Esomeprazole 20 mg on-demand is more acceptable to patients than continuous lansoprazole 15 mg in the long-term maintenance of endoscopy-negative gastro-oesophageal reflux patients: the COMMAND study


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared the use of esomeprazole 20 mg "on-demand" (Nexium; AstraZeneca) versus continuous (over a 6-month period) treatment with lansoprazole 15 mg once daily (Zoton Capsules; Wyeth). Esomeprazole is the s-isomer of omeprazole, a proton-pump inhibitor (PPI) licensed for on-demand use in patients with endoscopy-negative gastro-oesophageal reflux disease (GERD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with heartburn as the main symptom of GERD for at least 4 of the 7 days before enrolment were eligible to enter the study. Patients also had to meet other inclusion criteria. More specifically, a history of heartburn for at least 6 months and no oesophageal mucosal breaks (documented by endoscopy) for up to 14 days before enrolment.

Patients who had used a PPI for more than 10 days during the last 28 days before entry were not eligible to enter the study. Also not eligible were those who required continuous concomitant therapy with anticholinergics, cisapride, prostaglandin analogues, non-steroidal anti-inflammatory drugs or salicylates (>165 mg daily), and those with symptoms caused by a structural, metabolic or pathological gut disorder.

Setting
The setting was primary care (general practices) and secondary care (hospitals). The economic study was carried out in the UK.

Dates to which data relate
The exact dates to which the effectiveness data related were not reported. It was reported that the analysis was carried out in June 2002. In addition, 2002 price were used in the economic analysis.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although not explicitly reported, it seems that the costing has been carried out retrospectively on the same sample of
patients as that used in the economic analysis.

**Study sample**
Power calculations showed that a sample of at least 287 patients in each of the active treatment groups was required to detect a true difference of 10%, with a power of 90%, at the 5% significance level. Considering that 60% of patients would have complete resolution of heartburn after the acute phase, the authors concluded that a sample of 957 patients was necessary to arrive at a total of 554 randomised patients. The method used to select the sample was not explicitly reported.

Initially, 774 patients were enrolled into the acute phase and were treated with esomeprazole (20 mg once daily) for 2 or 4 weeks. Of these, 152 were excluded from the study and did not continue onto the maintenance phase (i.e. esomeprazole 20 mg on-demand or continuous lansoprazole 15 mg once daily for 6 months). Reasons for exclusion were adverse events (18) and eligibility/randomisation criteria not met (124). Ten were excluded without a provided justification. Overall, 622 patients were randomised into the maintenance phase, with 311 receiving esomeprazole and 311 lansoprazole. A total of 542 (87%) patients eventually completed the study, while the rest refused to continue.

**Study design**
The analysis was based on a multi-centre, single-blind (investigator), randomised, parallel-group study. The study was carried out in 92 general practices and 28 hospitals in the UK. Patients in the acute phase were followed up for 2 and/or 4 weeks. Those entering the maintenance phase were followed up for 6 months with scheduled meetings at the first, third and sixth month. Patients were randomised one to one (1:1) into the two groups, but the method of randomisation was not reported. The investigators were blinded to the intervention, but not the patients.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary outcome was the time to discontinuation from the maintenance phase, owing to unwillingness to continue. The patients were divided into three sub-groups at analysis, according to the degree of heartburn, time to symptom relief during the acute phase and Helicobacter pylori status. The secondary outcomes included time to discontinuation due to insufficient control of heartburn, patients' satisfaction with maintenance treatment, and symptom assessment after 1, 3 and 6 months' maintenance treatment. The analysis demonstrated that the patients group were comparable at baseline in terms of their GERD and demographic characteristics.

**Effectiveness results**
When comparing survival estimates of discontinuation, time to discontinuation from the maintenance phase was significantly longer for patients in the esomeprazole group than for those in the lansoprazole group, (p=0.001). At the end of the follow-up period (6 months), 13% (95% confidence interval, CI: 9.2 - 16.8) of patients in the continuous lansoprazole group were unwilling to continue, compared with 6% (95% CI: 2.8 - 8.8) in the esomeprazole on-demand group, (p=0.001).

After 1 month of maintenance therapy, 93.2% of the patients in the esomeprazole group were satisfied with their treatment, compared with 87.8% in the lansoprazole group, (p=0.02; estimate of difference 5.5, 95% CI: 0.88 - 10.1). Satisfaction with treatment remained higher in the esomeprazole group in the third and sixth months of treatment.

During maintenance therapy, the mean frequency of heartburn symptoms was higher in the esomeprazole group than in the lansoprazole group (quantitative results were not reported). However, the authors reported that at the end of the follow-up period, more than 85% of the patients reported no or only mild symptoms during the previous 7 days.

Both treatments were characterised as being well-tolerated by the patients. Adverse events were reported by 327 patients (42%) during the acute phase and by 443 patients (71%) during the maintenance phase. There were no statistical differences between the two treatment groups. It is notable that 18 patients discontinued treatment due to adverse events in the acute phase, 10 (3%) from the esomeprazole group and 30 (10%) from the lansoprazole group.
The laboratory test profiles were found to be similar between the two groups. No significant changes were detected during the study period.

Clinical conclusions
The authors concluded that in patients with endoscopy-negative GERD, more are satisfied with on-demand treatment with esomeprazole 20 mg than with continuous treatment with lansoprazole 15 mg daily.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of benefit in the economic analysis. In effect, a cost-consequences analysis was performed.

Direct costs
Only the costs of the drugs were included in the analysis. The costs and the quantities were not analysed separately. The quantities were estimated using data derived from the effectiveness study, whereas the source of the cost data was not reported. All the costs were reported for the year 2002. Discounting was not relevant, as the costs were incurred during less than 2 years, and was not conducted.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
UK pounds sterling (£).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The costs per patient were reported. The mean medication cost was 35.80 per patient in the esomeprazole group, and 56.20 in the lansoprazole group when the actual usage of 0.8 capsules per day was considered and 73.50 per patient when licensed usage (i.e. 1 capsule per day) was considered.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Esomeprazole 20 mg on-demand is more acceptable to patients with endoscopy-negative gastro-oesophageal reflux disease (GERD), and a more cost-effective option than continuous treatment with lansoprazole 15 mg once daily.
CRD COMMENTARY - Selection of comparators
The authors provided justification for the choice of the on-demand treatment with esomeprazole 20 mg. However, it was unclear why lansoprazole 15 mg daily continuously was chosen as the comparator. It is possible that it represented standard practice in the authors’ setting. You should decide if this represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a single-blind, randomised parallel-group study, which was appropriate given the study question. The study sample was representative of the study population and the patient groups were shown to be comparable at analysis. Although the method of randomisation was not explicitly reported, the reporting of the blinding method, length of study, loss to follow-up and drop-out rates suggests that the internal validity of the study is likely to be good. An appropriate statistical analysis was undertaken to take potential biases and confounding factors into consideration. In addition, power calculations were reported and the appropriate sample size was used.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit. The reader is referred to the comments in the ‘Validity of estimate of measure of effectiveness’ field (above).

Validity of estimate of costs
The perspective adopted was not reported, but it was not societal since the indirect costs were not included; only the drug costs were included. The unit costs were not reported, thus impeding the reproducibility of the study to other settings, nor was the source of the cost data. The costs were treated deterministically, and no sensitivity analysis was conducted to assess the robustness of the estimates used. The quantities were most probably derived directly from the effectiveness study, but no statistical analysis of the quantities was performed. The price year was reported. The inadequate cost analysis limits the interpretation of the study findings.

Other issues
The authors compared their findings with those from other studies and found them to be consistent. The issue of generalisability of the results to other settings was not directly addressed. The authors presented their results selectively by emphasising results that favoured esomeprazole (e.g. they only provided quantitative data for those results that favoured esomeprazole). In addition, in the ‘Discussion’ section, the costs of lansoprazole were reported to be higher than the costs reported in the main part of the study for the same treatment. The study enrolled adult patients with endoscopy-negative GERD and this was reflected in the authors’ conclusions. The authors acknowledged the restricted cost analysis as one of the limitations of their study.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice, nor did they recommend specific areas for further research. However, the analysis, especially the economic analysis, highlighted areas where more information is needed.

Source of funding
Supported by a grant from AstraZeneca UK Ltd, Luton, UK.

Bibliographic details