TO BE PRINTED ON LOCAL TRUST HEADED PAPER



<Doctor>

<Practice>

<Street>

<City>

<Postcode>

<Date>

Dear Dr <GP name>,

# Re: Name: …………………………………………………………………………………………………………….

# DoB: ……………………………………………………………………………………………………………….

# NHS No: …………………………………………………………………………………………………………

**Eculizumab in Shiga-toxin producing E.Coli Haemolytic Uraemic Syndrome (ECUSTEC): A Randomised, Double-Blind, Placebo-Controlled Trial.**

Date of enrolment: \_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (DD/MM/YYYY)

I am writing to inform you that your patient, named above, has agreed to take part in the ECUSTEC study which will assess the use of eculizumab in Shiga-toxin producing E. coli Haemolytic Uraemic Syndrome (STEC HUS). Our hypothesis is that eculizumab reduces the severity of STEC HUS. I am writing to give you some information about the study.

STEC HUS is the most common cause of paediatric acute kidney injury and affects ~100 UK children each year. It has a 2-3% mortality rate and considerable morbidity with 50-60% requiring dialysis. A proportion develop severe disease with other organ involvement including brain (20-25%), bowel perforation and diabetes. Long term complications such as chronic kidney disease (CKD, including end-stage kidney disease) or more rarely permanent brain injury, occur in up to 1/3 of survivors. Experimental evidence suggests a role for complement in the pathogenesis of STEC HUS. Eculizumab (a monoclonal antibody that inhibits complement) is remarkably effective in a related condition, atypical HUS. Following anecdotal case reports of benefit from eculizumab in STEC HUS it was studied in a prospective, non-controlled trial in adults with STEC HUS due to STEC O104 with inconclusive results.

We are undertaking a randomised, double-blind, placebo-controlled trial of eculizumab in 134 children aged 6 months – 18 years with presumed STEC HUS, recruited over 48 months. Participants have received 2 doses of eculizumab or placebo 1 week apart. Patients are followed for 1 year from randomisation, with daily assessments until hospital discharge, then 30 & 60 days, 6 months and 1 year post randomisation (if admission ≥14 days then assessments will be weekly from day 14 to discharge or day 60, whichever is soonest). Our aim is to determine if STEC HUS is less severe in those who receive eculizumab vs. placebo. The study will receive full UKCRN support.

**As your patient may have received two doses of eculizumab, they may be at increased risk of meningococcal disease for a period not greater than 8 weeks from the date of enrolment (date given above). All trial participants (those receiving eculizumab or placebo) have been given additional precautions against meningococcal disease:**

* + **All have received one dose of tetravalent ACWY vaccine.**
  + **All should receive 8 weeks of penicillin V (or erythromycin if penicillin allergic) – see below.**
  + **Those not already included in the UK Vaccination programme for Bexsero have received one dose of Bexsero. To complete the immunisation course, these patients will be offered an optional second dose of Bexsero at their study visit on day 60 after enrolment (although this is not mandatory since the effect of eculizumab will no longer be present). We will notify you if a second dose is given.**
  + **In children under 2 years old at first Bexsero dose, a booster is indicated between 12 and 23 months after the second dose. Again this is not mandatory but we will offer it to complete the immunisation course. We will notify you to ask you to undertake this third dose if it is indicated with details of how to claim reimbursement.**
  + **Details of vaccines received so far are given in Appendix 1.**
  + **Participants have also been given information about the symptoms and signs of meningococcal disease.**

**Please prescribe the following for your patient until \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (8 weeks after enrolment)**

|  |  |
| --- | --- |
| **Penicillin** | |
| Age | Dose |
| Under 1 year | 62.5 mg twice daily for 8 weeks |
| 1–5 years | 125 mg twice daily for 8 weeks |
| 5–18 years | 250 mg twice daily for 8 weeks |
| **Erythromycin if penicillin allergic** | |
| Age | Dose |
| 6 months – 2 years | 125 mg twice daily for 8 weeks |
| 2–8 years | 250 mg twice daily for 8 weeks |
| 8–18 years | 500 mg twice daily for 8 weeks |

ECUSTEC is being coordinated by the University of Birmingham Clinical Trials Unit (address below), and is being funded by the National Institute for Health Research, Efficacy and Mechanism Evaluation Programme (NIHR EME), Ref: 14/48/43. The trial has been approved by North East – Newcastle and North Tyneside 1 Research Ethics Committee. ECUSTEC is sponsored by the Newcastle Upon Tyne Hospitals NHS Foundation Trust.

If you have cause to see your patient during the course of the study and want to discuss any aspect of their management e.g. treatment regimen, contra-indications etc., please do not hesitate to contact me on Tel: *<insert responsible clinician telephone number>*. It would be particularly helpful if you could inform me of any adverse events your patient reports to you or any therapy changes you make or wish to make.

Yours sincerely,

*<insert responsible clinician name>*

ECUSTEC Study Office, The University of Birmingham Clinical Trials Unit, College of Medical & Dental Sciences, Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, B15 2TT.

Web address: www.birmingham.ac.uk/ECUSTEC

**Appendix 1**

**Details of vaccination given (please update your information systems accordingly):**

ACWY vaccine

Vaccine name:

Product name:

Batch number:

Expiry date:

Dose administered:

Site used:

Date immunisation given:

Group B meningococcal vaccine

Vaccine name:

Product name:

Batch number:

Expiry date:

Dose administered:

Site used:

Date immunisation given:

Vaccine not given as child already included in UK Vaccination programme for Bexsero

*Study team to tick if applicable*