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Title **A Systematic Review and Economic Evaluation of Epoetin Alfa, Epoetin Beta, and Darbepoetin Alfa in Anemia Associated with Cancer, Especially that Attributable to Cancer Treatment**

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

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Aim

To assess the effectiveness and cost effectiveness of epoetin alfa, epoetin beta, and darbepoetin alfa (referred to collectively here as epo) in anemia associated with cancer, especially that attributable to cancer treatment.

Conclusions and results

Forty-six RCTs were included that compared epo + supportive care for anemia with supportive care for anemia alone. Hematological response (HR), defined as an improvement by 2 g dl–1, had a relative risk of 3.4 with a response rate for epo of 53%. Hemoglobin (Hb) change showed a weighted mean difference of 1.63 g dl–1 in favor of epo. Erythropoietin treatment in patients with cancer-induced anemia reduces the number of patients who receive a red blood cell transfusion (RBCT) by an estimated 18%. A positive effect was observed in favor of an improved HRQoL for patients on epo. Published information on side effects was of poor quality. The previous Cochrane review had suggested a survival advantage for epo, HR 0.84 based on 19 RCTs. The update, based on 28 RCTs, suggests no difference. Although it is difficult to draw firm conclusions, the conclusions are broadly in line with those of a Food and Drug Administration (FDA) safety briefing (recommended, eg, that patients with Hb above 12 g dl–1 should not be treated and the target rate of rise in Hb should not be too great). Five economic evaluations from the literature showed inconsistent results, with estimates ranging from a cost per QALY under GBP 10 000 through to epo being less effective and more costly than standard care.

Recommendations

Epo is effective in improving hematological response and RBCT requirements, and appears to have a positive effect on HRQoL. The incidence of side effects and effects on survival remains highly uncertain. If there is no impact on survival, it seems unlikely that epo would be considered a cost-effective use of healthcare resources.

Methods

Using a recently published Cochrane review as the starting point, a systematic review of recent RCTs comparing epo with best standard was conducted. MEDLINE, EMBASE, the Cochrane Library, and other databases were searched from 2000 (1996 in the case of darbepoetin alfa) to September 2004. Inclusion, quality assessment, and data abstraction were undertaken in duplicate. Where possible, meta-analysis was employed. Economic assessment consisted of a systematic review of past evaluations, assessment of economic models submitted by manufacturers of the 3 epo agents, and development of a new individual sampling model (Birmingham epo model).

Further research/reviews required

Further research should focus on improving estimates of impact on survival, starting with more detailed secondary research, eg, the individual patient data meta-analysis started by the Cochrane group. Further trials may be required, eg, as recommended by the FDA. The Birmingham epo model developed as part of this project has features that are not present in previous models. These features improve its flexibility in exploring different scenarios in the future. Research to resolve uncertainty about other parameters, particularly quality of life and adverse events, should be pursued in parallel with attempts to improve evidence on survival. The rate of normalization was also an important parameter in the model for which no published data source was identified. Hence, further research in this area would be beneficial.

Written by Ms Jayne Wilson, University of Birmingham, United Kingdom

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