# Drug Class Review

# Proton Pump Inhibitors

**Preliminary Scan Report**

**December 2014**

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# OBJECTIVE

The purpose of this preliminary updated literature scan process is to provide the Participating Organizations with a preview of the volume and nature of new research that has emerged subsequent to the previous full review process. Provision of the new research presented in this report is meant to assist with Participating Organizations' consideration of allocating resources toward a full report update, a single drug addendum, or a summary review. Comprehensive review, quality assessment, and synthesis of evidence from the full publications of the new research presented in this report would follow only under the condition that the Participating Organizations ruled in favor of a full update. The literature search for this report focuses only on new randomized controlled trials, and actions taken by the US Food and Drug Administration (FDA) since the last report. Other important studies could exist.

## Date of Last Update Report

June 2013: Dexlansoprazole single drug addendum (searches through April 2013)
May 2009: Update Report #5 (searches through November 2008)

## Date of Last Preliminary Update Scan Reports (since last full report update)

March 2010: Scan #1
November 2011: Scan #2
December 2012: Scan #3

## Scope and Key Questions

The scope of the review and key questions were originally developed and refined by the Pacific Northwest Evidence-based Practice Center with input from a statewide panel of experts (pharmacists, primary care clinicians, pain care specialists, and representatives of the public). Subsequently, the key questions were reviewed and revised by representatives of organizations participating in the Drug Effectiveness Review Project (DERP). The Participating Organizations of DERP are responsible for ensuring that the scope of the review reflects the populations, drugs, and outcome measures of interest to both clinicians and patients. The Participating Organizations approved the following key questions to guide this review:

1. What is the comparative effectiveness of different PPIs in patients with symptoms of GERD?

2. What is the comparative effectiveness of different proton pump inhibitors in treating peptic ulcer and NSAID-induced ulcer?

3. What is the comparative effectiveness of different proton pump inhibitors in preventing ulcer in patients taking an NSAID?

4. What is the comparative effectiveness of different proton pump inhibitors in eradicating helicobacter pylori infection?

5. Is there evidence that one treatment strategy (e.g., stepping down to a lower dose, treatment as needed versus continuous treatment, high dose versus standard dose, or switching to an H2

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antagonist), is more effective or safer than another for longer-term treatment (more than 8 weeks) in patients with GERD or ulcer?

6. What is the comparative safety and adverse events of different PPIs in patients being treated for symptoms of gastroesophageal reflux, peptic ulcer, and NSAID-induced ulcer? 7. Are there subgroups of patients based on demographics, other medications, or co-morbidities (including patients with nasogastric tubes, or who cannot swallow solid oral medications) for which one medication or preparation is more effective or associated with fewer adverse effects?

## Inclusion Criteria

### Populations

Adults or children with symptoms of

- gastroesophageal reflux
- peptic ulcer (gastric or duodenal)
- NSAID- induced ulcer

### Interventions

- Omeprazole (Prilosec®, Prilosec OTC®)
- Omeprazole/sodium bicarbonate (Zegerid®)
- Lansoprazole (Prevacid®)
- Pantoprazole (Protonix®)
- Rabeprazole (Aciphex®)
- Esomeprazole (Nexium®)

### Effectiveness outcomes

- Symptoms
- Endoscopic healing
- Eradication rates
- Functional outcomes
- Quality of life

### Safety outcomes

- Withdrawals
- Withdrawals due to adverse effects
- Specific adverse effects or withdrawals due to specific adverse events (e.g., diarrhea)

### Study designs

- For comparative effectiveness of different PPIs, head-to-head randomized controlled trials comparing one PPI to another.
- For comparative safety of different PPIs, head-to-head randomized controlled trials or comparative observational studies.

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- For comparative effectiveness and safety of different longer-term treatment strategies, randomized controlled trials with any comparison group.

# METHODS

## Literature Search

To identify relevant citations, we searched Ovid MEDLINE and Ovid MEDLINE In-Process & Other Non-Indexed Citations from October 2012 through January 2014 including terms for included drugs. We also searched the FDA website (http://www.fda.gov/medwatch/safety.htm) for identification of new drugs, indications, and boxed warnings. To identify comparative effectiveness reviews we searched the websites of the Agency for Healthcare Research and Quality (http://www.ahrq.gov/), the Canadian Agency for Drugs and Technology in Health (http://www.cadth.ca/), Veterans Affairs Evidence-based Synthesis Program (http://www.hsrd.research.va.gov/publications/esp/), The Cochrane Collaboration **(http://www.cochrane.org/reviews/index.htm),** National Coordinating Center for Health Technology Assessment (NCCHTA) (**http://www.ncchta.org/),** and the NHS Centre for Reviews and Dissemination (CRD) (**http://www.york.ac.uk/inst/crd/).** All citations were imported into an electronic database (EndNote X4) and duplicate citations were removed.

## Study Selection

One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above.

# RESULTS

## New Drugs

### *New drugs identified in this Preliminary Update Scan*

ACIPHEX® SprinkleTM (rabeprazole sodium) delayed-release capsules was approved in March 2013 for the following conditions

Healing of erosive or ulcerative GERD in adults

Maintenance of healing of erosive or ulcerative GERD in adults

Treatment of symptomatic GERD in adults

Healing of duodenal ulcers in adults

Helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence in adults

Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome in adults

Short-term Treatment of symptomatic GERD in adolescent patients 12 years of age and older treatment of GERD in pediatric patients 1 to 11 Years of Age

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### *New drug identified in previous Preliminary Update Scan*

Dexlansoprazole (Dexilant®; previously named Kapidex) was approved in January 2009. The EPC produced a single drug addendum on the new drug dexlansoprazole in June 2013. No other drugs were identified in the previous scans.

## New Indications

### *New indications identified in this Preliminary Update Scan*

None identified.

### *Identified in previous Preliminary Update Scans*

June 2011: The indication for maintenance of healed erosive esophagitis for Dexilant® was expanded to include the relief of heartburn. The EPC produced a single drug addendum on the new drug dexlansoprazole in June 2013. No other new indications were identified in the previous scans.

## New Boxed Warnings

### *Identified in this Preliminary Update Scan*

None identified

### *Identified in previous Preliminary Update Scans*

No new boxed warnings were included in the previous scans

## Comparative Effectiveness Reviews

### *Reviews identified in this Preliminary Update Scan*

A protocol of a Cochrane review "High dose versus standard dose proton pump inhibitor for short term management of erosive reflux oesophagitis" is available though it is not clear when the study will be completed. The protocol is available at http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010581/pdf.

### *Reviews identified in previous Preliminary Update Scans*

In September 2011, the Agency for Healthcare Research and Quality published an update of its report, "Comparative Effectiveness of Management Strategies for Gastroesophageal Reflux Disease." The full report is available at http://www.effectivehealthcare.ahrq.gov/ehc/products/165/755/CER29-GERD_20110926.pdf

## Randomized Controlled Trials

### *Trials identified since the most recent Full Report*

For this scan, Medline searches resulted in 91 citations. Of those, there was only 1 new head to head trial comparing esomeprazole to lansoprazole in patients with helicobactor pylori. Previous scans identified 6 head to head trials in 7 publications. Most of the trials were conducted in patients with GERD. Additionally, we found 2 long term trials (>8 weeks duration), one comparing omeprazole to H2RA antagonist ranitidine in children and the other compared standard to lower dose of rabeprazole in patients with upper GI symptoms. Characteristics of the relevant trials are included in tables 2 and 3 below and the abstracts are included in Appendix A.

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Note that in the previous scan, there were 2 new trials reported in 1 publication on dexlansoprazole. Those two trials are not listed in the table below as they are already included in the single drug addendum report.

**Table 1. New head-to-head trials of proton pump inhibitors***

| Study, year | Comparison | Focus |
|---|---|---|
| Eggleston, 2009 | Esomeprazole vs rabeprazole | GERD |
| Hein, 2011 | Pantoprazole magnesium vs pantoprazole sodium | GERD |
| Labenz, 2009a, 2009b | Esomeprazole vs pantoprazole | GERD (healing and maintenance) |
| Lee, 2010 | Esomeprazole vs rabeprazole | Helicobacter pylori eradication in dyspepsia |
| Liu, 2013 | Rabeprazole vs lansoprazole | Helicobacter pylori eradication |
| Pace, 2011 | Rabeprazole vs omeprazole | GERD, healing rate by BMI |
| Zheng, 2009 | Esomeprazole vs lansoprazole vs pantoprazole vs omeprazole | GERD symptoms |

*Shading indicates trials identified in this preliminary update scan

**Table 2. Other Trials**

| | | |
|---|---|---|
| Sanuki, 2012 | Rabeprazole 10mg vs 20 mg | Upper GI symptoms |
| Umarino, 2012 | Omeprazole vs ranitidine | GERD in children |

*Shading indicates trials identified in this preliminary update scan

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# Appendix A. Abstracts of potentially relevant new trials of proton pump inhibitors (n=3)

## This scan

Liu, M.-K., I. C. Wu, et al. (2013). "Randomized trial comparing rabeprazole- versus lansoprazole-based Helicobacter pylori eradication regimens." Kaohsiung Journal of Medical Sciences **29**(7): 379-384.

Different types of proton pump inhibitor (PPI)-based triple therapies could result in different Helicobacter pylori eradication rates. This study aimed to compare the efficacy and safety of rabeprazole- and lansoprazole-based triple therapies in primary treatment of H. pylori infection. From September 2005 to July 2008, 426 H. pylori-infected patients were randomly assigned to receive a 7-day eradication therapy with either rabeprazole 20mgbid (RAC group, n=222) or lansoprazole 30mgbid (LAC group, n=228) in combination with amoxicillin 1gbid and clarithromycin 500mgbid. The patients received follow-up esophagogastroduodenoscopy (EGD) and/or (13)C-urea breath test 12-16 weeks later to define H. pylori status. Their personal and medical history, compliance and side effects were obtained by using a standardized questionnaire. Intention-to-treat analysis revealed that the eradication rate was 87.84% in the RAC group and 85.96% in the LAC group (p=0.56). All patients returned for assessment of compliance (100% in the LAC group vs. 99.50% in the RAC group; p=0.32) and adverse events (7.20% in the RAC group vs. 5.70% in the LAC group, p=0.51). Univariate analysis suggested that patients with nonsteroid anti-inflammatory agent (NSAID) use had lower eradication rates than those without (76.71% vs. 88.74%; p=0.006). Our results showed that efficacy and safety were similar in rabeprazole- and lansoprazole-based primary therapies. The influence of NSAID usage on H. pylori eradication needs to be further investigated. Copyright 2012. Published by Elsevier B.V.

Sanuki, T., T. Fujita, et al. (2012). "Rabeprazole reduces the recurrence risk of peptic ulcers associated with low-dose aspirin in patients with cardiovascular or cerebrovascular disease: a prospective randomized active-controlled trial." Journal of Gastroenterology **47**(11): 1186-1197.

BACKGROUND: Patients using low-dose aspirin (LDA) have an increased risk of gastroduodenal mucosal lesions and upper gastrointestinal symptoms. We aimed to clarify the efficacy of rabeprazole for preventing peptic ulcer, esophagitis, and gastrointestinal symptoms associated with LDA.

METHODS: Patients with a history of peptic ulcers who were receiving LDA for cardiovascular or cerebrovascular disease were randomly assigned to receive rabeprazole at 10 mg daily, rabeprazole at 20 mg daily, or gefarnate (a cytoprotective anti-ulcer agent) at 50 mg twice daily. The primary endpoint was the development of gastric and/or duodenal ulcer at 12 weeks. The modified Lanza score (MLS) and gastrointestinal symptoms were evaluated at baseline and at 12 weeks.

RESULTS: The full analysis set comprised 261 patients (rabeprazole 10 mg: n = 87, rabeprazole 20 mg: n = 89, gefarnate 100 mg: n = 85). The cumulative incidences of gastroduodenal ulcers at 12 weeks in the 10 mg rabeprazole group, 20 mg rabeprazole group, and gefarnate group were 7.4, 3.7, and 26.7 %, respectively (rabeprazole group 5.5 % vs. gefarnate group 26.7 %, hazard ratio [HR] 0.179; 95 % confidence interval [CI] 0.082-0.394; $p < 0.0001$). The proportions of patients with an MLS of >1 and erosive esophagitis were significantly lower in the rabeprazole group than in the gefarnate group at 12 weeks (gastric lesions 33.5 vs. 62.4 %, $p < 0.0001$; duodenal lesions 5.7 vs. 24.7 %, $p < 0.0001$; erosive esophagitis 5.8 vs. 19.4 %, $p < 0.0001$). Rabeprazole was significantly more effective than gefarnate for the resolution and prevention of gastrointestinal symptoms (resolution 53.6 vs. 25.0 %, $p = 0.017$; occurrence 9.2 vs. 28.3 %, $p = 0.0026$).

CONCLUSIONS: Rabeprazole is more effective than gefarnate for reducing the risk of recurrence of peptic ulcer, esophagitis, and gastrointestinal symptoms in LDA users.

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Ummarino, D., E. Miele, et al. (2012). "Impact of antisecretory treatment on respiratory symptoms of gastroesophageal reflux disease in children." Diseases of the Esophagus **25**(8): 671-677.

The effect of antisecretory treatment on extraesophageal symptoms of gastroesophageal reflux disease was evaluated. **Seventy-eight children** presenting with typical and extraesophageal symptoms of gastroesophageal reflux disease underwent a multichannel intraluminal impedance and pH monitoring (MII/pH). Children with a positive MII/pH were randomly treated with proton pump inhibitors (PPIs) or histamine H(2) -receptor antagonists (H(2) RAs) during 3 months. At the end of the treatment period, all patients were recalled. A second treatment period of 3 months was given to those patients who were not symptom-free after 3 months. Thirty-five of the forty-one (85.4%) children with a pathologic MII/pH presented with extraesophageal symptoms and were treated with PPIs (omeprazole; n:19) or H(2) RAs (**ranitidine;** n:16) for 12 weeks. After 3 months, 11/19 (57.9%) PPI-treated patients had a complete resolution of symptoms; 6/8 nonresponders were treated with PPI for another 3 months and became all symptom-free. The other two underwent a Nissen fundoplication. Only 5/16 (31.2 %) patients treated with H(2) RAs had a complete resolution of symptoms after 3 months; 1/11 was treated again with H(2) RAs during 3 months, and 10/11 were changed to PPIs. In 3/10, a partial resolution of symptoms was achieved, while in 7/10, a complete remission was obtained ($P < 0.05$). Antisecretory reflux treatment improves extraesophageal reflux symptoms. The efficacy of PPIs is superior to that of H(2) RAs in these children. 2012 Copyright the Authors. Journal compilation 2012, Wiley Periodicals, Inc. and the International Society for Diseases of the Esophagus.

## Identified in the previous Preliminary Update Scan (N=6 studies, 7 publications)

Hein, J. (2011). "Comparison of the efficacy and safety of pantoprazole magnesium and pantoprazole sodium in the treatment of gastro-oesophageal reflux disease: a randomized, double-blind, controlled, multicentre trial." Clinical Drug Investigation **31**(9): 655-664.

BACKGROUND: Proton pump inhibitors (PPIs) are well established as first-line agents for the treatment of moderate-to-severe gastro-oesophageal reflux disease (GORD). Although all PPIs heal oesophageal lesions and provide symptomatic relief, breakthrough symptoms may occur as acidity levels rebound. Pantoprazole magnesium (pantoprazole-Mg) has a longer elimination half-life than pantoprazole sodium (pantoprazole-Na), resulting in prolonged drug exposure. OBJECTIVE: This study compares the clinical efficacy and safety of once-daily pantoprazole-Mg 40[THIN SPACE]mg with that of once-daily pantoprazole-Na 40[THIN SPACE]mg in the management of GORD. METHODS: This was a randomized, double-blind, controlled, multicentre study of non-inferiority design in outpatients with GORD. The study was conducted in 53 centres in Germany from 12 May 2003 to 18 September 2003. Male or female outpatients (aged >=18 years) with endoscopically confirmed GORD stage I-III (according to the Savary-Miller classification modified by Siewert) were enrolled. Using a computer-generated randomization list, patients were randomized to treatment with pantoprazole-Mg 40[THIN SPACE]mg plus placebo or pantoprazole-Na 40[THIN SPACE]mg plus placebo, both given once daily for 4 or 8 weeks depending on healing of oesophagitis. The primary objective was endoscopic healing at 8 weeks. RESULTS: The intent-to-treat (ITT) group consisted of 636 patients (322 receiving pantoprazole-Mg and 314 receiving pantoprazole-Na). Endoscopically confirmed healing of reflux oesophagitis after 8 weeks occurred in 87.3% (95% CI 83.1, 90.7) of patients receiving pantoprazole-Mg and 85.0% (95% CI 80.6, 88.8) of patients receiving pantoprazole-Na (ITT population). The lower bound of the 95% CI for the between-group treatment difference was -1.3, which was within the predefined margin of non-inferiority of -10% to 0%. Healing rates after 4 weeks were superior in the pantoprazole-Mg group (72.7% [95% CI

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67.5, 77.5]) compared with the pantoprazole-Na group (66.2% [95% CI 60.7, 71.5]), and the one-sided (lower bound) of the 95% CI for the difference between healing rates for the two treatments was within the predefined non-inferiority margin of -10% to 0%. Both treatments had a similar effect on GORD healing in subgroups of patients based on baseline oesophagitis grade and Helicobacter pylori status. Pantoprazole-Mg had similar efficacy to pantoprazole-Na in relieving a broad range of GORD-related symptoms across the course of the study, although symptomatic relief at 4 weeks was numerically higher in the pantoprazole-Mg group than in the pantoprazole-Na group (statistical analyses were not performed). Both treatments were well tolerated; most adverse events were of mild or moderate severity and unrelated to the study medication, and there were no unexpected safety concerns. CONCLUSION: Pantoprazole-Mg is clinically as effective and well tolerated as pantoprazole-Na in the treatment of GORD stages I-III, demonstrating non-inferiority for oesophageal healing at 8 weeks and superior healing rates at 4 weeks associated with high levels of symptomatic relief.

Pace, F., B. Coudsy, et al. (2011). "Does BMI affect the clinical efficacy of proton pump inhibitor therapy in GERD? The case for rabeprazole." European Journal of Gastroenterology & Hepatology **23**(10): 845-851.

BACKGROUND: Increased BMI is associated with a higher risk of gastroesophageal reflux disease. AIMS: To investigate whether overweight/obesity (BMI>=25 kg/m(2)) affects rabeprazole clinical efficacy versus omeprazole in patients with erosive esophagitis (EE). PATIENTS AND METHODS: Post-hoc analysis of EE healing rate and symptom response stratified by patient BMI was performed on data from a multicenter, double-blind, randomized, 4- to-8-week trial comparing EE healing with rabeprazole (20 mg daily) and omeprazole (20 mg daily). Analysis of variance, two-sample t-test, Blackwelder's test for equivalence, log-rank, and Cochran-Mantel-Haenszel tests were used to analyze comparisons. RESULTS: In the two BMI groups (<25 kg/m(2) and >=25 kg/m(2) respectively), rabeprazole and omeprazole were equally effective for mucosal healing regardless of patient's BMI (N=542, P>0.05). However, in overweight/obese patients, rabeprazole was significantly faster than omeprazole in inducing heartburn relief during the first treatment week (P<0.0001). CONCLUSIONS: Results of this study show that the clinical efficacy of rabeprazole is maintained in overweight/obese patients with gastroesophageal reflux disease and suggest that this subgroup of patients may derive, from rabeprazole, even greater benefit than lean patients.

Eggleston, A., P. H. Katelaris, et al. (2009). "Clinical trial: the treatment of gastro-oesophageal reflux disease in primary care--prospective randomized comparison of rabeprazole 20 mg with esomeprazole 20 and 40 mg." Alimentary Pharmacology & Therapeutics 29(9): 967-78.

BACKGROUND: A trial of empirical PPI therapy is usual practice for most patients with symptoms of gastro-oesophageal reflux disease (GERD) in primary care. AIM: To determine if the 4-week efficacy of rabeprazole 20 mg for resolving heartburn and regurgitation symptoms is non-inferior to esomeprazole 40 mg or 20 mg. METHODS: In all, 1392 patients were randomized to rabeprazole 20 mg, esomeprazole 20 mg or 40 mg once daily. Patients, doctors and assessors were blinded. Symptom resolution data were collected on days 0-7 and day-28 using the Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity Index with a shortened version used on days 8-27. RESULTS: Rabeprazole 20 mg was non-inferior to esomeprazole 40 mg for complete resolution of regurgitation and satisfactory resolution of heartburn and regurgitation. For complete heartburn resolution, the efficacy of rabeprazole 20 mg and esomeprazole 40 mg was statistically indistinguishable, although the non-inferiority test was inconclusive. Rabeprazole 20 mg was non-inferior to esomeprazole 20 mg for all outcomes. CONCLUSIONS: In uninvestigated GERD patients, rabeprazole 20 mg was non-inferior to esomeprazole 40 mg for complete and satisfactory relief of regurgitation and satisfactory relief of heartburn, and not different for complete resolution of heartburn.

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Labenz, J., D. Armstrong, et al. (2009). "Clinical trial: factors associated with freedom from relapse of heartburn in patients with healed reflux oesophagitis--results from the maintenance phase of the EXPO study." Alimentary Pharmacology & Therapeutics 29(11): 1165-71.

BACKGROUND: Ability to predict freedom from heartburn relapse during maintenance therapy for healed reflux oesophagitis may facilitate optimal treatment choices for individual patients. AIM: To determine factors predicting freedom from heartburn relapse during maintenance proton pump inhibitor therapy in patients with healed reflux oesophagitis. METHODS: This post-hoc analysis used data from the maintenance phase of the EXPO study (AstraZeneca study code: SH-NEG-0008); 2766 patients with healed reflux oesophagitis and resolved heartburn received once-daily esomeprazole 20 mg or pantoprazole 20 mg for 6 months. Multiple logistic regression analysis determined factors associated with freedom from heartburn relapse. RESULTS: Heartburn relapse rates were lower with esomeprazole than pantoprazole in all subgroups analysed. Esomeprazole treatment was the factor most strongly associated with freedom from heartburn relapse (odds ratio 2.08; P < 0.0001). Other factors significantly associated with freedom from heartburn relapse were Helicobacter pylori infection, greater age, non-obesity, absence of epigastric pain at baseline, pre-treatment nonsevere heartburn and GERD symptom duration < or =5 years. CONCLUSIONS: Several factors predict freedom from heartburn relapse during maintenance proton pump inhibitor therapy for healed reflux oesophagitis, the strongest being choice of proton pump inhibitor. These findings outline the importance of optimizing acid control and identifying predictors of relapse for effective long-term symptom management in reflux oesophagitis patients.

Labenz, J., D. Armstrong, et al. (2009). "Clinical trial: factors associated with resolution of heartburn in patients with reflux oesophagitis--results from the EXPO study." Alimentary Pharmacology & Therapeutics 29(9): 959-66.

BACKGROUND: The ability to predict symptom response to reflux oesophagitis-healing therapy may optimize treatment decisions. AIM: To identify factors associated with heartburn resolution in patients receiving acid-suppressive therapy for reflux oesophagitis. METHODS: In this multicentre, randomized, double-blind trial (EXPO; AstraZeneca study code: SH-NEG-0008), patients with endoscopically confirmed reflux oesophagitis and reflux symptoms received once-daily proton pump inhibitor therapy [esomeprazole 40 mg (n = 1562) or pantoprazole 40 mg (n = 1589)] for >or=4 weeks. Factors associated with heartburn resolution after 4 weeks were identified by multiple logistic regression analysis. RESULTS: Esomeprazole therapy, positive Helicobacter pylori status and greater age were associated with an increased likelihood of heartburn resolution [odds ratio (95% confidence interval): 1.31 (1.12, 1.54), 1.44 (1.19, 1.74) and 1.013 (1.007, 1.019) per year, respectively; all P < 0.001]. Men and patients with no acid regurgitation or epigastric pain pre-treatment were also more likely to achieve heartburn resolution (all P < 0.05). CONCLUSIONS: The use of esomeprazole rather than pantoprazole increases the probability of achieving resolution of heartburn during reflux oesophagitis-healing therapy. Other factors, including H. pylori status, age, gender and symptom profile may be helpful in determining the likelihood of heartburn resolution in such patients.

Lee, V. W. Y., T. S. Chau, et al. (2010). "Pharmacogenetics of esomeprazole or rabeprazole-based triple therapy in Helicobacter pylori eradication in Hong Kong non-ulcer dyspepsia Chinese subjects." Journal of Clinical Pharmacy & Therapeutics **35**(3): 343-350.

OBJECTIVE: Our study aimed to assess the effectiveness of esomeprazole or rabeprazole in combination with amoxicillin and clarithromycin for the eradication of Helicobacter pylori in Hong Kong non-ulcer dyspepsia (NUD) patients. METHODS: A prospective clinical trial was conducted at the Alice Ho Miu ling Nethersole Hospital outpatient endoscopy center from June 2004 to December 2005. Participants received amoxicillin 1 g, clarithromycin 500 mg, and,

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esomeprazole 20 mg (EAC) or rabeprazole 20 mg (RAC), all given twice daily for 1 week. The H. pylori status was determined by the [13C] urea breath test at least 4 weeks after completion of the treatment. Mutation status of CYP2C19 in exon 4 and exon 5 associated with the poor metabolizer phenotype was determined. RESULTS: The intention-to-treat eradication rates in patients treated with RAC and EAC were 77% and 84.6% respectively, and per protocol-based eradication rates were 83.7% and 88.9% respectively. The eradication rates did not vary with CYP2C19 phenotype found. For clarithromycin-sensitive strains, the cure rates were statistically significant regardless of CYP2C19 polymorphism (P < 0.0001). CONCLUSION: Triple therapy with either EAC or RAC is effective for Hong Kong Chinese NUD patients with H. pylori infection. Success eradication was related to clarithromycin resistance and not CYP2C19 genotype.

Zheng, R. N. and R.-N. Zheng (2009). "Comparative study of omeprazole, lansoprazole, pantoprazole and esomeprazole for symptom relief in patients with reflux esophagitis." World Journal of Gastroenterology 15(8): 990-5.

AIM: To clarify whether there is any difference in the symptom relief in patients with reflux esophagitis following the administration of four Proton pump inhibitors (PPIs). METHODS: Two hundred and seventy-four patients with erosive reflux esophagitis were randomized to receive 8 wk of 20 mg omeprazole (n = 68), 30 mg of lansoprazole (n = 69), 40 mg of pantoprazole (n = 69), 40 mg of esomeprazole (n = 68) once a day in the morning. Daily changes in heartburn and acid reflux symptoms in the first 7 d of administration were assessed using a six-point scale (0: none; 1: mild; 2: mild-moderate; 3: moderate; 4: moderate-severe; 5: severe). RESULTS: The mean heartburn score in patients treated with esomeprazole more rapidly decreased than those receiving other PPI. Complete resolution of heartburn was also more rapid in patients treated with esomeprazole for 5 d compared with omeprazole (P = 0.0018, P = 0.0098, P = 0.0027, P = 0.0137, P = 0.0069, respectively), lansoprazole (P = 0.0020, P = 0.0046, P = 0.0037, P = 0.0016, P = 0.0076, respectively), and pantoprazole (P = 0.0006, P = 0.0005, P = 0.0009, P = 0.0031, P = 0.0119, respectively). There were no significant differences between the four groups in the rate of endoscopic healing of reflux esophagitis at week 8. CONCLUSION: Esomeprazole may be more effective than omeprazole, lansoprazole, and pantoprazole for the rapid relief of heartburn symptoms and acid reflux symptoms in patients with reflux esophagitis.

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