An Economic Evaluation of Eculizumab (Soliris®) for the treatment of Paroxysmal Noctural Haemoglobinuria (PNH) in the Irish Healthcare Setting

National Centre for Pharmacoeconomics
St. James's Hospital
Dublin 8
Ireland

March 2010

Summary

1. On the 29th October 2009 the National Centre for Pharmacoeconomics (NCPE) received a request from the HSE-Corporate Pharmaceutical Unit (CPU) to conduct a pharmacoeconomic assessment of the product eculizumab (soliris®). The manufacturer, Alexion Pharma UK Ltd submitted documentation to support the reimbursement of eculizumab under the High Tech Drugs scheme on the 20th January 2010. Additional information was requested by the NCPE on 22nd January 2010.

2. Eculizumab (soliris®) is a humanized monoclonal antibody that blocks the activation of terminal complement at C5 and prevents the formation of C5a and the terminal complement complex C5b-9. It is indicated for the treatment of patients with paroxysmal noctural haemoglobinuria (PNH).

3. Alexion Pharma UK Ltd did not undertake a formal cost-effectiveness analysis to support the reimbursement of eculizumab under the High Tech Drugs scheme. The submission did provide an overview of the clinical evidence for the efficacy of eculizumab. The only double-blind, randomised, placebo controlled trial was the "TRIUMPH" study where 87 patients were enrolled in the 26 week trial. Stabilisation of haemoglobin levels in the absence of transfusions was achieved in 49% of the patients assigned to eculizumab and none of those assigned to placebo. Eculizumab reduced intravascular haemolysis and improved patients quality of life.

4. The "SHEPHERD" study was an open label non placebo controlled 52 week phase III trial where 97 patients were enrolled. The primary efficacy endpoint was haemolysis as assessed by the AUC of LDH. The LDH was reduced from a mean of 2201 ± 105U/L at baseline to 297 ± 21U/L at 52 weeks. Further evidence to support the clinical efficacy of eculizumab is derived from the uncontrolled 102 week extension study which evaluated the effect of eculizumab on thromboembolism events in patients with PNH. Patients from 3 independent

clinical studies including a phase II pilot study and its extension, the TRIUMPH and SHEPHERD studies and the common phase III extensions, participated. The thromboembolism event rate with eculizumab treatment was reported as 1.07 events/100 patient years as compared with 7.37 events/100 patients years prior to eculizumab therapy. The review team highlighted the limitations associated with this uncontrolled study.

5. In their submission Alexion Pharma UK Ltd highlighted the benefit of eculizumab in reducing causes of mortality in patients with PNH including thromboembolism, renal dysfunction and pulmonary hypertension. However the fact remains that there is no evidence to date to demonstrate that eculizumab therapy reduces mortality in patients with paroxysmal noctural haemoglobinuria.

6. The review group noted the West Midlands Health Technology Assessment Collaboration (WMHTAC) health economic data for the cost-effectiveness of eculizumab. The company is not aware of any other economic data. The WMHTAC report contained 3 preliminary cost-effectiveness analyses. The first analysis investigated the cost per stabilisation of haemoglobin and the cost per stabilisation of LDH. The incremental cost per haemoglobin stabilised was estimated at £257,142 (€285,713). The incremental cost per normalisation of LDH is estimated at £340,541 (€378,378). Estimates of the cost per life year gained (cost/LYG) were within the range of £600,000/LYG to £1,000,000/LYG (€666,666/LYG and €1,111,101/LYG). The cost/LYG for averting thrombosis related mortality with eculizumab ranged from £1.2 million/LYG to £1.4 million/LYG. The equivalent ICERs in Euro would be €1,333,333/LYG and €1,555,555/LYG.

7. It has been estimated that 15% of eligible patients would receive eculizumab therapy. This would result in an annual budget impact in the region of €3.5 to €3.9 million. With a PNH prevalence rate of 15.9 per million population, if all

patients who could potentially benefit received the therapy, the budget impact could exceed €23 million/annum.

8. At a price of €4,557.5 per 30ml/300mg vial we do not believe that eculizumab (soliris®) is value for money for treatment of patients with paroxysmal noctural haemoglobinuria (PNH) in the Irish healthcare setting. Alexion Pharma UK Ltd have failed to demonstrate the cost-effectiveness of this therapy. We believe that the request for reimbursement under the High Tech Drugs scheme should be rejected. It must be emphasised that there is no clinical data to suggest that this product reduces mortality in patients with PNH at this point in time.