Scottish Medicines Consortium

esomeprazole 20mg tablets (Nexium®) No. (257/06)
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 prevention of gastric and duodenal ulcers associated with non-steroidal anti-inflammatory (NSAID) therapy in patients at risk.

When compared to placebo, esomeprazole reduces the rate of gastro-duodenal ulcers associated with NSAID therapy in at-risk patients. 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

Prevention of gastric and duodenal ulcers associated with non-steroidal anti-inflammatory (NSAID) therapy in patients at risk.

Dosing information

20mg once daily

UK launch date

October 2004

Comparator medications

The proton pump inhibitors, lansoprazole, pantoprazole and omeprazole are licensed in the UK for the prevention of gastroduodenal ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy. The prostacyclin analogue, misoprostol, is also licensed for this indication and the histamine H_2 antagonist, ranitidine, is licensed for prevention of duodenal ulcers associated with NSAIDs. Misoprostol is available in combination with the NSAID, diclofenac, as the product Arthrotec®.

Cost of relevant comparators

		Dose	Annual cost (£)
Proton pump inhibitor	**Esomeprazole**	**20mg daily**	**241**
	Omeprazole	20mg daily	116
	Pantoprazole	20mg daily	160
	Lansoprazole	15-30mg daily	59-88
Prostacyclin analogue	Misoprostol	200mcg two-four times daily	122-243*
Histamine-H_2antagonist	Ranitidine	150mg twice daily	16

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 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 £188.45 and £44.30, 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.

The data that were assessed remain commercially confidential.*

Summary of evidence on comparative safety

No new adverse effects were identified for esomeprazole in the studies for this indication.

Summary of clinical effectiveness issues

In a pooled analysis of the trials described previously the majority of the patients (71%) were receiving treatment with non-selective NSAID, with the remaining patients receiving a 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 therefore no evidence that esomeprazole would have any advantages in clinical practice over the other PPIs, omeprazole, pantoprazole and lansoprazole, which could be used within their current licences, for the prevention of gastro-duodenal ulcers associated with COX-2 selective NSAIDs.

Esomeprazole has not been directly compared with any other PPIs, histamine H_2 antagonist or prostaglandin analogue for prevention of gastro-duodenal ulcers. 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's 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 at high risk (previous ulceration) and for whom NSAID continuation is necessary, offering gastric protection or considering substitution to a COX-2 selective NSAID. It is noted that in patients using NSAIDs without peptic ulcer disease, double-dose histamine H_2 antagonist therapy or proton pump inhibitors significantly reduce the incidence of endoscopically detected lesions; misoprostol at low dose is less effective than proton pump inhibitors at reducing the incidence of endoscopically detected lesions, and has greater side-effects. 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 December 2000 Scottish Intercollegiate Guidelines Network (SIGN) guideline number 48 on the management of early arthritis, currently under review, noted that gastroprotective agents may be used for patients at risk of NSAID-associated gastroduodenal ulcers who require treatment with NSAIDs. Gastroprotection should be given to patients aged >65 years and those with a history of peptic ulceration. It is noted that the proton pump inhibitors are the most effective gastroprotective agents, with prostaglandin analogues being effective but less well tolerated than proton pump inhibitors and potentially associated with problems in premenopausal women. The histamine H2 antagonists and mucosal protective agents (e.g. sucralfate) are noted to be less effective than proton pump inhibitors.

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.

Schieman JM, Yeomans ND, Talley NJ et al. Prevention of ulcers by esomeprazole in at-risk patients using non-selective NSAIDs and COX-2 inhibitors. Am J Gastroenterol (in press)