Economic evaluation of tegaserod vs placebo in the treatment of patients with irritable bowel syndrome: an analysis of the TENOR study

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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 tegaserod (6 mg twice daily) with placebo for the treatment of irritable bowel syndrome (IBS). Tegaserod, a 5-HT4 receptor partial agonist and promotility agent, addresses the multiple symptoms of IBS with constipation.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with IBS with constipation. Patients under medication with an impact of gastrointestinal motility and/or visceral perception, those who took antiflatulence agents, opioids or narcotic analgesics, prokinetics, anticholinergics, antispasmodics or antidepressants were excluded from the study, unless the treatments were received at stable doses for indications other than IBS and had been taken for a minimum of 3 months before the initiation of the study. For further inclusion and exclusion criteria the reader is referred to the parent clinical trial used by the authors, namely the TENOR study (Nyhlin et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details).

Setting
The setting was the community. Although it was unclear in the paper, the economic study appear to have been carried out in Sweden.

Dates to which data relate
The dates relating to the effectiveness and resource use data were not explicitly reported. For relevant details the reader is referred to the parent clinical trial (Nyhlin et al. 2004). The price year was not reported.

Link between effectiveness and cost data
The costing appears to have been undertaken prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The authors reported limited details on the study sample in the current paper. For relevant details the reader is referred to the parent clinical trial (Nyhlin et al. 2004). It was reported that, overall, a final sample of 647 patients were randomised either to receive tegaserod (n=327) or placebo (n=320).
Study design
The analysis was based on a multinational, multi-centre, double-blind, randomised, placebo-controlled clinical trial. Details on the randomization and blinding method, and the follow-up of patients were not reported in the current paper.

Analysis of effectiveness
It was not reported in the current paper whether the analysis was conducted on an intention to treat basis or on treatment completers only. In addition, the primary clinical outcomes were not reported in this paper.

Effectiveness results
The primary clinical outcomes were not reported in the current paper. The authors only reported that the average length of treatment was 73.1 days in the tegaserod group and 77.0 days in the placebo group. Utilities were derived and reported (see 'Measure of Benefit' section).

Clinical conclusions
Based on the results of the parent clinical trial and of other clinical studies in the literature, the authors concluded that tegaserod is the only effective and well-tolerated treatment for abdominal pain, bloating and constipation for IBS patients without diarrhoea.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). Using the EuroQol EQ-5D questionnaire, patients’ values were evaluated at baseline, after 4 and 12 weeks, or at discontinuation of treatment. A sub-sample of the TENOR trials was used for the valuation of the utilities, namely 485 (75%) out of 644 patients. Of these, 247 patients were from the tegaserod group and 238 from the placebo group. It was reported that the sub-sample of patients was comparable, in terms of the baseline clinical characteristics, with the total trial population. As the average utilities in the tegaserod and placebo groups differed at baseline, the authors controlled for the difference using an analysis of covariance. Missing data due to study drop-outs and non-completion of the EuroQol EQ-5D questionnaire were handled using the last-observation-carried-forward method (LOCF).

Direct costs
Only tegaserod treatment costs were accounted for in the analysis. Tegaserod costs were based on Swiss data (public price at the time of the study). The average number of treatment days was derived from the parent clinical trial and estimates were reported. Patient visit costs and other direct health care costs were not included in the analysis. Discounting was not relevant. The price year was not reported.

Statistical analysis of costs
The data were treated deterministically.

Indirect Costs
Inline with the perspective adopted, productivity costs were not included in the analysis.

Currency
Euros (EUR).

Sensitivity analysis
The issue of uncertainty was investigated by generating 2,000 bootstrapped replications of the incremental cost-

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effectiveness ratios (ICERs). For each of the 2,000 iterations, costs and QALYs were used separately for patients in the treatment and placebo groups, and a bootstrap estimate of the average QALY gain and average cost was estimated for each group. ICERs were calculated and cost-effectiveness acceptability curves were generated. A conventional sensitivity analysis was also performed to explore the robustness of the results to using unadjusted baseline EQ-5D utility scores and to variations in treatment costs. Separate analyses were conducted for men and women. Finally, a separate analysis was performed including only those utilities with complete utility measurements (i.e. excluding utilities that were extrapolated using the LOCF method).

**Estimated benefits used in the economic analysis**
Incremental results were reported. With adjusted utilities, tegaserod compared with placebo resulted in 0.0077 incremental QALYs.

**Cost results**
At baseline (daily tegaserod cost of EUR 2), the average cost in the treatment group was EUR 146.3.

**Synthesis of costs and benefits**
An incremental cost-effectiveness analysis was performed. At baseline cost estimates, the incremental cost per QALY gained with tegaserod over placebo was EUR 19,000.

When the cost was raised to EUR 3 and EUR 4, the incremental cost per QALY gained increased to EUR 28,500 and EUR 38,000, respectively.

Using a threshold value of EUR 50,000 per QALY gained, the probability that tegaserod was cost-effective was 90% (daily treatment cost EUR 2).

The respective probability fell to 81% and 69% when the daily treatment costs were raised to EUR 3 and EUR 4, respectively.

The sensitivity analysis demonstrated that, when unadjusted utilities were used, the probability that tegaserod was cost-effective within the same threshold was 98%, 95% and 90% at daily treatment costs of EUR 2, EUR 3 and EUR 4 respectively. When only women were accounted for in the analysis, the ICERs ranged from EUR 20,700 to EUR 41,400 for the different treatment costs. When only men were accounted for in the analysis, the ICERs ranged from EUR 12,800 to EUR 25,600, respectively. The exclusion of the LOCF utilities did not have a significant impact on the results.

**Authors’ conclusions**
Tegaserod treatment is a cost-effective option for patients with irritable bowel syndrome (IBS).

**CRD COMMENTARY - Selection of comparators**
The authors used placebo as a comparator for the intervention drug. This allowed the active value of the treatment to be evaluated. In addition, it was reported that there were no alternative agents for the treatment of IBS with constipation. You should decide if this is a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis was based on a clinical trial, which was appropriate for the study question. The randomised nature of the study and the multi-centre design enhance the validity of the analysis. However, as the study had been published elsewhere, little information on the methods of the study trial was reported in the present paper, making it difficult to comment on the internal validity of the study.

**Validity of estimate of measure of benefit**
The general summary benefit measure (QALYs) was appropriate since it allows more general comparisons. Extensive details of the methods used to derive the measure of benefit were reported.

Validity of estimate of costs
It was reported that the third-party payer perspective was adopted in the economic analysis. However, the authors only included tegaserod treatment costs, while patients' visits and further direct and indirect costs were omitted. No justification for the omission of these costs was provided. The authors acknowledged that the omission of these costs might have resulted in an underestimation of the cost-effectiveness of the intervention therapy. Uncertainty in treatment costs was investigated in the sensitivity analysis, but no justification was provided for the ranges over which the costs were varied. The authors also evaluated uncertainty in the cost data jointly with the effectiveness data by bootstrapping to produce a cost-effectiveness acceptability curve. The price year was not reported, thus limiting the possibility of performing relflation exercises in other time periods.

Other issues
The authors did not compare their results with those of previous studies; however, this was unavoidable given the lack of economic evaluations in the same research area. They also do not appear to have presented their results selectively. As the authors did not provide extensive details of their study sample, it is unclear whether their conclusions reflected their scope of analysis. Their conclusions were generalised across all IBS patients and not just IBS patients with constipation, although it is not clear that this generalisation was appropriate. The authors reported a number of limitations to their study and attempted to address the issue of the potential impact of these on the findings.

Implications of the study
The authors did not make recommendations for changes in policy or practice. For an accurate analysis they recommended that the costs and effects of the treatment should be evaluated over a longer time horizon.

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Other publications of related interest
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Subject indexing assigned by NLM

MeSH
Adult; Cost-Benefit Analysis; Female; Health Care Costs; Humans; Indoles /economics; Irritable Bowel Syndrome /drug