

Discontinuance of Inappropriate and/or Unnecessary Proton Pump Inhibitor Use Can Result in Sizeable Cost Savings for Patients, Government & Third-Party Payers.

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SUMMARY

Background – Proton-pump inhibitors are commonly prescribed first-line for a number of gastrointestinal conditions. Proton-pump inhibitors are often continued longer than may be medically necessary, when alternative treatments or no treatment may be warranted. Proton-pump inhibitors are expensive and patients often don't qualify for coverage.

Aim – To identify those patients who no longer need to be taking a proton-pump inhibitor and to encourage them to try to discontinue the medication. To determine the cost-savings to the patient and to the health care system when unnecessary proton-pump inhibitors are stopped.

Methods – We searched our pharmacy database for all patients taking any proton-pump inhibitor at any time between July 2007 and February 2008. We then determined which patients were candidates to safely taper off of their proton-pump inhibitor.

Results – Sixty-six percent (147/222) of patients taking proton-pump inhibitors were identified as being eligible for discontinuation. Twenty-nine percent (42/147) of those patients enrolled in the study and just over half (26/42) were willing to try a trial discontinuation. Twelve months later, 15 patients (58% of the original subset (15/26)) remained off of their proton-pump inhibitors.

Conclusion – Withdrawing proton-pump inhibitors that are no longer required can result in sizeable savings for both the individual patient and the collective health care system. Many patients continue indefinitely on proton-pump inhibitors that are no longer medically required and this can result in potential adverse effects; not to mention the unnecessary spending of dollars that could be allocated elsewhere.

INTRODUCTION

Proton-pump inhibitors (PPIs) are a class of drug which suppress gastric acid secretion by inhibiting the H⁺/K⁺ ATP pump in parietal cells. They decrease the acidity of the gastrointestinal tract. The five drugs in this class include esomeprazole (Nexium[®]), lansoprazole (Prevacid[®]), omeprazole (Losec[®]), pantoprazole (Pantoloc[®]), and rabeprazole (Pariet[®]). At equivalent doses, all PPIs have similar efficacy rates and safety profiles.^{1, 2}

PPIs are highly effective for the treatment of a variety of conditions that are caused or aggravated by acid. They are used to treat ulcers, gastro-esophageal reflux disease (GERD), and erosive esophagitis. They are also often given before anaesthetic to reduce the risk of acid-aspiration pneumonia. The length of time which PPI therapy is needed depends on the condition being treated. For treatment of an ulcer, GERD, or erosive esophagitis; therapy should extend for four to eight weeks. If the PPI was given pre-anaesthetic, therapy is generally continued for one month. If the medication is used in conjunction with an *H. pylori* eradication regimen, therapy should continue for 7-14 days. There are some conditions that require long-term PPI therapy; such as Zollinger-Ellison syndrome or patients at high risk for a GI bleed in whom anticoagulant, NSAID, or glucocorticosteroid therapy cannot be avoided.

PPI therapy is expensive. Six percent of drug expenditures in the UK are on PPIs, in 2006 the equivalent of \$872 million was spent on PPIs in Great Britain.^{3,4} The monthly cost in Saskatchewan ranges from \$26.42 (rabeprazole 10 mg) to \$89.78 (lansoprazole 30 mg) per patient. * The vast majority of patients require these medications for only a defined period of time; four to eight weeks for treatment of peptic ulcer disease. However, most patients never stop taking them. A study at a Michigan hospital found that half of patients discharged were taking a PPI, and 90% had no apparent indication.⁴ This is a huge economic drain and is money that could be used elsewhere. The Saskatchewan Health Drug Plan and Extended Benefits Branch Exception Drug Status (EDS) Program Criteria for Proton Pump Inhibitors (*Appendix A*)⁵ usually only provides coverage for up to 8 weeks. Therefore, the majority of patients on long-term PPI therapy do not have coverage for their medications and are paying for them out of pocket. Furthermore, if patients are approved for EDS coverage but they have been prescribed a PPI which exceeds the Maximum Allowable Cost (MAC)

* Saskatchewan pharmacies dispense on a 34-day month.

Policy (*Appendix B*)⁶, then they are still paying for some of the cost of their medication. In addition to the economic implications, patients taking PPIs unnecessarily are complicating their medication regimens and exposing themselves to the side effects of the medication.

METHODS

Literature Review

T.J Lee et al⁷ conducted a systematic review to investigate whether some GERD patients were receiving maintenance treatment with a PPI unnecessarily, and whether these patients were taking unnecessarily high or unnecessarily frequent doses. They found that a substantial portion of patients with GERD could be managed with treatment that was less intensive than daily PPIs. Stepping down to no therapy was also acceptable in endoscopy-negative reflux disease (ENRD). However, the authors emphasized that although reduction in the cost of treatment is desirable, it is only acceptable if symptom control is not compromised.

A double-blind, placebo-controlled trial by E. Bjornsson et al³ investigated the proportion of patients on long term PPI therapy who were able to discontinue without developing symptoms. Participants underwent upper endoscopy and were excluded if endoscopic findings indicated that they could not safely discontinue their PPIs. This trial found that GERD patients had more difficulty discontinuing long-term PPIs than non-GERD patients; those taking the medications for ulcer prophylaxis, dyspepsia, or peptic ulcer disease. Discontinuation of PPIs was successful in 27% of long-term PPI users in this trial, although there were no recommendations given on the most successful method of discontinuation.

Selection Criteria

Based on a review of the literature, we have decided to target patients who were taking proton pump inhibitors:

1. As an extension of a post-anaesthetic or in-hospital prescription
2. After treatment with an *H. pylori* eradication regimen
3. For greater than 8 weeks to heal an ulcer and were not at risk for ulcer recurrence
4. For treatment of GERD which was currently controlled
5. With no identifiable indication for PPI use

We prepared a consent form for eligible patients (Appendix C) and a weekly survey for patients after they started decreasing their PPI use (Appendix D). We then wrote a letter to the nurse practitioner and physicians at the local medical clinic explaining the purpose of our trial and asking for their input and support (Appendix E).

Using our medication records, we identified 222 patients at our pharmacy who had taken a PPI since July 1, 2007. We then looked for patients with known contraindications to PPI discontinuation and removed them from our list of targets. The local paper ran an article to raise awareness of our program and a copy of same was sent to 175 patients (Appendix F) whom we thought may be eligible for PPI discontinuation. When these patients came in to the pharmacy, we evaluated whether they were potential candidates for decreased PPI use. If they met the criteria; we faxed their doctors for approval and then recommended that they try decreasing their use to every other day and using Gaviscon^{®†} for relief of symptoms due to initial rebound acid hypersecretion. If these patients were able to control their symptoms after a month of decreased PPI use, they were encouraged to discontinue their PPIs altogether.

RESULTS

Two hundred and twenty-two patients were identified as having received one or more prescriptions for a PPI between July 2007 and February 2008. Forty-seven patients were excluded from the study if they resided in the local nursing home, were deceased or had moved away, had already discontinued their PPI or had only filled their PPI prescription once.

One hundred and seventy-five patients were invited to participate in the study. Discontinuation of a PPI was contraindicated in twenty-eight participants due to cancer, methotrexate, prednisone, warfarin or NSAID use, active GERD, history of ulcer or hernia. Of the 147 eligible participants 42 completed Appendix C Patient Screening Tool. Patient characteristics are shown in Table 1. Twenty-six patients were both willing and eligible to attempt to discontinue their PPI. Four patients (15%) returned the required three weekly Appendix D Patient Symptom Questionnaires. Results are shown in Table 2. Twelve months later 15 (58%) patients remained PPI-free.

[†] Gaviscon[®] samples were obtained from GlaxoSmithKline.

DISCUSSION

Proton-pump inhibitors are the treatment of choice for many conditions. However, a number of these conditions resolve after a short period of treatment. Other conditions can be treated and or maintained with less potent, less expensive drugs such as H² blockers or OTC stomach preparations. Prescribing guidelines, such as the Saskatchewan Health Drug Plan and Extended Benefits Branch EDS Program Criteria (Appendix A), should be followed to prevent drug-related adverse effects and decrease costs to the patient and the health care system; while still maintaining optimal treatment of the patient's condition.

The median cost of PPIs is \$58.10 per month; \$26.42 for novo-rabeprazole 10 mg to \$89.78 for Prevacid® 30 mg. Having 15 patients successfully discontinue their PPI results in a cost-savings of approximately \$10458 per year at our pharmacy. Extrapolated across the entire province of Saskatchewan this could potentially lead to an annual savings of \$3,639,384 (assuming 15 patients from each of 348 pharmacies were able to discontinue PPI use). Nationally the cost savings would be \$84,667,968.⁸

Of the patients who were able to permanently discontinue their PPI, one had been taking omeprazole 20 mg, five had been taking pantoprazole 40 mg, two had been taking rabeprazole 10mg and seven had been taking rabeprazole 20 mg. Three patients had third party coverage, four had government coverage and the remainder paid the full price out of pocket. The actual monthly cost-savings for the 15 patients who successfully discontinued their PPI was \$767.17 (\$525.09 for the patients, \$152.20 for the government, and \$89.88 for third party payers), or an annual savings of \$9205 for all parties.

Table 1 Patient Characteristics

| Characteristic | n=42 |
|-----------------------------|-----------|
| Female, n (%) | 20 (48) |
| Age, mean | 69 |
| Years of PPI use, mean | 4.5 |
| Reason for PPI use, n (%) | |
| Unknown | 4 (9.5) |
| GERD | 7 (16.7) |
| Heartburn | 11 (26.2) |
| Previous Ulcer | 2 (4.8) |
| Previous Hiatal Hernia | 4 (9.5) |
| Anticoagulant use | 2 (4.8) |
| NSAID use | 2 (4.8) |
| <i>H.pylori</i> eradication | 2 (4.8) |
| Other | 7 (16.7) |
| PPI used, n (%) | |
| Esomeprazole 40 mg | 2(5) |
| Lansoprazole 30 mg | 2(5) |
| Omeprazole 20 mg | 5(12) |
| Pantoprazole 40 mg | 5(12) |
| Rabeprazole 10 mg | 8(19) |
| Rabeprazole 20 mg | 19(45) |

Table 2 Patient Symptom Questionnaire

| Symptom | Week 1, n (%) | Week 2, n (%) | Week 3, n (%) |
|----------------------------|---------------|---------------|---------------|
| Mild heartburn | 2 (50) | 1 (25) | - |
| Moderate heartburn | 1 (25) | 2 (50) | 2 (50) |
| Severe heartburn | 1 (25) | - | 1 (25) |
| Acid Regurgitation | 1 (25) | 2 (50) | 2 (50) |
| Excessive burping/belching | 3 (75) | 3 (75) | 3 (75) |
| Abdominal Bloating | 2 (50) | 2 (50) | 2 (50) |

Appendix A⁵

Saskatchewan Health Drug Plan and Extended Benefits Branch Exception Drug Status (EDS) Program Criteria for Proton Pump Inhibitors

The following criterion (a-f) applies to:

- esomeprazole delayed release tablet, 20 mg and 40 mg
 - lansoprazole delayed release capsule and tablet, 15 mg and 30 mg
 - omeprazole capsules and tablet, 20 mg
 - pantoprazole enteric-coated tablet, 40 mg
 - rabeprazole sodium tablet, 10 mg and 20 mg
- (a) For a maximum of 8 weeks in treatment of peptic ulcer disease, which includes gastric and duodenal ulcers, in patients not responding or experiencing unusual or severe adverse reactions to a reasonable trial with H₂ blockers, sucralfate or misoprostol. *Coverage for a repeat treatment will be approved only after a 3-6 month period of no treatment or prophylaxis with an H₂ blocker, sucralfate or misoprostol.*
- (b) For treatment of symptoms of gastroesophageal reflux disease (GERD). *It was noted that patients with non-erosive GERD could potentially be reduced to step-down therapy with an H₂ antagonist depending on symptom resolution.*
- (c) For treatment of severe erosive esophagitis and Zollinger-Ellison Syndrome.
- (d) For one week for eradication of *H. pylori*-related infections in individuals with peptic ulcer disease. *Provision will be made for additional coverage in treatment failures.*
- (e) For first-line prevention of gastroduodenal haemorrhage in high risk patients with prior history of gastroduodenal bleeds for whom anticoagulant, glucocorticosteroid or NSAID therapy cannot be avoided. *Coverage is renewable on a yearly basis for patients if discontinuation of offending agents or replacement with less damaging alternatives is not feasible.*
- (f) For a maximum of 8 weeks in patients discharged from hospital, on a proton pump inhibitor, following a gastroduodenal bleed.

Omeprazole, capsule and tablet 10 mg, criteria for treatment of:

- a) Symptoms of gastroesophageal reflux disease (GERD). *It was noted that patients with non-erosive GERD could potentially be reduced to step-down therapy with an H₂ antagonist depending on symptom resolution.*
- b) Severe erosive esophagitis and Zollinger-Ellison syndrome. *This is renewable on a yearly basis, and:*
- c) For maintenance therapy of healed reflux esophagitis. *This is renewable on a yearly basis.*

Appendix B⁶

Saskatchewan Health Drug Plan Maximum Allowable Cost (MAC) Policy

For many common medical conditions, drug manufacturers market a wide variety of prescription drugs that often vary in price but achieve the same medical effect. Under the MAC policy, the Drug Plan obtains expert advice on which prescription drug products within a group of similar medications are safe and beneficial, and the most cost-effective. The price of the most cost-effective drugs are used as a guide to set the maximum allowable cost the Drug Plan will cover for other similar drugs used to treat the same condition. The price is not necessarily set at the lowest cost drug.

Patients have two options if they are prescribed a drug whose price is above the MAC for the group; (1) they can either continue to take the higher priced drug and pay the difference in cost over the MAC or, (2) they can talk to their physician about switching to a drug that is within the MAC. If the patient wishes to switch medications they will need a new prescription from their physician.

If the patient chooses to remain on a higher priced drug, then only the maximum allowable cost will go towards their deductible and/or calculation of their co-payment.

The expert drug review committees assess the need for exemptions (and any exemption criteria) as they review each possible MAC group. Exemption criteria (where applicable) are noted in the chart below for each group. Exemption requests are considered on a case-by-case basis. Prescribers or pharmacists may make exemption requests, with supporting detailed information, to the Drug Plan via the Exception Drug Status process.

The MAC policy applies equally to all Saskatchewan residents eligible for benefits under the Drug Plan and Extended Benefits Branch.

MAXIMUM ALLOWABLE COST GROUP(S)

Proton Pump Inhibitors (PPIs)

| | |
|------------------------|--|
| Group includes | esomeprazole, lansoprazole, omeprazole*, pantoprazole, rabeprazole* |
| Maximum Allowable Cost | \$1.51 per tablet or capsule (subject to the patient's usual co-payment and deductible). |
| Exemption Criteria | - Patients who are intolerant or refractory to at least two drugs priced within the MAC policy. - Patients requiring administration of a PPI by nasogastric tube. |

Appendix C Patient Screening Tool

February 2008

Patient's Name _____ Taking PPI _____

1. How long have you been taking this medication for?
2. Why did you start taking this medication?
3. Is this condition under control?
4. Would you be willing to try discontinuing this medication?

Appendix D Patient Symptom Questionnaire

Name _____

Date _____

Please rate your symptoms since discontinuing your proton pump inhibitor. We encourage you to complete this questionnaire weekly. However, we understand this may not be possible, but please ensure that you date each form that you complete.

1. Did you experience any heartburn this week? Yes No

2. If yes, how would you rate it? Mild (an annoyance) Moderate (some discomfort) Severe
(significant pain)

3. Did you experience any acid regurgitation this week? Yes No

4. Did you experience excessive burping or belching this week? Yes No

5. Did you experience any abdominal bloating this week? Yes No

Did you experience anything else out of the ordinary that you feel may be due to decreasing/discontinuing your proton pump inhibitor? If yes, please explain.

Appendix E Letter to Physicians

Dear Dr. _____

February 2008

We are interested in decreasing the unnecessary use of proton pump inhibitors in community pharmacy. This will reduce costs to both patients and the provincial drug plan. It will also simplify medication regimens and stop exposing these patients unnecessarily to potential side effects of proton pump inhibitors (including, among others, headache, diarrhea, constipation, and predisposition to hip fractures).

Target patients are those who are taking PPI's for the following reasons:

1. As an extension of a post-anaesthetic prescription
2. Following *H. pylori* eradication
3. Used the PPI for up to 8 weeks to heal an ulcer
4. Without a clear indication for PPI use

We understand that there are instances that necessitate the use of PPIs. Patients will not be included in this trial if they have been diagnosed with an esophageal stricture, Barrett's esophagus, or are presumed to have extra-esophageal manifestations of GERD (such as asthma symptoms, non-cardiac chest pain, or chronic cough). Participation in this trial is completely voluntary, and we will encourage treatment in those who experience symptoms, although we may recommend that they try something else before resuming PPI therapy.

We would like to evaluate patients on PPI therapy and determine if they are candidates for discontinuation. We will reach these patients primarily when they come in to refill their prescription, but would appreciate if you would spread the word to suitable patients in your clinic as well. With your approval, we will encourage those patients who we feel do not require therapy, to attempt to discontinue their PPI. Of course, if at any time the participants or you feel that PPI therapy is vital, it will be immediately resumed.

If you have any questions or comments regarding this proposed program, please do not hesitate to contact the pharmacy. We welcome any input and suggestions you can offer!

Appendix F Newspaper Article, also sent to candidate patients

Proton pump inhibitors (PPIs) are a class of drugs which decrease the acidity of your stomach. Drugs which are included in this class include esomeprazole (Nexium®), lansoprazole (Prevacid®), omeprazole (Losec®), pantoprazole (Pantoloc®), and rabeprazole (Pariet®). PPIs are used to treat ulcers, heartburn, and gastroesophageal reflux disease (GERD). They are often given before general anaesthetic to reduce stomach acidity.

The length of time that you should take a PPI varies. If the medication is treating an ulcer, heartburn, or GERD, therapy may extend 4 – 8 weeks. If you have been given a PPI prior to anaesthetic, therapy is generally for a month. Long-term PPI use is appropriate in some instances, such as for prevention of stomach bleeding in high risk patients, and treatment of complications due to GERD.

The problem is that people often start treatment with a PPI for a condition that does not require indefinite PPI therapy, but never stop taking it. This complicates their medication regimens, carries significant economic implications, and exposes them to the side effects of PPIs (which include, but are not limited to, headache, diarrhea, stomach pains, gas, and impaired absorption of Vitamin B₁₂ and iron). The monthly cost ranges from \$26.42 (rabeprazole 10 mg) to \$89.78 (lansoprazole 30 mg) per patient. The vast majority of patients do not require long term therapy with PPIs, and when people continue taking these medications forever, the only real winners are the drug manufacturers. Studies have indicated that it is possible, safe, and cost effective to avoid long-term use of PPIs.

We believe in evidence based, appropriate use of medications. If you are taking a PPI, we encourage you to consult with us the next time you are in the pharmacy. If you are willing and a suitable candidate for PPI discontinuation, we will work with you and your physician to discontinue this medication.

We will pilot this program in our pharmacy, and see how many patients are able to successfully discontinue their PPIs. Our next goal will be to see if we can get each pharmacy in Saskatchewan to encourage a minimum of 3 patients to discontinue PPIs.

Assuming that there are 345 pharmacies in Saskatchewan:

$$[\$89.78 \text{ (lansoprazole 1 month)} + \$26.42 \text{ (rabeprazole 10 mg 1 month)}] / 2 = \mathbf{\$58.10/month}$$

345 pharmacies x \$58.10 per PPI prescription x 3 patients per pharmacy = \$60,133.50 savings per month to Saskatchewan people and the health system, which translates to \$721,602.00 per year. If you were to extrapolate this nationally, savings could range as high as 25 million dollars annually. This is a step in the right direction to limiting expenditures for unnecessary prescription drugs.

References

1. Hughes DA, Bytzer P, de Herdt D, Dubois D. Economic Analysis of On-Demand Maintenance Therapy with Proton Pump Inhibitors in Patients with Non-Erosive Reflux Disease. *Pharmacoeconomics* 2005; 23(10): 1031-1041.
2. Schneiweis, S. et al. Proton-Pump Inhibitors: Evidence for Concern. Independent Drug Information Service. Jan 2008. www.rxfacts.org.
3. Bjornsson E, Abrahamsson H, Simren M, Mattson N, Jensen C, Agerforz A, Kilander A. Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial. *Alimentary Pharmacology & Therapeutics* 2006; 24, 945-954.
4. Forgacs, I. Loganayagam, A. Overprescribing proton pump inhibitors: Is expensive and not evidence based. *BMJ* 2008; 336; 2-3.
5. Saskatchewan health Drug Plan EDS criteria. Updated February 15, 2008.
<http://formulary.drugplan.health.gov.sk.ca/publications/APPENDIX%20A.pdf>. Accessed February 25, 2008.
6. Saskatchewan Health Drug Plan MAC Policy.
<http://formulary.drugplan.health.gov.sk.ca/publications/APPENDIX%20I.pdf>. Accessed November 3, 2008.
7. Lee TJ, Fennerty MB, Howden CW. Systematic review: is there excessive use of proton pump inhibitors in gastro-oesophageal reflux disease? *Alimentary Pharmacology & Therapeutics* 2004; 20:1241-1251.
8. NAPRA national and provincial pharmacy statistics. www.napra.ca. Accessed January 3, 2009.