Scottish Medicines Consortium

esomeprazole 20mg tablets (Nexium®) **No. (274/06)**

AstraZeneca UK Ltd

5 May 2006

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

Esomeprazole (Nexium®) is not recommended for use within NHS Scotland for the healing of gastric ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy.

In the treatment of gastric ulcers associated with NSAID therapy, esomeprazole produced greater healing rates than a histamine-H_2 antagonist. However, there are no comparisons of esomeprazole with other proton pump inhibitors for this indication. The economic case has not been demonstrated.

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium

Esomeprazole 20mg tablet (Nexium®)

Indication

Healing of gastric ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy

Dosing information

20mg once daily for 4 to 8 weeks

UK launch date

October 2004

Comparator medications

The proton pump inhibitors omeprazole and lansoprazole are licensed in the UK for the treatment of gastric ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy. The histamine H_2 antagonists ranitidine, cimetidine and nizatidine and the prostacyclin analogue, misoprostol, are also licensed for this condition. The latter is available in combination with the NSAID, diclofenac, as the product Arthrotec®.

Cost of relevant comparators

		Dose	Cost per course (£)
Proton pump inhibitor	**Esomeprazole**	**20mg daily**	**19-37**
	Omeprazole	20mg daily	8.94-18
	Lansoprazole	15-30mg daily	4.57-14
Prostacyclin analogue	Misoprostol	200mcg four times daily	19-37*
Histamine (H_2) antagonist	Nizatidine	150mg twice daily	23
	Cimetidine	400mg twice daily	5.47
	Ranitidine	150mg twice daily	2.43

Courses of 4-8 weeks, except for histamine H_2 antagonists, which are 8 weeks; Costs from eVadis accessed on 27th April 2006; Doses from summary of product characteristics and do not imply therapeutic equivalence; * incremental costs of misoprostol as part of a combination products: Arthrotec 50® three times daily and Arthrotec 75® twice daily (calculated by subtracting costs of generic diclofenac from costs of the combination products) are £14.49-28.99 and £3.41-6.82, respectively.

Summary of evidence on comparative efficacy

Esomeprazole, the S-isomer of omeprazole, is a proton pump inhibitor (PPI) that inhibits the acid pump in parietal cells, thereby reducing gastric acid secretion.

Two double-blind trials recruited 399 and 410 adults who required continuous treatment with a NSAID, had a gastric ulcer ≥5 mm in diameter and no gastric or duodenal ulcers >25 mm. They were randomised to ranitidine 150mg twice daily, esomeprazole 20mg or 40mg once daily for eight weeks. The primary endpoint was the proportion of the intention-to-treat (ITT) population, comprising all patients who received at least one dose of study drug, who had no gastric ulcers at week 8. This was significantly greater with both esomeprazole 20mg and 40mg than with ranitidine, with healing rates (95% confidence intervals (CI)) in the respective groups of 88% (83%, 94%), 92% (87%, 96%) and 74% (67%, 82%) in the first study. In the second study this was numerically greater with both doses of esomeprazole compared to ranitidine, with healing rates in the respective groups of 85%, 86% and 76%. In a pooled analysis of these data the differences between the esomeprazole groups and ranitidine were significant, with healing rates of 87%, 88% and 75%, respectively. The healing rates at 4 weeks were significantly greater with esomeprazole 20mg and 40mg than with ranitidine in both studies and the pooled analysis, with rates in the respective groups of 73-79%, 71-78% and 55-67%.

Other data were also assessed but remain commercially confidential. *

Summary of evidence on comparative safety

No new adverse effects were identified for esomeprazole in the studies for this indication. In the trials described previously, similar adverse-events were observed in the esomeprazole and ranitidine groups, with no significant differences between them.

Summary of clinical effectiveness issues

In a pooled analysis of the trials described previously the majority of the patients (85%) were receiving treatment with non-selective NSAID, with the remaining patients receiving a cyclo-oxygenase-2 (COX-2) selective NSAID. No evidence was provided to indicate that the pathology of gastro-duodenal ulceration associated with COX-2 selective NSAIDs differs from that with non-selective NSAIDs. There is no evidence that esomeprazole would have any advantages in clinical practice over the other proton pump inhibitors, omeprazole and lansoprazole, which could be used within their current licences, for the healing of gastric ulcers associated with COX-2 selective NSAIDs.

Esomeprazole has not been directly compared with any other PPIs or a prostaglandin analogue for healing of gastric ulcers associated with NSAIDs. Therefore, relative efficacy and safety in this indication are unknown.

Summary of comparative health economic evidence

The manufacturer presents a direct cost comparison of esomeprazole with other PPIs. No evaluation is presented of the cost effectiveness of esomeprazole relative to the treatment options it may displace. As a consequence, the cost effectiveness of esomeprazole has not been demonstrated.

Patient and public involvement

A Patient Interest Group Submission was not made.

Budget impact

The budget impact is not disaggregated by licensed indication. The following estimate therefore included both the prevention and treatment of ulcers indications.

The manufacturer presents data suggesting that currently around 56,000 patients are co-prescribed NSAIDs and PPIs. Around 3,400 of these are being prescribed COX-2 selective NSAIDs in conjunction with PPIs, though this is anticipated to fall to only 1,300 within 5 years. Based upon the current market share of esomeprazole of 5.2% a net cost of £11,163 is anticipated in year 1 in the COX-2 selective NSAID market, falling to £4,200 by year 5. However, any increase in market share over the 5.2% of the COX-2 selective NSAID co-prescribed PPI market would increase the budget impact within this market segment proportionately.

A market share of 0% of the non-selective NSAID co-prescribed PPI market is assumed.

Guidelines and protocols

The August 2004 National Institute for Health and Clinical Excellence (NICE) clinical guideline number 17 on dyspepsia recommends, for patients using NSAIDs with diagnosed peptic ulcer, stopping the use of NSAID where possible and offering full-dose proton pump inhibitor or histamine H_2 antagonist therapy for two months, with subsequent eradication therapy offered to patients with Helicobacter pylori. It is also noted that in patients using NSAIDs without peptic ulcer disease, substitution to a COX-2 selective NSAID is associated with a lower incidence of endoscopically detected lesions. The promotion of healing and prevention of recurrence in those with existing ulcer disease is unclear.

Additional information

After review of a full submission the Scottish Medicines Consortium (SMC) issued advice on 11th October 2004 that intravenous esomeprazole (Nexium IV®) is accepted for use within NHS Scotland for the treatment of gastroesophageal reflux disease in patients with oesophagitis and/or severe symptoms of reflux as an alternative to oral therapy when oral intake is not appropriate. Intravenous esomeprazole seems to be as effective as oral esomeprazole in terms of gastric acid suppression and healing of erosive oesophagitis. However comparisons with other IV proton pump inhibitors are restricted to pre-clinical studies. Esomeprazole has similar acquisition costs to other IV proton pump inhibitors.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including 13 April 2006.

Drug prices are those available at the time the papers were issued to SMC for consideration.

** Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:* http://www.scottishmedicines.org.uk/

The undernoted reference was supplied with the submission.

Goldstein JL, Johanson JF, Suchower LJ, Brown KA. Healing of gastric ulcers with esomeprazole versus ranitidine in patients who continued to receive NSAID therapy: a randomized trial. Am J Gastroenterol 2005; 100: 2650-7.