The cost-effectiveness of bosentan in the United Kingdom for patients with pulmonary arterial hypertension of WHO functional class III
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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.

CRD summary
This study examined the cost-effectiveness of bosentan in comparison with no active intervention, as first-line treatment of idiopathic pulmonary arterial hypertension or pulmonary arterial hypertension associated with connective tissue disease, of World Health Organization functional class III. The authors concluded that bosentan was a cost-effective treatment from the perspective of the UK National Health Service. The study was generally well conducted and the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of bosentan, compared with no active intervention, as first-line treatment for idiopathic pulmonary arterial hypertension or pulmonary arterial hypertension associated with connective tissue disease, of World Health Organization functional class III.

Interventions
Bosentan added to palliative care (diuretics, warfarin, and calcium antagonists) was compared with palliative care alone. Patients on bosentan could switch to epoprostenol and palliative care, if there was deterioration in functional class at 12 weeks. Patients on palliative care alone were also assumed to move to epoprostenol and palliative care on deterioration.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The analysis was based on a mathematical model with a lifetime horizon. The authors stated that the perspective of the UK National Health Service (NHS) was adopted.

Effectiveness data:
The clinical data came from a selection of known, relevant studies. The efficacy and safety of bosentan over palliative care were derived from two pivotal, double-blind, placebo, randomised controlled trials (RCTs). The long-term data were from open-label extensions of these trials and other published sources. Time until clinical deterioration was the key endpoint. In the base case it was assumed that there was no survival advantage with bosentan over palliative care.

Monetary benefit and utility valuations:
The utility values were derived from a published study that used the Short Form (SF-36) health survey.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the costs of drugs and home delivery. Drug costs were based on average wholesale
prices. Resource quantities and other items were from two specialist pulmonary arterial hypertension centres. All costs were in UK pounds sterling (£) and were discounted at 3.5% per annum. They referred to 2006 to 2007 prices.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken on the key model inputs, using published confidence intervals. A scenario analysis removed the assumption that all patients had the same survival duration irrespective of treatment duration.

Results
In patients with idiopathic pulmonary arterial hypertension, the costs were £134,000 and the QALYs were 3.32 with bosentan, and the costs were £203,000 and QALYs were 2.95 with palliative care.

In patients with pulmonary arterial hypertension from connective tissue disease, the costs were £62,000 and QALYs were 1.36 with bosentan, and the costs were £94,000 and QALYs were 1.21 with palliative care.

Bosentan was the dominant strategy, as it was more effective and less expensive, in both patient populations.

The incremental cost per QALY gained with bosentan was £30,000 or more, when the survival benefit from bosentan treatment was increased to over two years for patients with idiopathic pulmonary arterial hypertension and when it approached one year for patients with pulmonary arterial hypertension from connective tissue disease. This was due to the increased costs associated with longer survival in the bosentan group.

Authors’ conclusions
The authors concluded that bosentan was a cost-effective treatment from the perspective of the UK health care system.

CRD commentary
Interventions:
The authors justified their selection of the interventions by stating that palliative care was the conventional approach until the launch of bosentan. The selection of the comparators was appropriate. The authors stated that other active treatments, such as sildenafil, sitaxsentan, and ambrisentan, should have been included, but they were not able to do so due to a lack of relevant data.

Effectiveness/benefits:
The analysis of effectiveness was based on selected sources of data. Most of the evidence was from RCTs, which are valid sources given the strengths of their methods. Limited information on these sources was provided, but they appear to have been appropriately selected as the few trials available on this treatment. Little information on the derivation of the utility values was provided. QALYs are a valid benefit measure, given the impact of the disease on quality of life and survival.

Costs:
The categories of costs were consistent with the economic viewpoint. It was assumed that no difference in hospitalisation was associated with functional classes and so hospitalisation costs were excluded. The inclusion of these costs could have further favoured bosentan. The unit costs and resource quantities were not presented separately. Official drug prices were used to estimate these costs. The patterns of resource use appeared to reflect actual drug consumption in medical centres. The price year was reported, which will allow reflation exercises for other time periods.

Analysis and results:
An appropriate incremental analysis was performed and the expected costs and benefits of the two strategies were reported. Conventional discounting for both benefits and costs was applied. The issue of uncertainty was appropriately investigated in a probabilistic analysis, which focused on the most uncertain inputs to the model. The analysis was based on a key assumption that no survival advantage was associated with bosentan, but this was removed in the sensitivity analysis, which showed the importance of this model driver.
Concluding remarks:
The study was generally well conducted and the authors’ conclusions appear to be valid.

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