TITLE: Eculizumab for Paroxysmal Nocturnal Hemoglobinuria: A Review of Clinical and Cost-Effectiveness

DATE: 25 November 2008

CONTEXT AND POLICY ISSUES:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired stem cell disorder, characterized by complement-related intravascular hemolysis, marrow failure, and a thrombotic tendency.\(^1-3\) This pathogenesis significantly affects patient’s quality of life, with thrombosis being the leading cause of premature mortality.\(^4\) Until recently, there has been no specific therapy for PNH with clinical management largely symptomatic in terms of anemia and control of thrombotic risk.\(^5,6\)

The development of eculizumab, a monoclonal antibody to the C5 complement protein,\(^7-9\) which received accelerated approval by the US Food and Drug Administration in 2007,\(^10\) raises hope as well as safety concerns in the treatment of patients with PNH.\(^11,12\)

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of eculizumab for the treatment of paroxysmal nocturnal hemoglobinuria?
2. What is the cost-effectiveness of eculizumab for the treatment of paroxysmal nocturnal hemoglobinuria?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including OVID MedLine, OVID Embase, The Cochrane Library (Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include articles published between 2003 and November 2008, and are limited to English language publications only. No filters were applied to limit the retrieval by study type.

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SUMMARY OF FINDINGS:

Clinical effectiveness of eculizumab

Our literature search identified one systematic review on the clinical and cost-effectiveness of eculizumab for the treatment of PNH, with literature search covering up to November 2007. No other systematic reviews or randomized controlled trials were found.

The systematic review included five trials, of which one is a randomized, placebo-controlled trial, and four are prospective, non-placebo controlled studies. The systematic review is qualitative and did not pool data from the five trials, which showed agreement in their conclusions in terms of the effectiveness of eculizumab. The RCT that was included in the systematic review included 87 patients with a 26-week follow-up period. Data showed eculizumab reduced transfusion requirements and anemia. Forty-nine percent of the treatment group but 0% of the placebo group remained independent of red blood cell transfusion (p<0.001) and mean unit-transfused/26 weeks pretreatment (i.e., at baseline) was reduced by 70% with eculizumab but remained unchanged with placebo (p<0.001). The same trial found eculizumab reduced intravascular hemolysis, as shown by a statistically significant reduction in lactate dehydrogenase levels in the treatment group. Clinically significant improvements were also found in the patients’ quality of life.

Cost-effectiveness of eculizumab

Our literature search did not identify any economic analysis of PNH treatments, but the systematic review conducted a primary economic analysis. The preliminary economic evaluations suggested that the incremental cost-effectiveness ratio (ICER) for eculizumab versus standard care lies between £0.5M and £1.4M per life year gained for patients like those recruited to clinical trials, and between £2.8M and £3.2M per life year gained for all diagnosed patients. The budget impact is based on prevalence (1.59/100,000) and annual incidence estimates (0.13/100,000) of PNH, and assuming between 16% and 33% of PNH patients are treated with eculizumab. Annual savings from standard care cost-avoided ranges from £1K to £10K/patient. The budget impact for the studied population (5.5M) is estimated between £3.3M and £7.0M in year one and £9.5M to £15.3M by year 10.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The limited evidence that was identified suggests eculizumab is more effective than standard care in the treatment of PNH. Newer treatment modalities, such as addition of erythropoietin treatment following complement inhibition with eculizumab in patients with PNH could further enhance patients’ outcomes. Considering a conventional threshold of US$50,000 per ICER, eculizumab may not be deemed cost-effective despite a substantial budget impact that the use of eculizumab could provide to health care. These factors as well as the lack of other treatment options should be taken into account when deciding on the use of eculizumab for PNH.

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