INAHTA Briefs

Issue 2006/94

Title **Clinical Effectiveness and Cost-Effectiveness of Drotrecogin Alfa (activated) (Xigris) for the Treatment of Severe Sepsis in Adults: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

Reference Health Technol Assess 2005;9(11). March 2005. www.hta.ac.uk/execsumm/summ911.htm

Aim

To assess the clinical and cost-effectiveness of drotrecogin alfa (activated) in treating adults with severe sepsis in a UK context.

Conclusions and results

The evidence came primarily from the PROWESS randomized controlled trial, which showed a statistically significant absolute reduction in 28-day mortality of 6.5%. Longer term survival benefit was maintained to 90 days. By 9 months, the trend toward increased median survival was nonsignificant, although the survival curves did not cross. Results presented by the number of organ dysfunctions were not statistically significant, but when mortality rates for those with two or more organ failures were combined, the relative risk of death was significantly lower in those treated with drotrecogin alfa (activated) compared with placebo. Cost-effectiveness studies of drotrecogin alfa (activated) treatment have used various methods to estimate benefits, estimating an incremental gain per treated patient (with severe sepsis) of 0.38 to 0.68 life-years. For patients with severe sepsis and multiple organ dysfunction, the manufacturer estimated an incremental gain of 1.115 life-years per treated patient, compared to 1.351 life-years estimated by the Southampton Health Technology Assessments Centre (SHTAC). Three cost-effectiveness studies in US and Canadian patient groups report that additional costs per patient treated range from USD 10 000 to 16 000 for patients with severe sepsis. Using 28-day survival data in patients with severe sepsis and multiple organ dysfunction, the manufacturer estimates an additional mean cost of GBP 5106 per treated patient. An analysis of UK patients with severe sepsis and multiple organ dysfunction estimates an additional mean cost of GBP 6661 per patient treated. The manufacturer's cost-effectiveness estimate for drotrecogin alfa (activated) in UK patients with severe sepsis and multiple organ dysfunction showed GBP 6637 per quality-adjusted life-year (QALY) based on 28-day effectiveness data, and GBP 10 937 per QALY based on longer term followup data. SHTAC developed an independent cost-effectiveness model and estimated a base-case cost per QALY of GBP 8228 in patients with severe sepsis and multiple organ failure (28-day survival data). Simulation results indicate that where the NHS is willing to pay GBP 20 000 per QALY, drotrecogin alfa (activated) is cost effective in 98.7% of cases.

Recommendations

For severe sepsis and severe sepsis with multiple organ failure in a UK context, drotrecogin alfa (activated) plus best supportive care is likely to be considered clinically and cost effective compared to best supportive care alone. Introducing drotrecogin alfa (activated) will add substantial costs to the NHS. Up to 16 570 patients could be eligible for treatment in England and Wales, with an estimated annual drug acquisition cost of over GBP 80 million, excluding VAT.

Methods

A systematic review of the literature and an economic evaluation were undertaken. Data were synthesized through a narrative review with full tabulation of results from included studies.

Further research/reviews required

Further research is required on the longer term impact of drotrecogin alfa (activated) on mortality and morbidity in UK patients with severe sepsis, on the clinical and cost effectiveness of drotrecogin alfa (activated) in children (under 18 years) with severe sepsis, and on the effect of the timing of dosage and duration of treatment on outcomes in severe sepsis.

Written by Mr Colin Green, SHTAC, Wessex Institute for Health R&D, United Kingdom

ISSN 1654-501X