Cost effectiveness of deferasirox compared to desferrioxamine in the treatment of iron overload in lower-risk, transfusion-dependent myelodysplastic syndrome patients
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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 deferasirox compared with non-proprietary desferrioxamine for the control of transfusion-related iron overload in lower risk patients with myelodysplastic syndrome. The authors concluded that deferasirox was a cost-effective treatment in these transfusion-dependent patients. The cost-effectiveness framework was conventional and should have ensured the validity of the authors’ conclusions, but these were based on a key assumption for clinical efficacy.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of deferasirox compared with non-proprietary desferrioxamine (deferoxamine) for the control of transfusion-related iron overload in lower risk patients with myelodysplastic syndrome.

Interventions
The two interventions were once daily oral deferasirox (20mg per kg per day) versus slow subcutaneous infusion, over eight to 12 hours, of desferrioxamine (40mg per kg per day, for five days per week). Patients were assumed to continue therapy until death or the occurrence of acute myeloid leukaemia.

Location/setting
UK/out-patient setting.

Methods
Analytical approach:
The analysis was based on a Markov model with a lifetime horizon (20 years). The authors stated that the perspective of the UK NHS was adopted.

Effectiveness data:
Some of the clinical data on survival associated with iron chelation therapy, both with desferrioxamine and deferasirox, were from a large observational study (n=165 regularly transfused patients). The risk of disease progression was from the retrospective analysis of 178 patients at a large Canadian hospital. Additional data were from published studies. A key assumption of the model was that the clinical outcomes (efficacy and compliance) were the same between treatment arms. This was assumed because there were no head-to-head studies between desferrioxamine and deferasirox. The impact of treatment-related complications was a key input for the model.

Monetary benefit and utility valuations:
The utility values were derived from a published study that used a time trade-off method, with a sample of the UK general public, to elicit the utilities for iron chelation therapy provided orally once daily or as a slow subcutaneous infusion. The utility decrements associated with therapy complications were from the Beaver Dam Health Outcomes study (a longitudinal study of health-related quality of life in a random sample cohort of 1,356 US adults). The utility decrements for acute myeloid leukaemia were from a published study that used the Health Utilities Index 2.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3.5%. Survival and iron chelation therapy complications were reported.

Cost data:
The economic analysis included the drug costs (acquisition and administration), monitoring (blood tests), and treatment of acute myeloid leukaemia, complications, and blood transfusions. The drug costs were from the British National Formulary. The cost of the administration of deferasirox was from a published economic evaluation. The costs of acute myeloid leukaemia were from a US study and included treatment, hospitalisation, blood transfusion, and other related medical costs. Other costs were from official price lists, NHS reference costs, and published studies. Most of the resource quantities were based on published studies. All costs were in UK pounds sterling (£) and were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on those inputs affecting the drug-related costs, such as patient weight, average daily dose, days per week of treatment with deferasirox, and deferasirox administration costs. The proportion of deferasirox patients who used a balloon infuser or a battery-operated pump for the subcutaneous infusion was varied. The utility values, compliance rates, and monitoring costs were analysed.

Results
In a cohort of 1,000 patients, the total costs were £195,244 with deferasirox and £173,744 with desferrioxamine. The QALYs were 5.02 with deferasirox and 3.98 with desferrioxamine. The incremental cost per QALY gained with deferasirox was £20,822. The two treatments had the same survival rate and rate of complications; the difference in QALYs was due to the method of administration (deferasirox was more convenient for patients).

The dose of deferasirox was an influential input: a lower average daily dose of 15mg per kg per day led to deferasirox being dominant (more effective and less expensive than desferrioxamine), while at higher doses of 25mg per kg per day, the incremental cost per QALY gained rose to over $40,000. Changes in the other inputs did not substantially alter the base-case findings.

Authors’ conclusions
The authors concluded that deferasirox was a cost-effective treatment in lower risk, transfusion-dependent, patients with myelodysplastic syndrome.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. Desferrioxamine was the primary treatment in UK clinical practice for the patient population. Oral deferasirox had the advantage of overcoming the problematic administration of parenteral desferrioxamine. The authors stated that another treatment, deferiprone, was available, but was not licensed for myelodysplastic syndrome and was not considered as a relevant comparator. Conventional dosages were considered, but the authors pointed out that there was limited information available on the desferrioxamine dosage.

Effectiveness/benefits:
No systematic review was reported to identify the relevant data sources, the key methods of which were provided. In general, no randomised study was available and most of the data were from prospective or retrospective comparative studies. These designs are limited, leaving them open to selection bias. A key assumption was the equal efficacy and compliance for desferrioxamine and deferasirox. This was based on the results for β-thalassaemia patients, as there were no head-to-head studies for myelodysplastic syndrome. This was an important assumption and it should have been tested in the sensitivity analysis. QALYs were an appropriate benefit measure because of the mortality and quality-of-life implications of iron overload in these patients. The utility valuations were appropriately reported and valid sources and instruments appear to have been used.

Costs:
The cost categories were consistent with the perspective of the public payer. Most of the data sources reflected
conventional NHS prices. Some costs were from published reports and the accounting approach and other methods of these reports were not stated. The unit costs were reported for some items. The cost calculations were transparently reported for the drugs, while less clear information on the quantities of resources was provided for the other costs. The price year was not explicitly reported, but most of the data were adjusted to the years 2008 or 2009. The costs and resource use were extensively varied in the sensitivity analysis.

Analysis and results:
The results were clearly presented, with both total and incremental findings, and the undiscounted results for the projected benefits of the two treatments. The uncertainty was investigated, using a deterministic approach, which considered variations in individual inputs one at a time. The variation of the inputs simultaneously, as well as in alternative scenarios, would have been helpful. Conventional discounting was applied to both the costs and benefits. The authors acknowledged that the main limitation of their study was the lack of head-to-head randomised clinical trials for the two treatments, and they stated that future trials were needed to corroborate their findings.

Concluding remarks:
The cost-effectiveness framework was conventional and should have ensured the validity of the authors’ conclusions, but these were based on a key assumption for clinical efficacy.

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