

Bulletin # 718

June 16, 2008

**Proton Pump Inhibitors (PPIs)  
Benefit Status Change for Omeprazole and Rabeprazole**

Effective June 30, 2008 the standard 20 mg daily doses of omeprazole and rabeprazole products listed below will no longer require special authorization for coverage under the New Brunswick Prescription Drug Program.

Regular Benefit Additions*:		Plans ABFGVW	
Drug	Brand Name	DIN	Manufacturer
Omeprazole 20 mg cap	Losec	00846503	AZE
	Apo-Omeprazole	02245058	APX
	Sandoz-Omeprazole	02296446	SDZ
Omeprazole 20 mg tab	Losec	02190915	AZE
	ratio-Omeprazole	02260867	RPH
Rabeprazole 10 mg tab	Pariet	02243796	JAN
	Novo-Rabeprazole	02296632	NOP
	Ran-Rabeprazole	02298074	RAN
Rabeprazole 20 mg tab	Pariet	02243797	JAN
	Novo-Rabeprazole	02296640	NOP
	Ran-Rabeprazole	02298082	RAN

Omeprazole and rabeprazole prescribed in doses higher than 20 mg daily will require special authorization.

In order to implement and monitor the benefit status change for the standard dose of omeprazole or rabeprazole 20 mg daily, a quantity limit has been established for each drug.

\* Subject to Maximum Allowable Price (MAP)

Guidance provided by the **Canadian Optimal Medication Prescribing and Utilization Service (COMPUS)** informed the NBPDP on the appropriate benefit status for PPIs.

**Highlights from COMPUS work:**

- All PPIs are equally efficacious
- Standard-dose PPI therapy should be the initial therapy for all patients
- H<sub>2</sub>RAs are a less costly option in many patients, controlling symptoms in almost 60% of patients as initial therapy in uninvestigated GERD
- Safety: it is prudent to keep patients at the lowest dose and degree of acid suppression that is necessary for treatment

For the detailed evidence on the prescribing and use of PPIs, consult the COMPUS Optimal Therapy Report - Scientific Report at: [www.cadth.ca/compustools](http://www.cadth.ca/compustools)

- The quantity limit will allow claims for 100 tablets/capsules of omeprazole 20 mg or rabeprazole 20 mg every 90 days.
- A quantity limit allowing claims of a maximum of 200 tablets of rabeprazole 10 mg tablets will also be established.
- The quantity limit will have a floating time period; it will begin on the date of the beneficiary's first claim for omeprazole or rabeprazole.
- The quantity limit will be renewed every 90 days and can only be overridden with an approved special authorization request.
- When pharmacy claims are submitted electronically, a response message will be sent to advise the pharmacist when the beneficiary has reached 75% or more of their quantity limit.
- Claims that bring a patient above the quantity limit will be cut back to the quantity allowed. The response message will indicate the number of units allowed for payment.

Please note that patients with existing special authorization for PPIs will not be affected by the quantity limit until their current coverage period expires.

## REGULAR BENEFIT ADDITIONS

### Omeprazole and Rabeprazole doses ≤ 20 mg daily

Omeprazole 20 mg tablets and capsules and rabeprazole 10 mg and 20 mg tablets are listed as regular benefits for Plans ABEFGVW when prescribed in doses up to 20 mg daily. Doses above 20 mg daily require special authorization.

## SPECIAL AUTHORIZATION – REVISED CRITERIA

### Omeprazole and Rabeprazole doses > 20 mg daily

Requests for omeprazole and rabeprazole doses >20 mg daily will be considered for indications listed below when beneficiaries remain symptomatic despite an adequate trial of regular benefit PPI (i.e. omeprazole OR rabeprazole) at a dose of 20 mg daily for a minimum of 8 weeks.

### Lansoprazole 15 mg & 30 mg capsules and Pantoprazole 20 mg & 40 mg tablets

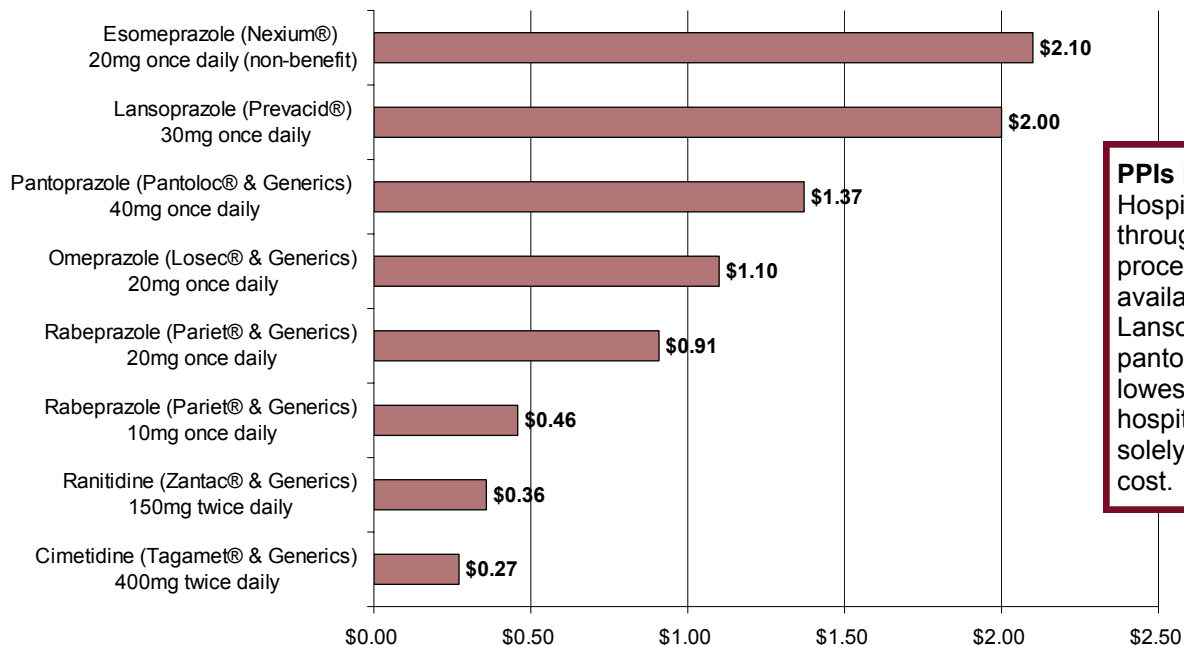
Requests for lansoprazole and pantoprazole will be considered for beneficiaries in whom there has been a therapeutic failure with regular benefit PPIs (i.e. omeprazole 20 mg daily AND rabeprazole 20 mg daily).

### Approval Periods

Requests for lansoprazole, pantoprazole, and doses of omeprazole or rabeprazole greater than 20 mg per day meeting criteria above will be considered for the following maximum approval periods:

Indication and Diagnostic Information	Maximum Approval Period
1 Symptomatic GERD or other reflux-associated indications (i.e. non-cardiac chest pain)	Considered for short-term (8-12 week) approval
2 Erosive/ulcerative esophagitis or Barrett's esophagus	Considered for long term approval
3 Zollinger-Ellison Syndrome	Considered for long-term approval
4 Gastric/duodenal ulcers in individuals who are <i>H. pylori</i> negative or having uninvestigated peptic ulcer disease (PUD)	Considered for up to 12 weeks
5 <i>H. pylori</i> positive patients with PUD	Omeprazole 20 mg or rabeprazole 20 mg BID will be reimbursed without a special authorization as part of an <i>H. pylori</i> eradication regimen. <i>H. pylori</i> regimens containing lansoprazole or pantoprazole will be reimbursed only under special authorization.
6 Gastro-duodenal protection (ulcer prophylaxis) for high risk patients (e.g. high risk NSAID users)	Considered for one year with reassessment

### Daily Drug Cost Comparison



**PPIs in Hospitals**  
Hospitals purchase PPIs through group tendering processes that are only available to hospitals. Lansoprazole and pantoprazole have the lowest tendered prices so hospitals purchase them solely based on their cost.

The following optimal therapy information on PPIs is primarily based on work completed by COMPUS—a program of the Canadian Agency for Drugs and Technologies in Health (CADTH). COMPUS promotes the optimal prescribing and use of drugs to improve health outcomes. A description of the COMPUS process and a variety of Optimal Therapy Reports and supporting tools are available at: [www.cadth.ca/compustools](http://www.cadth.ca/compustools).

**Bottom Line: All PPIs are equally efficacious.**

- There are not clinically important differences among standard-doses of PPIs in the treatment of acid-related GI conditions.
- The lowest cost PPI may be chosen without compromising quality of care.
- \* Standard daily doses are defined as: omeprazole 20mg, lansoprazole 30mg, pantoprazole 40mg, rabeprazole 20mg, and esomeprazole 20mg
- \* PPIs have been compared in studies of symptomatic GERD, endoscopy-negative reflux disease (ENRD), erosive esophagitis, *H.pylori* eradication, and healing and prophylaxis of NSAID-induced ulcers.

**Bottom Line: Double-dose PPI is not necessary for initial therapy.**

- Doubling the standard daily dose of PPIs, as initial therapy, is no better than standard daily dose PPI for healing of erosive esophagitis or NSAID-induced ulcer healing
- \* Double-dose PPI therapy has not been studied for all indications; however, the severity of the above conditions lends support to the efficacy of standard-dose PPI. Higher than standard-dose PPI is officially indicated as initial therapy in *H.pylori* eradication and Zollinger Ellison

Syndrome.

- \* The Canadian GERD Guidelines,<sup>2004</sup> state there is little evidence to support double-dose PPI as initial therapy, but a trial of double-dose PPI may be considered in patients who continue to have severe symptoms despite standard-dose PPI, or in other conditions such as non-cardiac chest pain. The guidelines also recommend that maintenance therapy be given at the lowest dose and frequency that is sufficient to achieve optimal control of the patient's symptoms.
- \* Patients on double-dose therapy should be reassessed for continued need.

**Bottom Line: H<sub>2</sub>RAs are a less costly option in treating patients requiring less intense acid suppression.**

Initial therapy of uninvestigated GERD:

- Symptom relief at 8 weeks: H<sub>2</sub>RA 58%; PPI 75%

Endoscopically negative reflux disease (ENRD):

- Heartburn relief at 4 weeks: H<sub>2</sub>RA 42%; PPI 53%

• No significant difference in quality of life

Uninvestigated dyspepsia (*H. pylori* negative):

- Complete symptom control at 4 weeks: H<sub>2</sub>RA 11%; PPI 24%
- Maintenance therapy with “on-demand” PPI was not found to offer benefit over on-demand H<sub>2</sub>RA

Functional dyspepsia (no organic cause is found to explain symptoms):

- No difference in symptom control between standard dose PPI and H<sub>2</sub>RAs with 4-8 weeks of therapy

PPIs are accepted as the treatment of choice

for conditions such as erosive esophagitis, (initial and maintenance therapy) and peptic ulcer disease (e.g. *H. pylori* or NSAID-induced ulcers).

**Treatment options for maintenance therapy**

There is no clear consensus on what constitutes optimal maintenance therapy for subjects who attain symptomatic relief of GERD with PPIs. Based on individual patient characteristics, the following are reasonable options:

- Continuation of daily PPI therapy
- Switching to “on-demand” PPI use
- Stepping-down to H<sub>2</sub>RAs
- A trial of medication discontinuation

**Safety**

Although PPIs have a good safety profile, recent concerns have been raised over their possible association with:

- Increased risk of hip fracture, which is higher with increased duration of therapy and higher daily dose. Evidence from two case control studies and is postulated to be related to decreased calcium absorption with acid suppression.
- Community acquired pneumonia. Evidence is based on two case control studies and is postulated that acid suppression decreases the destruction of ingested pathogens.
- *Clostridium difficile* associated diarrhea. Evidence is based on several observational studies; one did not find a significant association between PPI use and *C. difficile*.

Further study is required to establish the clinical significance of these adverse reactions. In the meantime, the lowest dose required for symptom control and the shortest duration is prudent. References available upon request.

For full project details and supporting intervention tools, please visit the CADTH web site:

[www.cadth.ca/compustools](http://www.cadth.ca/compustools)