverse effects

Clinical trials data gathered to date suggest that rabeprazole is generally well-tolerated, and comparable to other PPIs in its adverse effects, with headache (incidence 2.4% vs. placebo 1.6%), diarrhea, nausea, and abdominal pain as the most common complaints (all <1%).^{3,5,12-14} Overall rate of withdrawal from participation in clinical trials due to adverse events was 3%.¹³ Data from trials of one year duration show a similar adverse effect pattern, but long-term experience is limited relative to the other PPIs.¹² One recent randomized trial found similar efficacy and tolerability of rabeprazole 10 mg or 20 mg daily compared to omeprazole 20 mg daily over a 5-year study period involving GERD patients.¹⁵ Like other PPIs, rabeprazole is associated with elevation of serum gastrin concentrations.¹³ Further clinical experience will better define its adverse reaction profile.

Interactions

Unlike omeprazole, cytochrome P450 activity is not altered by rabeprazole; small studies suggest rabeprazole does not alter the pharmacokinetics of **theophylline**,¹⁶ **diazepam**, **phenytoin**, or **warfarin**.^{16,17} Reduced gastric pH can alter the absorption of some drugs including **ketoconazole** (bioavailability decreased by 30% with rabeprazole)¹⁸ and **digoxin** (peak digoxin plasma concentrations increased by 28%)¹⁷. The clinical significance of potential rabeprazole interactions awaits further experience.

Dosage and administration

Rabeprazole is available in 10 mg and 20 mg enteric-coated tablets.

Rabeprazole is usually given as a single dose in the morning. It is primarily excreted as inactive metabolites in the urine. Limited data currently available suggest that no dosage adjustment is necessary for patients with renal disease, mild to moderate hepatic impairment, or in the elderly. Patients with severe liver disease may require a dosage adjustment; caution is advised.

Table I: *Pharmacokinetics of proton pump inhibitors*^{12,19}

	Rabeprazole	Omeprazole	Lansoprazole	Pantoprazole	Esomeprazole
Oral bioavailability (%)	52	30-40	80-85	77	89-90%
Protein binding (%)	96	95	97	98	97
Peak (hr)	2.9-3.8	0.5-3.5	1.7	2.4	1-1.6
Plasma elimination half-life (hr)	1-2	0.5-1	1.5-1.7	1-1.9	1.2-1.5
Urinary excretion (%)	90 *	77	33	71	80
Duration of action (hr)	> 24	> 24	> 24	>24	> 24

* as inactive metabolites

Table II: *Comparable adult doses of proton pump inhibitors for approved indications*²⁰

	Rabeprazole (Pariet®)	Omeprazole (Losec®)	Lansoprazole (Prevacid®)	Pantoprazole (Pantoloc®)	Esomeprazole (Nexium®)
Duodenal Ulcer active maintenance	20 mg daily --	20-40 mg daily 10-40 mg daily	15 mg daily 15 mg daily	40 mg daily --	-- --
Gastric Ulcer active maintenance	20 mg daily --	20-40 mg daily 20-40 mg daily	15 mg daily --	40 mg daily --	-- --
NSAID-induced Ulcer	see text	20 mg daily	15-30 mg daily	--	--
Gastroesophageal reflux (GERD) symptomatic relief/healing	20 mg daily	20-40 mg daily	15-30 mg daily	40 mg daily	20-40 mg daily
long-term maintenance	10-20 mg daily	10-40 mg daily	15 mg daily	20-40 mg daily	20 mg daily
<i>H. pylori</i> eradication adjunct	see text	20 mg bid	30 mg bid	40 mg bid	20 mg bid
Hypersecretory conditions (e.g. Zollinger-Ellison Syndrome)	60-120 mg daily	60-120 mg daily (up to 120 mg tid)	60 mg daily - 90 mg bid	--	--

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