INTERIM FUNDING CRITERIA IN ONTARIO FOR SOLIRIS AHUS –CASE BY CASE BASIS

Initiation Criteria

A patient must meet **all three** of the following to obtain funding for initial treatment of eculizumab for aHUS:

1. Confirmed diagnosis of atypical hemolytic uremic syndrome (aHUS) at initial presentation, defined by presence of thrombotic microangiopathy (TMA)

a) ADAMTS-13 activity ≥ 10% on blood samples taken prior to plasma exchange or plasma infusion (PE/PI).

Note:

If the sample for ADAMTS-13 was not collected prior to PE or PI, platelet counts > 30 x 10^9/L and SrCr > 150 umol/L at TMA presentation will be accepted as predictive of ADAMTS-13 ≥10% in TMA patients. In this case, measurement of ADAMTS-13 can be taken 1-2 weeks following last PE. The ADAMTS-13 result **must** be provided to the Ministry within 30 days of commencement of eculizumab AND at least 1 week after last PE; Subsequent doses of eculizumab cannot be administered to a patient unless the compliant result has been provided.

AND

b)STEC–negative test if the patient has had diarrhea in the preceding 14 days

2. Evidence of on-going active TMA, defined by laboratory test abnormalities despite plasmapheresis (minimum of 4 plasma exchanges required over 4 successive days)
Patients must demonstrate

a) Thrombocytopenia (platelet count <150 x 10^9/L) or decline of platelet count of > 25% from baseline that is not explained by some other cause including secondary TMA; **AND** hemolysis as indicated by the documentation of two of the following: schistocytes on the blood film; low or absent haptoglobin; or lactate dehydrogenase (LDH) above normal. OR

b) Tissue biopsy confirming TMA in patients who do not have evidence of platelet consumption and hemolysis

Note:

- Pediatric patients (defined as less than 12 years old) are not required to be treated with plasmapheresis in order to have funding consideration for eculizumab but must have evidence of on-going active TMA as defined above.

- If a patient has a family history of TMA and is genetically positive for aHUS the patient is not required to be treated with plasmapheresis in order to have funding consideration for eculizumab as long as they have evidence of on-going active TMA as defined above along with renal or neurological involvement.

3. Evidence of at least ONE of the following documented clinical features of active organ damage or impairment

- Kidney impairment as demonstrated by one of the following:
  - decline in estimated Glomerular Filtration Rate (eGFR) of >20% in a patient with pre-existing renal impairment; and/or
  - serum Creatinine (SrCr) > upper limit of normal (ULN) for age or GFR < 60 and renal function deteriorating despite prior PE/PI in patients who have no history of pre-existing renal impairment (i.e. who have no baseline eGFR measurement); or SrCr > the age-appropriate ULN in pediatric patients (subject to advice from a

pediatric nephrologist)

OR

- Onset of neurological impairment related to TMA

Notes

- Eculizumab increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis).
- Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of SOLIRIS®; revaccinate according to current medical guidelines for vaccine use

Patients less than 2 years of age and those who are treated with SOLIRIS® less than 2 weeks after receiving a meningococcal vaccine must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary.

Request must come from a pediatric nephrologist, a nephrologist, a pediatric hematologist, a hematologist OR must be in consultation with a pediatric nephrologist, a nephrologist, a pediatric hematologist, a hematologist

Case by Case:

Transplant patient with a past known normal ADAMTS-13 TMA would be eligible for eculizumab if they develop an active TMA in immediate transplant period (after stopping CNI) for sparing of transplant kidney function. Approve funding for period immediately prior to and throughout transplant period. Criteria for continued funding are to be determined

Patients who have extra renal complications related to TMA (specifically onset of TMA –related cardiac impairment, onset of TMA –related gastrointestinal impairment, or onset of TMA-related pulmonary impairment) will be considered on case by case basis

Continuation criteria at 6 months (written application)

After 6 months of initial funding , treatment response is required for further subsidized treatment with eculizumab

A patient must demonstrate '**treatment response'** at 6 months to be eligible for a further 6 month supply of funded eculizumab therapy.

'Treatment response' at 6 months is defined as:

- Hematological normalization (as demonstrated by LDH within 25% ULN and normalization of platelet count)

AND EITHER

- An "improvement" in eGFR, defined as an increase in eGFR of >25% from baseline (where the baseline is the date of commencement of eculizumab); or
- "Stabilization" of eGFR, defined as an eGFR < 25% increase from baseline.
- "Stabilization" of extra-renal impairment if complication originally presented

Continued funding of treatment with eculizumab will not be permitted beyond 6 months if a patient has experienced 'treatment failure'.

'Treatment failure' at 6 months is defined as:

dialysis-dependence at 6 months and failed to demonstrate resolution or failed to demonstrate stabilization of neurological (or extra renal if applicable) complications if originally present; **OR**

- on dialysis for ≥ 4 of the previous 6 months while receiving eculizumab and failed to demonstrate resolution or failed to demonstrate stabilization of neurological (or extra renal if applicable) complications if originally present **OR**
- Worsening of kidney function with a reduction in eGFR ≥ 25% from baseline.

Request must come from a pediatric nephrologist, a nephrologist, a pediatric hematologist, a hematologist OR must be in consultation with a pediatric nephrologist, a nephrologist, a pediatric hematologist, a hematologist

Continuation criteria at 12 months

To be determined