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Alexion Pharma UK is grateful for the opportunity to provide a response to the report 'Prevalence and prognosis of paroxysmal nocturnal haemoglobinuria and the clinical and cost-effectiveness of eculizumab treatment' produced by West Midlands Health Technology Assessment Collaboration (WMHTAC) and to state our opinion of the budget impact detailed within the report.

Alexion recognises that studying the cost-effectiveness of ultra-orphan therapies, such as eculizumab, is very difficult. Extremely low numbers of patients combined with the very high development costs of producing innovative, first in class medicines necessitate high drug acquisition costs. This led NICE to recommend that a new framework for assessing the cost-effectiveness of ultra-orphan drugs be established¹. This has not yet happened and as such calculation using standard health economic tools continues.

Alexion acknowledges that the report recognised the high quality of the clinical data available for eculizumab and the clinical benefits it brings as the first drug licensed to treat paroxysmal nocturnal haemoglobinuria (PNH). The clinical trial data have demonstrated that eculizumab treatment results in significant improvements in quality of life, however the authors did not feel it was possible at this time to factor quality of life into the cost-effectiveness analysis. Quality of life is obviously hugely influential in assessing cost-effectiveness and Alexion believe when this is properly factored in the cost-effectiveness of eculizumab as an ultra-orphan therapy for an extremely rare, life-threatening disorder, will be further established.

The report contains wide ranging estimates of cost-effectiveness and the budget impact for the West Midlands SCG. Alexion feels that the lower of these estimates is likely to be closer to the realistic treatment cost values. In reference to some of the specific variables used, Alexion believes that the likely proportion of PNH patients who will be treated with eculizumab is consistent with the 16% figure cited in the HTA and the savings over standard care will be far greater than £1000 per annum. Furthermore, the figures for mean survival and part of the thrombosis analysis are taken from cohorts of all PNH patients, not those at the more severe end of the spectrum of PNH disease who are likely to receive eculizumab in the UK. It is reasonable to expect that those patients with more severe disease are likely to have increased occurrence of thrombosis (as demonstrated during the Extension study) and lower mean survival than that of the entire PNH patient population.

Importantly, for SCGs using this report to estimate the likely budget impact of eculizumab, Alexion believes that the budget impact model significantly overestimates the number of patients likely to be treated and therefore the cost at years 1 to 10. Looking only at treating 16% of PNH patients, the greatest estimate of budget impact at year 1 is £3.3M and year 10 is £9.5M (assuming £1,000 savings over standard care treatment). This budget impact model assumes that 2% of untreated PNH patients will become eligible for treatment each year as well as adding 1 new treated patient per year from the newly diagnosed patient population. We do not believe this reflects accurately the true clinical picture where it is expected that whilst the PNH population identified may increase slightly over time with greater disease awareness, the percentage of patients treated will remain at 16%. The effect of the assumption that an additional 2% of patients will require therapy per year over the 10 year model is that 16% of the initial population of 87 patients are treated, but by year 10, some 27% of the larger population of 160 (includes new annual new diagnoses) receive eculizumab therapy. Alexion firmly believe this figure should remain at 16% which would reduce the budget impact to less than £6M at year 10².

The budget impact figure will also be affected by other factors, including:-

- The demonstrated effect of eculizumab in reducing blood transfusions, thrombotic events and other complications are likely to result in substantially greater than £1000 per annum savings over standard care
- The model assumes all patients live indefinitely
- The budget impact model assumes that 14 patients will be treated immediately. The number of patients identified for the West Midlands SCG is currently 5. This significantly affects the budget impact today and for the future. Using this figure the drug acquisition cost at year 1 is £1.23 million and using the rate of new diagnoses assumed in the model, at year 10 would be approximately £3.7 million².

Alexion believes that all of these factors must be borne in mind when making funding decisions on the basis of budget impact, which of course ignores the significant quality of life gain that patients treated with eculizumab will achieve.

¹ National Institute for Clinical and Health Excellence, Appraising Orphan Drugs, March 2006

² Alexion Pharma UK company calculation

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