Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Implementation Information:

1.0 Under the supervision of the Clinical Pharmacy Management (CPM) Director, the CPM staff is responsible for the development of guidelines and criteria for use by the Medical Department.

2.0 Staff utilizing this procedure is monitored via individual departmental audit tools.

3.0 On an annual basis or more often when indicated, the Medical Department Procedures are reviewed by medical staff for the purpose of developing, revising, or archiving:

3.1 Medical Department staff has access to the Medical Department Procedure Manual and receives notice from management when procedures are developed, revised, or archived.

Background Information:

Definitions

- Hemolytic anemia is the abnormal breakdown of intravascular red blood cells (RBC) and release of hemoglobin into the plasma, causing anemia.
- Paroxysmal Nocturnal Hemoglobinuria (PNH) Members suffer from a genetic mutation which leads to the generation of abnormal RBCs (PNH cells). PNH cells are targeted by the immune system and destroyed. The loss of these PNH cells (also called intravascular hemolysis) results in low RBC counts (anemia), fatigue, hemoglobinuria, plasma free hemoglobin, and indirectly thrombosis, abdominal pain, dysphagia, erectile dysfunction, and pulmonary hypertension.
Medical Department Procedure Manual

Section: Chapter 7A Prescription Medications Prior Authorization   Number: 07.064
Title: eculizumab (Soliris)   Page 2 of 7

Background Information, continued:

Medication Summary
- Soliris is a monoclonal antibody that specifically binds to the complement protein C5, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Soliris thus inhibits terminal complement mediated intravascular hemolysis.
- Soliris is the first treatment for paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis. PNH is a rare, life-threatening, and genetically acquired form of hemolytic anemia.
- Soliris is supplied as a 300mg single-use vial containing 30ml of 10mg/ml sterile, preservative-free solution. Soliris is diluted to a final concentration of 5mg/ml.

Reference Statement
- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

Coverage Guidelines
- Member must be eligible and have applicable benefit coverage.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Exclusion Criteria
- Unresolved serious Neisseria meningitides infection.
- Members not currently vaccinated against Neisseria meningitides (meningococcal vaccination).
- Members with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Additional Information
- AvMed’s Clinical Pharmacists are licensed by the State of Florida.
- AvMed’s Medical Directors are Board Certified physicians licensed by the State of Florida.
Medical Department Procedure Manual

Section: Chapter 7A Prescription Medications Prior Authorization Number: 07.064
Title: eculizumab (Soliris) Page 3 of 7

Procedure:

1.0 Request for initial therapy for paroxysmal nocturnal hemoglobinuria (PNH) requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying ALL of the following criteria:

1.1 Member must have definitive diagnosis of paroxysmal nocturnal hemoglobinuria as evidenced by both of the following:

1.1.1 Elevation of lactate dehydrogenase (LDH) level (within last 30 days) is 1.5 times or more the upper limit of normal (ULN) which indicates degree of intravascular hemolysis (Normal LDH range is 105 - 333 IU/L); AND

1.1.2 Confirmed PNH type III erythrocytes detectable by flow cytometry (at least 10%); OR greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP) deficient poly-morphonuclear cells (PMNs)

1.1.2.1 Cytometry should be performed prior to transfusion or at least one (1) month since last transfusion to avoid dilution of abnormal cell proportion;

1.2 Member hemoglobin level less than 9g/dL in the presence of symptoms, or less than 7g/dL without symptoms (lab should be drawn before transfusion or at least one (1) month since last transfusion); AND

1.3 Member must be transfusion-dependent, requiring at least four (4) RBC transfusions in the past 12 months; OR has a history of major adverse vascular event from thromboembolism (eg. Cerebrovascular accident, DVT); AND

1.4 Member must have at least two (2) of the following:

1.4.1 Platelet counts of at least 20,000/mm³
1.4.2 Granulocytes greater than or equal to 500/mm³
1.4.3 Reticulocytes greater than or equal to 1%
1.5 Member must have received meningococcal vaccine at least two (2) weeks prior to initiation of Soliris therapy;

1.6 If criteria are met, may approve Soliris initially for two (2) months based on the recommended dosage regimen of induction and maintenance phases:

1.6.1 During the induction phase, Soliris 600mg by IV infusion every week for the first four (4) weeks followed by 900mg infusion on week five (5);

1.6.2 The maintenance phase consists of a 900mg infusion every 14 days thereafter.

2.0 Request for continuation of therapy for paroxysmal nocturnal hemoglobinuria (PNH) beyond the initial authorization period requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying ALL of the following:

2.1 Member must be showing improvement in disease stability by all of the following:

2.1.1 Reduction of intravascular hemolysis as measured by serum LDH levels (should be a reduction from baseline); AND

2.1.2 Reduction in PRBC transfusions required secondary to the disease; AND

2.1.3 Hemoglobin levels should be above baseline; AND

2.2 Member is tolerating therapy without any adverse effects;

2.3 If criteria are met, may approve Soliris for an additional six (6) months at the maintenance infusion dose of 900mg every 14 days.
Medical Department Procedure Manual

Section: Chapter 7A Prescription Medications Prior Authorization Number: 07.064

Title: *eculizumab* (Soliris) Page 5 of 7

**Procedure, continued:**

3.0 Request for *initial therapy* for **atypical hemolytic uremic syndrome** (aHUS) requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying **ALL** of the following criteria:

3.1 Diagnosis is supported by **BOTH** of the following:

3.1.1 Absence of Shiga toxin-producing E.Coli infection

3.1.2 ADAMTS-13 level is greater than 5%

3.2 Member weighs at least five (5) kilograms;

3.3 Member has meningococcal vaccine at least two (2) weeks prior to initiation of Soliris therapy;

3.4 If criteria are met, may approve Soliris initially for two (2) months based on the recommended dosage regimen of induction and maintenance phases:

3.4.1 For Members ≥ 40 kg: During the induction phase, Soliris 900mg by IV infusion every week for the first four (4) weeks followed by 1200mg infusion on week five (5);

The maintenance phase consists of a 1200mg infusion every 14 days thereafter;

3.4.2 For Members <40 kg, see dosage chart below:

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Induction</th>
<th>Maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>600 mg weekly x 2 weeks</td>
<td>900 mg at week 3 then 900mg every 14 days</td>
</tr>
<tr>
<td>20-29</td>
<td>600 mg weekly x 3 weeks</td>
<td>600 mg every 14 days</td>
</tr>
<tr>
<td>10-19</td>
<td>600 mg weekly x 1 week</td>
<td>300 mg at week 2 &amp; every 14 days thereafter</td>
</tr>
<tr>
<td>5-9</td>
<td>300 mg weekly x 2 weeks</td>
<td>300 mg every 21 days thereafter</td>
</tr>
</tbody>
</table>

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Medical Department Procedure Manual

Section: Chapter 7A Prescription Medications Prior Authorization  Number: 07.064
Title: eculizumab (Soliris)  Page 6 of 7

Procedure, continued:

4.0 Request for continuation of therapy for atypical hemolytic uremic syndrome (aHUS) beyond the initial authorization period requires documentation from the Member’s medical records maintained by the requesting independent practitioner verifying ALL of the following:

4.1 Response to treatment, as defined by one (1) or more of the following:

   4.1.1 Platelet count improvement from baseline; OR
   4.1.1 Member shows ≥ 25% reduction in SrCr; OR
   4.1.1 Reduction in the number of plasma infusion interventions or dialysis sessions;

4.2 If Member weighs <40 kg, updated weight for weight-based dosing;

4.3 If criteria are met, may approve Soliris for an additional six (6) months at the maintenance infusion dose of 1200mg every 14 days OR if Member is <40 kg, see weight-based dosing chart above for maintenance dose.

References:


References, continued:


