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Re: Eculizumab for treating atypical haemolytic uraemic syndrome (aHUS) [ID703] - ECD2

The Royal College of Physicians (RCP) plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 30,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

I write on behalf of the RCP and the Renal Association with regard to the above ECD2 consultation. We are grateful for the opportunity to respond and would like to make the following joint submission.

We welcome the recommendation of the committee that eculizumab should be available for use in aHUS subject to certain conditions (addressed below). We believe this to be the right decision for patients with aHUS and those yet undiagnosed who will experience significant health benefit from eculizumab. We are pleased that the culmination of years of successful medical research has been translated into an effective treatment, and that patients will now benefit from this.

We believe that all relevant evidence has been taken into account and that the summaries of the criteria considered by the Committee and the clinical and economic considerations are reasonable interpretations of the evidence.

Our experts note the robust defence of costs by the manufacturer and feel that the main areas of contention now appear to rest within the remit of health economics. We do, however, wish to respond with regard to two outstanding clinical issues, as below:

- The main clinical issue is that of dosage and interval, and whether the drug can be withdrawn. We note that the manufacturer firmly rejects the proposal that the drug can ever be withdrawn, and our experts are uncomfortable with this stance. The manufacturer quotes previous EMA recommendation for lifelong treatment. However, this ignores the fact that the evidence base will inevitably improve as studies are carried out and that there is no scientific or ethical imperative to continue lifelong treatment in all patients. The manufacturer also states that lifelong complement inhibition is necessary in those with a complement gene abnormality. This is theoretical and we do not currently understand

either the nature of second hits required for disease relapses or the adverse consequences of long-term complement inhibition.

- Our experts believe that the cost analysis provided by the manufacturer, compared to other ultra-rare disease therapies, is a compelling set of calculations to justify its use. Our only comment here is that this would only hold true if a similar number of patients were being treated with each of the drugs being compared, across the UK. If Eculizumab is being used (or will be used) in a significantly higher number of patients (particularly as it is or has been evaluated for several other conditions) then the cost to the NHS will be far higher, and the comparison with other ultra-rare disease therapies is less relevant.

The recommendation of eculizumab by the committee is subject to a number of conditions, considered below:

- We agree that use of eculizumab should be co-ordinated through an expert centre. We strongly propose that eculizumab should be delivered locally with local expertise but recognise the value of the resource provided by an expert centre or specialised service, including diagnostic and management support.

- We agree with the recommendation that the number of people with aHUS and the number receiving eculizumab should be monitored and information collected about dosing and duration. There is great value in collecting this independently of the manufacturer-sponsored registry and would be best achieved by having an expert centre or specialised service.

- We propose that a national protocol for starting and stopping eculizumab should be developed, but that this should be informed by well-conducted clinical trials.

We do not think that any aspects of the recommendations pose a risk of unlawful discrimination.
The provisional recommendations are sound and provide clear guidance on the use of eculizumab in aHUS and are a suitable basis for guidance on the use of eculizumab for the treatment of aHUS in the context of national commissioning by NHS England.

Since an interim national aHUS service is already in place we believe that the health technology will be available within three months of the publication of the recommendation.

Yours sincerely