The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

Atypical Haemolytic Uraemic Syndrome Shared Care protocol

Contact Details	**Patient ID Label:**
Name:_____	**Surname:** _____
Location:_____	**Forenames:**_____
Date: _____	**NHS Number:**_____
Phone No. _____	**Date of Birth:**_____

Introduction	Eculizumab is available for treatment for patients with aHUS in England and only if all the following arrangements are in place • coordination of eculizumab use through an expert centre • monitoring systems to record the number of people with a diagnosis of atypical haemolytic uraemic syndrome and the number who have eculizumab, and the dose and duration of treatment • a national protocol for starting and stopping eculizumab for clinical reasons • a research programme with robust methods to evaluate when stopping treatment or dose adjustment might occur. Ravulizumab* is available for treatment for patients with aHUS in England and only if all the following arrangements are in place • coordination of ravulizumab use through an expert centre • monitoring systems to record the number of people with a diagnosis of atypical haemolytic uraemic syndrome and the number who have ravulizumab, and the dose and duration of treatment • a national protocol for starting and stopping ravulizumab for clinical reasons *Please refer to the ravulizumab switching protocol The expert centre (National aHUS Service) is based at The National Renal Complement Therapeutics Centre, Building number 26, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust and is known as the National aHUS Service. This protocol outlines the responsibilities of the referring consultant and the National aHUS Service.
Dose & Administration	The dose of **Eculizumab** for induction and maintenance is fixed for adults. For children and adolescents dose is adjusted

	according to body weight. Details of dosing schedules are available at: **https://www.medicines.org.uk/EMC** The dose of **Ravulizumab** for induction and maintenance is adjusted according to body weight for both adults and children. Details of dosing schedules are available at: **https://www.medicines.org.uk/emc/product/11944/smpc#CLINICAL_PARTS**
National Service Responsibilities	1. Consider all patients referred with a thrombotic microangiopathy and possible diagnosis of atypical Haemolytic Uraemic Syndrome (aHUS) and provide a clinical opinion on diagnosis and treatment. 2. Authorise the initiation of treatment with Eculizumab or Ravulizumab for patients with a likely diagnosis of aHUS who may benefit from treatment and who meet NHS eligibility. 3. Inform NHS England that treatment has been recommended for a patient. 4. Perform and review genetic testing for causes of aHUS and report the results to the referring Consultant. 5. Provide the patient with information about aHUS and treatment with Eculizumab or Ravulizumab. 6. Initiate shared care with the referring consultant and other clinicians involved in the patient's care according to this agreement. 7. Review the progress of patients referred to the National aHUS Service. For patients not treated, further progress review will cease upon mutual agreement between the National aHUS Service and the referring consultant. 8. Discuss with the patient, when indicated, the possibility of switching treatment from Eculizumab to Ravulizumab or stopping treatment. 9. Offer the patient the opportunity for appointments with a consultant from the National aHUS Service (either face to face or remotely). When appropriate offer appointments to family members for genetic counselling and provide educational material to family members. 10. Maintain written communication with the referring Consultant and patient's General Practitioner following all appointments.

	11. The Specialist aHUS nurses will be in regular contact with the patient following initiation of treatment and will have regular clinic appointments with them. 12. Provide ongoing advice and information to the referring consultant and patient's General Practitioner as required. 13. The Specialist nurses will lead on monitoring meningococcal vaccination and antibody titres. They will share results with primary care and local consultants and arrange booster vaccinations when appropriate. When indicated they will monitor anti-factor H autoantibodies and share this information with the referring team. 14. Provide support and education for healthcare professionals involved in administering Eculizumab and Ravulizumab and all other aspects of the care of patients with aHUS.
Responsibilities of the Referring Consultant	1. Contact the National aHUS Service if a diagnosis of aHUS is suspected. 2. Undertake local investigations as recommended in the National aHUS Service protocol to establish a cause of the thrombotic microangiopathy and indication for commencing treatment with Eculizumab. **https://www.atypicalhus.co.uk/forms/** 3. Send the required samples to the National aHUS Service. 4. As HUS is a notifiable disease, UKHSA must be informed, this can be done prior to laboratory confirmation of disease. When advised by the National aHUS Service, liaise with the local microbiology laboratory to ensure urgent samples are sent for: a. *Shiga-toxin producing E. coli* (STEC) culture to local microbiology laboratory. b. When advised stool or rectal swab should be sent for enhanced STEC testing to Bacteriology Reference Department, UKHSA Colindale. c. UKHSA will assess whether contact tracing is indicated. 5. When treatment is authorised: a, to prescribe and administer Eculizumab or Ravulizumab according to the manufacturer's instructions and protocol unless a deviation from protocol is agreed with the National aHUS Service.

b, to prescribe prophylactic antibiotics for the duration of treatment with Eculizumab or Ravulizumab and for 4 weeks (eculizumab) and 4 months (ravulizumab) following any discontinuation of treatment.

6. Notify the National aHUS Service of all diagnostic checklist investigations requested within one month of starting Eculizumab treatment.

7. Minimise the risk of meningococcal infection by vaccination and the use of prophylactic antibiotics as recommended in the aHUS National aHUS Service protocol **https://www.atypicalhus.co.uk/following-approval-of-eculizumab/**

    a. Vaccinate with a tetravalent (ACWY) vaccine and Bexsero (against serotype B).

    b. Prescribe prophylactic antibiotic for the duration of Eculizumab or Ravulizumab treatment. Oral antibiotics should be continued for 4 weeks following the discontinuation of Eculizumab and 4 months following discontinuation of Ravulizumab

    Make the patient/parent/carer aware of the increased risk of meningococcal infection and possible symptoms of meningococcal infection and advise what to do if concerned.

8. Make the patient or guardian/ carer aware of the National aHUS Service and that they will be contacted directly with further information about aHUS and its treatment.

9. Arrange ongoing monitoring at the recommended frequencies by the National aHUS Service, including collection of samples to be sent to the National aHUS Service for complement studies.

10. Supply patient data to the National aHUS Service, as mandated by NHS England, to allow submission of regular reports of Eculizumab and Ravulizumab use and patient outcomes.

11. Report any adverse events to the National aHUS Service (consultant or specialist nurse).

12. Notify the National aHUS Service of any variations in treatment, including patient deterioration, non-compliance with treatment, deviations in dosing/frequency and pregnancy.

	13. Decisions on switching treatments or stopping treatment should be made in consultation with the National aHUS Service. 14. Provide a named person (i.e. Consultant, Doctor or Specialist Nurse) for each patient who can be contacted by the National aHUS Service in case of questions relating to that patient. 15. All patients referred to the National aHUS Service should be registered with RADAR and Patients Know Best to allow automatic collection of outcome data.
Monitoring Required from Referring Centre	Monitoring of patients receiving Eculizumab or Ravulizumab treatment is required and the National aHUS Service requires this information to report to NHS England. Monitoring in the early stages of treatment will be based on clinical need and local protocols. Complement blockade should be confirmed once established on a maintenance dose of eculizumab and thereafter only if clinically indicated. This should include AP100 and CH50 to confirm complement blockade and will be performed by the National aHUS Service. Samples should be sent to the National aHUS Service for processing and interpretation. In stable patients the following tests are recommended on a three monthly basis. • Renal function • Platelet count • Lactate dehydrogenase • Haptoglobin • Urinalysis • Urine Protein/Creatinine ratio These should be monitored by the referring team. The National aHUS Service will provide advice when indicated. Further information on monitoring is available at: **https://www.atypicalhus.co.uk/following-approval-of-eculizumab/**
Adverse Effects	Eculizumab and Ravulizumab treatment increases the risk of meningococcal infection. The protocol to minimise risk of infection is available at: **https://www.atypicalhus.co.uk/following-approval-of-eculizumab/** Details of other treatment related adverse effects are available at: **https://www.medicines.org.uk/emc**

	https://www.medicines.org.uk/emc/product/11944/smpc#UNDESIRABLE_EFFECTS

Referring Consultant

Signed…… Date…….

Print name…….. Position……

National aHUS Service Consultant

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