The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis (1.1).

SOLIRIS® (eculizumab) injection, for intravenous use

These highlights do not include all the information needed to use SOLIRIS safely and effectively. See full prescribing information for SOLIRIS.

**INDICATIONS AND USAGE**

1.1 Paroxysmal Nocturnal Hemoglobinuria (PNH)

Soliris is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

1.2 Atypical Hemolytic Uremic Syndrome (aHUS)

Soliris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (1.2). Limitation of Use

Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Soliris is a complement inhibitor indicated for:

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis (1.1).
- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (1.2).

**WARNING: SERIOUS MENINGOCOCCAL INFECTIONS**

See full prescribing information for complete boxed warning

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris and may become rapidly life-threatening or fatal if not recognized and treated early (5.1).

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies (5.1).
- Immunize patients with meningococcal vaccines at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risks of developing a meningococcal infection. (See Warnings and Precautions (5.1) for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program (5.2).

**DOSAGE AND ADMINISTRATION**

2.1 Recommended Dosage Regimen - PNH

For patients 18 years of age and older, Soliris therapy consists of:

- 900 mg every 2 weeks thereafter.
- 900 mg for the fifth dose 1 week later, then
- 900 mg every 2 weeks thereafter.

**DOSAGE FORMS AND STRENGTHS**

Injection: 300 mg/30 mL (10 mg/mL) in single-dose vial (3).

**CONTRAINDICATIONS**

- Discontinue Soliris in patients who are being treated for serious meningococcal infections (5.4).
- Use caution when administering Soliris to patients with any other systemic infection (5.2).

**ADVERSE REACTIONS**

The most frequently reported adverse reactions in the PNH randomized trial (≥10% overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea (6.1).

The most frequently reported adverse reactions in aHUS single arm prospective trials (≥20%) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia (6.1).

The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) is: musculoskeletal pain (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

To see 17 PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 2/2018

Vaccinate patients according to current ACIP guidelines to reduce the risk of serious infection (see Warnings and Precautions (5.1) and (5.2)).

Only administer as an intravenous infusion.

2.1 Recommended Dosage Regimen - PNH

For patients 18 years of age and older, Soliris therapy consists of:

- 600 mg weekly for the first 4 weeks, followed by
- 900 mg for the fifth dose 1 week later, then
- 900 mg every 2 weeks thereafter.

Administer Soliris at the recommended dosage regimen time points, or within two days of these time points (see Warnings and Precautions (5.4)).

2.2 Recommended Dosage Regimen - aHUS

For patients 18 years of age and older, Soliris therapy consists of:

- 900 mg weekly for the first 4 weeks, followed by
- 1200 mg for the fifth dose 1 week later, then
- 1200 mg every 2 weeks thereafter.

For patients less than 18 years of age, administer Soliris based upon body weight, according to the following schedule (Table 1):
2.4 Dose Adjustment in Case of Plasmapheresis, Plasma Exchange, or Fresh Frozen Plasma Infusion

Administer Soliris at the recommended dosage regimen time points, or within two days of these time points.

For adult and pediatric patients with aHUS and adult patients with gMG, supplemental dosing of Soliris is required in the setting of concomitant plasmapheresis or plasma exchange, or fresh frozen plasma infusion (PE/PI) (Table 2).

Table 2: Supplemental Dose of Soliris after PE/PI

<table>
<thead>
<tr>
<th>Type of Plasma Intervention</th>
<th>Most Recent Soliris Dose</th>
<th>Supplemental Soliris Dose With Each Plasma Intervention</th>
<th>Timing of Supplemental Soliris Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmapheresis or plasma exchange</td>
<td>300 mg</td>
<td>300 mg per each plasmapheresis or plasma exchange session</td>
<td>Within 60 minutes after each plasmapheresis or plasma exchange</td>
</tr>
<tr>
<td>&gt;600 mg</td>
<td>600 mg per each plasmapheresis or plasma exchange session</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh frozen plasma infusion</td>
<td>≥300 mg</td>
<td>300 mg per infusion of fresh frozen plasma</td>
<td>60 minutes prior to each infusion of fresh frozen plasma</td>
</tr>
</tbody>
</table>

2.5 Preparation

Dilute Soliris to a final concentration of 5 mg/mL by adding the appropriate amount (equal volume of diluent to drug volume) of 0.9% Sodium Chloride Injection, USP; 0.45% Sodium Chloride Injection, USP; 5% Dextrose in Water, USP; or Ringer’s Injection, USP to the infusion bag.

The final admixed Soliris 5 mg/mL infusion volume is 60 mL for 300 mg doses, 120 mL for 600 mg doses, 180 mL for 900 mg doses or 240 mL for 1200 mg doses (Table 3).

Table 3: Preparation and Reconstitution of Soliris

<table>
<thead>
<tr>
<th>Soliris Dose</th>
<th>Diluent Volume</th>
<th>Final Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg</td>
<td>30 mL</td>
<td>60 mL</td>
</tr>
<tr>
<td>600 mg</td>
<td>60 mL</td>
<td>120 mL</td>
</tr>
<tr>
<td>900 mg</td>
<td>90 mL</td>
<td>180 mL</td>
</tr>
<tr>
<td>1200 mg</td>
<td>120 mL</td>
<td>240 mL</td>
</tr>
</tbody>
</table>

Gently invert the infusion bag containing the diluted Soliris solution to ensure thorough mixing of the product and diluent. Discard any unused portion left in a vial, as the product contains no preservatives.

Prior to administration, the admixture should be allowed to adjust to room temperature [18°-25°C, 64-77°F]. The admixture must not be treated in a microwave or with any heat source other than ambient air temperature.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

2.6 Administration

Do Not Administer As An Intravenous Push or Bolus Injection

Administer the Soliris admixture by intravenous infusion over 35 minutes in adults and 1 to 4 hours in pediatric patients via gravity feed, a syringe-type pump, or an infusion pump. Admixed solutions of Soliris are stable for 24 h at 2-8°C in a refrigerator and for 24 h at ambient temperatures.

3 Dose Forms and Strengths

Injection: 300 mg single-dose vials each containing 30 mL of 10 mg/mL sterile, colorless, preservative-free eculizumab solution.

4 CONtraindications

Soliris is contraindicated in:

- Patients with unresolved serious Neisseria meningitidis infection
- Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection [see Warnings and Precautions (5.5)].

5 WARNINGS AND PRECAUTIONS

5.1 Serious Meningococcal Infections

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. The use of Soliris increases a patient’s susceptibility to serious meningococcal infections (septicaemia and/or meningitis).

Vaccinate for meningococcal disease according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with complement deficiencies. Revaccinate patients in accordance with ACIP recommendations, considering the duration of Soliris therapy.

Immunize patients without a history of meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris. If urgent Soliris therapy is indicated in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible.

In prospective clinical studies, 75/100 patients with aHUS were treated with Soliris less than 2 weeks after meningococcal vaccination and 64 of these 75 patients received antibiotics for prophylaxis of meningococcal infection until at least 2 weeks after meningococcal vaccination. The benefits and risks of antibiotic prophylaxis for prevention of meningococcal infections in patients receiving Soliris have not been established.

Vaccination reduces, but does not eliminate, the risk of meningococcal infections. In clinical studies, 2 out of 196 PNH patients developed serious meningococcal infections while receiving treatment with Soliris; both had been vaccinated [see Adverse Reactions (6.1)]. In clinical studies among non-PNH patients, meningococcal meningitis occurred in one unvaccinated patient. In addition, 3 out of 130 previously vaccinated patients with aHUS developed meningococcal infections while receiving treatment with Soliris [see Adverse Reactions (6.7)].

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if an infection is suspected. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Discontinue Soliris in patients who are undergoing treatment for serious meningococcal infections.

5.2 Soliris REMS

Because of the risk of meningococcal infections, Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program.

Prescribers must counsel patients about the risk of meningococcal infection, provide the patients with the REMS educational materials, and ensure patients are vaccinated with meningococcal vaccine(s).

Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLRIS (1-888-765-4747) or at www.solirisrems.com.

5.3 Other Infections

Soliris blocks terminal complement activation; therefore patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, Aspergillus infections have occurred in immunocompromised and neutropenic patients. Children treated with Soliris may be at increased risk of developing serious infections due to Streptococcus pneumoniae and Haemophilus influenzae type b (Hib). Administer vaccinations for the prevention of Streptococcus pneumoniae and Haemophilus influenzae type b (Hib) infections according to ACIP guidelines. Use caution when administering Soliris to patients with any systemic infection [see Warnings and Precautions (5.1)].

5.4 Monitoring Disease Manifestations after Soliris Discontinuation

Treatment Discontinuation for PNH

Monitor patients after discontinuing Soliris for at least 8 weeks to detect hemolysis.

Treatment Discontinuation for aHUS

After discontinuing Soliris, monitor patients with aHUS for signs and symptoms of thrombotic microangiopathy (TMA) complications for at least 12 weeks. In aHUS clinical trials, 18 patients (6 in the prospective studies) discontinued Soliris treatment. TMA complications occurred following a missed dose in 5 patients, and Soliris was reinstituted in 4 of these 5 patients.

Clinical signs and symptoms of TMA include changes in mental status, seizures, angina, dyspnea, or thrombosis. In addition, the following changes in laboratory parameters may identify a TMA complication: occurrence of five or more reported complications of any one of the following: a decrease in platelet count by 25% or more compared to baseline or peak platelet count during Soliris treatment; an increase in serum creatinine by 25% or more compared to baseline or nadir during Soliris treatment; or an increase in serum LDH by 25% or more over baseline or nadir during Soliris treatment. If TMA complications occur after Soliris discontinuation, consider reinstitution of Soliris treatment, plasma therapy (plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI), or appropriate organ-specific supportive measures.

5.5 Thrombosis Prevention and Management

The effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established. Therefore, treatment with Soliris should not alter anticoagulant management.

5.6 Infusion Reactions

Administration of Soliris may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no patients experienced an infusion reaction which required discontinuation of Soliris. Interrupt Soliris infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious Meningococcal Infections [see Warnings and Precautions (5.5)]
- Other Infections [see Warnings and Precautions (5.3)]
- Monitoring Disease Manifestations After Soliris Discontinuation [see Warnings and Precautions (5.4)]
- Thrombosis Prevention and Management [see Warnings and Precautions (5.5)]
- Infusion Reactions [see Warnings and Precautions (5.6)]

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Meningococcal infections are the most important adverse reactions experienced by patients receiving Soliris. In PNH clinical studies, two patients experienced meningococcal sepsis. Both patients had previously received a meningococcal vaccine. In clinical studies among patients without PNH, meningococcal meningitis occurred in one unvaccinated patient. Meningococcal sepsis occurred in one previously vaccinated patient enrolled in the retrospective aHUS study during the post-study follow-up period [see Warnings and Precautions (5.1)].

PNH

The data described below reflect exposure to Soliris in 196 adult patients with PNH, age 18-85, of whom 55% were female. All had signs or symptoms of intravascular hemolysis. Soliris was studied in a placebo-controlled clinical study (PNH Study 1, in which 43 patients received Soliris and 44 placebo); a single arm clinical study (PNH Study 2); and a long term extension study (E05-001). 182 patients were exposed for greater than one year. All patients received the recommended Soliris dose regimen.

Table 4: Adverse Reactions Reported in 5% or More of Soliris Treated Patients with PNH and Greater than Placebo or the Concomitant Study

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Soliris</th>
<th>Placebo</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>19 (44)</td>
<td>12 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>16 (23)</td>
<td>8 (16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>8 (19)</td>
<td>4 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (16)</td>
<td>5 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (12)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>5 (12)</td>
<td>4 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex infections</td>
<td>3 (7)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinusitis</td>
<td>3 (7)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>3 (7)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (7)</td>
<td>2 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (7)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>3 (7)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The safety of Soliris therapy in patients with aHUS was evaluated in four prospective, single-arm studies, three in adult and adolescent patients (Studies C08-002A/B, C08-003A/B, and C10-004), one in pediatric and adolescent patients (Study C10-003), and one retrospective study (Study C09-001r).

In Study C10-003, included 22 pediatric and adolescent patients, of which 18 patients were less than 12 years of age. One patient discontinued Soliris due to an adverse event (severe agitation).

In a 26-week placebo-controlled trial evaluating the effect of Soliris for the treatment of gMG (gMG Study 1), 62 patients received Soliris at the recommended dosage regimen and 63 patients received placebo. Patients were 19 to 79 years of age, and 66% were female. Table 8 displays the most common adverse reactions from gMG Study 1 that occurred in ≥5% of Soliris-treated patients and at a greater frequency than in placebo-treated patients.

### Table 6: Per Patient Incidence of Adverse Reactions in 10% or More Patients Enrolled in StudyC10-003

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Soliris (n=62)</th>
<th>Placebo (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4 (60)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (72)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (120)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Malaise</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (90)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>11 (165)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cough</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12 (180)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cough</td>
<td>10 (150)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (180)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>15 (225)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>4 (60)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>12 (180)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (180)</td>
<td>3 (5)</td>
</tr>
</tbody>
</table>

### Table 7: Adverse Reactions Occurring in at Least 15% of Patients Less than 18 Years of Age Enrolled in Study C09-001r

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>32 (32%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>36 (36%)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>23 (23%)</td>
</tr>
<tr>
<td>Vomitting</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (9%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

### Table 8: Adverse Reactions Reported in 5% or More of Soliris-Treated Patients in gMG Study 1 and at a Greater Frequency than in Placebo-Treated Patients

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Soliris (n=62)</th>
<th>Placebo (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4 (60)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (72)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (120)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Malaise</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (90)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>11 (165)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cough</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12 (180)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>7 (105)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>8 (120)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>17 (255)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Anemia</td>
<td>12 (180)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (150)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (180)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>3 (45)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Headache</td>
<td>10 (150)</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

In Studies C08-002A/B, C08-003A/B and C10-004 combined, 60% (47/78) of patients experienced a serious adverse event (SAE). The most commonly reported SAEs were infections (24%), hypertension (5%), chronic renal failure (5%), and renal impairment (5%). Five patients discontinued Soliris due to adverse events; three due to worsening renal function, one due to new diagnosis of Systemic Lupus Erythematosus, and one due to meningococcal meningitis. Study C10-003 included 22 pediatric and adolescent patients, of which 18 were less than 12 years of age. All patients received the recommended dosage of Soliris. Median exposure was 44 weeks (range: 1 day-87 weeks).

Table 8 summarizes all adverse events reported in at least 10% of patients enrolled in Study C10-003.
The immunogenicity of Soliris has been evaluated using two different immunoassays for the detection of anti-eculizumab antibodies: a direct enzyme-linked immunosorbent assay (ELISA) using the Fab fragment of eculizumab as target was used for the PNH indication; and an electro-chemiluminescence (ECL) bridging assay using the eculizumab whole molecule as target was used for the aHUS indication, as well as for additional patients with PNH. In the PNH population, antibodies against eculizumab were detected in 13/320 (4%) patients using the ELISA assay and 15/361 (4%) patients using the ECL assay. In the aHUS population, antibodies to Soliris were detected in 3/100 (3%) patients using the ECL assay. An ECL-based neutralization assay with a low sensitivity of 2 mcg/mL was performed to detect neutralizing antibodies for the 3 patients with aHUS and the 5 patients with PNH with positive samples using the ECL assay. Two of 161 patients with PNH (1.2%) and 1 of 100 patients with aHUS (1%) had low positive values for neutralizing antibodies. None of 62 patients with gmg had antibodies to Soliris detected immediately following the 26-week active treatment. No apparent correlation of antibody development to clinical response was observed.

12. CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Eculizumab, the active ingredient in Soliris, is a monoclonal antibody that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Soliris inhibits terminal complement-mediated intravascular hemolysis in PNH patients and complement-mediated thrombotic microangiopathy (TMA) in patients with aHUS.

The precise mechanism by which eculizumab exerts its therapeutic effect in gmg patients is unknown, but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction.

12.2 Pharmacodynamics
In the placebo-controlled clinical study (PNH Study 1), Soliris when administered as recommended reduced serum LDH levels from 2220 ± 1024 U/L (mean ± SD) at baseline to 700 ± 888 U/L by week one and maintained the effect through the end of the study at week 26 (267 ± 432 U/L) in patients with PNH. In the single arm clinical study (PNH Study 2), the effect was maintained through week 52 [see Clinical Studies (4)].

In patients with PNH, aHUS, and gmg, free C5 concentrations of < 0.5 mcg/mL was correlated with complete blockade of terminal complement activity.

12.3 Pharmacokinetics
Following intravenous maintenance doses of 900 mg once every 2 weeks in patients with PNH, the week 26 observed mean ± SD serum eculizumab maximum concentration (Cmax) was 194 ± 76 mcg/mL and the trough concentration (Cmin) was 58 ± 30 mcg/mL. Following intravenous maintenance doses of 1200 mg once every 2 weeks in patients with aHUS, the week 26 observed mean ± SD Cmax was 242 ± 101 mcg/mL. Following intravenous maintenance doses of 1200 mg once every 2 weeks in patients with gmg, the week 26 observed mean ± SD Cmax was 783 ± 286 mcg/mL, and the Cmin was 341 ± 172 mcg/mL.

Steady state was achieved 4 weeks after starting eculizumab treatment, with accumulation ratio of approximately 2-fold at all studied indications. Population pharmacokinetic analyses showed that eculizumab pharmacokinetics were dose-linear and time-independent over the 600 mg to 1200 mg dose range, with inter-individual variability of 21% to 38%.

Distribution
The eculizumab volume of distribution for a typical 70 kg patient was 5 L to 8 L.

Elimination
The half-life of eculizumab was approximately 270 h to 375 h.

Premature exchange for infusion increased the clearance of eculizumab by approximately 250-fold and reduced the half-life to 1.26 h. Supplemental dosing is recommended when Soliris is administered to patients receiving plasma exchange or infusion [see Dosage and Administration (2.4)].

Specific Populations
Age, Sex, and Race:
The pharmacokinetics of eculizumab were not affected by age (2 to 85 years), sex, or race.

Renal Impairment:
Renal function did not affect the pharmacokinetics of eculizumab in PNH (creatinine clearance of 8 mL/min to 396 mL/min calculated using Cockcroft-Gault formula; eculizumab estimated glomerular filtration rate [eGFR] of 5 mL/min/1.73 m2 to 105 mL/min/1.73 m2 using the Modification of Diet in Renal Disease [MDRD] formula), or gmg patients (eGFR of 44 mL/min/1.73 m2 to 168 mL/min/1.73 m2 using MDRD formula).

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term animal carcinogenicity studies of eculizumab have not been conducted.

Genotoxicity studies have not been conducted with eculizumab. Effects of eculizumab upon fertility have not been studied in animals. Intrauterine injections of male and female mice with a murine anti-C5 antibody at up to 48 times the equivalent of the clinical dose of Soliris had no adverse effects on mating or fertility.

14 CLINICAL STUDIES
14.1 Paroxysmal Nocturnal Hemoglobinuria (PNH)
The safety and efficacy of Soliris in PNH patients with hemolysis was assessed in a randomized, double-blind, placebo-controlled 26-week study (PNH Study 1, NCT01722330). PNH patients were also treated with Soliris in a single arm 52-week study (PNH Study 2, NCT01122034) and in a separate expansion study (NCT00175021). Patients received eculizumab monoclonal antibody infusion every 2 weeks as maintenance treatment for at least 26 weeks. Subsequent maintenance infusions were dosed every 6 weeks.
Patients treated with Soliris had significantly reduced (p<0.001) hemolytic resulting in improvements in anemia as indicated by increased hemoglobin stabilization and reduced need for RBC transfusions compared to placebo treated patients (Table 10). These effects were seen among patients within each of the three pre-study RBC transfusion strata (4 - 14 units; 15 - 25 units; > 25 units). After 3 weeks of Soliris treatment, patients reported less fatigue and improved health-related quality of life. Because of the study sample size and duration, the effects of Soliris on thrombotic events could not be determined.

Table 10: PHiW Study 1 Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>Soliris</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with stabilized hemoglobin levels</td>
<td>44</td>
<td>43</td>
</tr>
<tr>
<td>Packed RBC units transfused per patient (median) (range)</td>
<td>0 (2 - 21)</td>
<td>0 (0 - 16)</td>
</tr>
</tbody>
</table>

Table 11: Baseline Characteristics of Patients Enrolled in Study C08-002/A

<table>
<thead>
<tr>
<th>Study C08-002/A</th>
<th>Placebo</th>
<th>Soliris</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from aHUS diagnosis until screening in months, median (min, max)</td>
<td>10 (2, 26)</td>
<td>10 (2, 26)</td>
</tr>
<tr>
<td>Time from current clinical TMA manifestation until screening in months, median (min, max)</td>
<td>&lt;1 (&lt;1, 4)</td>
<td>&lt;1 (&lt;1, 4)</td>
</tr>
<tr>
<td>Baseline Hct (median)</td>
<td>38 (31, 43)</td>
<td>38 (31, 43)</td>
</tr>
<tr>
<td>Baseline LDH (ULN, median range)</td>
<td>169 (112, 261)</td>
<td>269 (134, 634)</td>
</tr>
</tbody>
</table>

Patients in Study C08-002/A received Soliris for a minimum of 26 weeks. In Study C08-002/A, the median duration of Soliris therapy was approximately 114 weeks (range: 26 to 129 weeks).

Table 15: Efficacy Results in Pediatric Patients Enrolled in aHUS Study 3

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Study C08-003/A (n = 17)</th>
<th>Study C08-003/A at 2 yrs (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete TMA response, n (%)</td>
<td>8 (47)</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Median duration of complete TMA response, weeks (range)</td>
<td>30 (12, 48)</td>
<td>34 (22, 56)</td>
</tr>
<tr>
<td>Hematologic normalization, n (%)</td>
<td>10 (59)</td>
<td>19 (95)</td>
</tr>
</tbody>
</table>

1 At data cut-off (September 8, 2010).
2 At data cut-off (April 20, 2012).
3 Calculated at each post-dose day of measurement (excluding Days 1 to 4) using a repeated measurement ANOVA model.
4 In Study C08-003/A, 85% of patients had normal platelet counts and 80% of patients had normal LDH levels at baseline, so hematologic normalization in this population reflects maintenance of normal parameters in the absence of PE/PI.

Retrospective Study in Patients with aHUS (C09-001r)

The efficacy results for the aHUS retrospective study (Study C09-001r) were generally consistent with results of the two prospective studies. Soliris reduced signs of complement-mediated TMA activity, as shown by an increase in mean platelet counts from baseline. Mean platelet count (SD) increased from 171 ± 83 x10^9/L at baseline to 239 ± 119 x10^9/L at week 26 (mean platelet count (SD) at week 26: 254 ± 79 x10^9/L).

Table 13: Table 13 summarizes the key baseline clinical and disease-related characteristics of patients enrolled in Study C08-003/A.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C08-003/A (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from aHUS diagnosis until screening in months, median (min, max)</td>
<td>48 (66, 286)</td>
</tr>
<tr>
<td>Time from current clinical TMA manifestation until screening in months, median (min, max)</td>
<td>49 (9, 143)</td>
</tr>
</tbody>
</table>

Table 14: Efficacy Results for Study C08-003/A

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Study C08-003/A/B (n = 26 wks)</th>
<th>Study C08-003/A/B at 2 yrs (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete TMA response, n (%)</td>
<td>18 (90)</td>
<td>38 (190)</td>
</tr>
<tr>
<td>Median duration of complete TMA response, weeks (range)</td>
<td>37 (25, 62)</td>
<td>38 (25, 62)</td>
</tr>
<tr>
<td>Hematologic normalization, n (%)</td>
<td>18 (90)</td>
<td>38 (190)</td>
</tr>
</tbody>
</table>

1 At data cut-off (April 20, 2012).
2 At data cut-off (April 20, 2012).
3 Calculated at each post-dose day of measurement (excluding Days 1 to 4) using a repeated measurement ANOVA model.
4 In Study C08-003/A, 85% of patients had normal platelet counts and 80% of patients had normal LDH levels at baseline, so hematologic normalization in this population reflects maintenance of normal parameters in the absence of PE/PI.

The overall efficacy results for these pediatric patients appeared consistent with what was observed in patients enrolled in Studies C08-002/A and C08-003/A/B (Table 15). No pediatric patient required new dialysis during treatment with Soliris.
Reduction in terminal complement activity and an increase in platelet count relative to baseline were observed after dialysis at study baseline were able to discontinue dialysis during Soliris treatment.

Table 17: Efficacy Results for Study C10-004

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C10-004</th>
<th>N = 41</th>
<th>Study C10-004AHS</th>
<th>N = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from aHUS diagnosis until start of study drug in months, median (range)</td>
<td>0.79 (0.03 – 3.11)</td>
<td></td>
<td>2.4 (0.23 – 20.71)</td>
<td></td>
</tr>
<tr>
<td>Time from current clinical TMA manifestation until first study dose in months, median (range)</td>
<td>0.52 (0.03 – 19)</td>
<td></td>
<td>13 (0.5 – 43)</td>
<td></td>
</tr>
<tr>
<td>Baseline platelet count (&lt; 10^11/L), median (range)</td>
<td>125 (16 – 332)</td>
<td></td>
<td>375 (131 – 3318)</td>
<td></td>
</tr>
</tbody>
</table>

Patients in Study C10-004 received Soliris for a minimum of 26 weeks. In Study C10-004, the median duration of Soliris therapy was approximately 50 weeks (range: 13 weeks to 86 weeks).

Renal function, as measured by eGFR, was improved during Soliris therapy. The mean eGFR (± SD) increased from 17 ± 12 mL/min/1.73m² at baseline to 47 ± 24 mL/min/1.73m² by 26 weeks. Twenty-four of the 26 patients who required dialysis at study baseline were able to discontinue dialysis during Soliris treatment.

Reduction in terminal complement activity and an increase in platelet count relative to baseline were observed after commencement of Soliris. Soliris reduced signs of complement-mediated TMA activity, as shown by an increase in mean platelet counts from baseline to 26 weeks. Study C10-004, mean platelet count (± SD) increased from 110 ± 66 x10^9/L at baseline to 200 ± 84 x10^9/L by one week, and this effect was maintained through 26 weeks (mean platelet count ± SD at week 26: 252 ± 70 x10^9/L). In Study C10-004, responses to Soliris were similar in patients with and without identified mutations in genes encoding complement regulatory factor proteins or auto-antibodies to factor H.

Table 18: Baseline Characteristics of Patients Enrolled in Study C10-003

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C10-003</th>
<th>N = 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from aHUS diagnosis until start of study drug in months, median (range)</td>
<td>0.30 (0.03 – 2)</td>
<td></td>
</tr>
<tr>
<td>Time from current clinical TMA manifestation until first study dose in months, median (range)</td>
<td>0.33 (0.03 – 4)</td>
<td></td>
</tr>
<tr>
<td>Baseline platelet count (x10^11), median (range)</td>
<td>110 (9 – 275)</td>
<td></td>
</tr>
<tr>
<td>Baseline LDH, L/L, median (range)</td>
<td>310 (120 – 900)</td>
<td></td>
</tr>
</tbody>
</table>

In Study C10-003, patients enrolled who displayed signs of thrombotic microangiopathy (TMA) in whom age at diagnosis (38 years in each group), female sex (62% with TMA and 61% without TMA), and complement geno-14.3 Generalized Myasthenia Gravis (gMG) type (95% ABO+) were similar in patients with and without identified mutations in genes encoding complement regulatory factor proteins or auto-antibodies to factor H.

Table 19: Efficacy Study for C10-003

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C10-003</th>
<th>N = 41</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete TMA response, n (%)</td>
<td>35 (85)</td>
<td></td>
</tr>
<tr>
<td>Median Duration of complete TMA response, weeks (range)</td>
<td>40 (17.7 – 86)</td>
<td></td>
</tr>
</tbody>
</table>

The efficacy of Soliris for the treatment of gMG was established in gMG Study 1 (NCT01997229), a 26-week randomized, double-blind, parallel-group, placebo-controlled, multicenter trial that enrolled patients who met the following criteria at screening:

1. Severe generalized weakness that interferes with basic activities of daily living
2. Presence of anti-acetylcholine receptor (anti-AChR) antibodies in serum
3. Additionally, patients with a history of thymectomy were included.

The primary efficacy endpoint for gMG Study 1 was a comparison of the change from baseline between treatment groups in the Myasthenia Gravis-Specific Activities of Daily Living scale (gMG-ADL). The results of the analysis of the MG-ADL and QMG from gMG Study 1 are shown in Table 20.

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• headache with a stiff neck or stiff back
• fever
• fever and a rash
• confusion
• muscle aches with flu-like symptoms
• eyes sensitive to light

Inform patients that they will be given a Soliris Patient Safety Information Card that they should carry with them at all times. This card describes symptoms which, if experienced, should prompt the patient to immediately seek medical evaluation.

Other Infections
Inform patients that there may be an increased risk of other types of infections, particularly those due to encapsulated bacteria. Additionally, Aspergillus infections have occurred in immunocompromised and neutropenic patients. Inform parents or caregivers of children receiving Soliris for the treatment of aHUS that their child should be vaccinated against Streptococcus pneumoniae and Haemophilus influenzae type b (Hib) according to current medical guidelines.

Discontinuation
Inform patients with PNH that they may develop hemolysis due to PNH when Soliris is discontinued and that they will be monitored by their healthcare professional for at least 8 weeks following Soliris discontinuation.
Inform patients with aHUS that there is a potential for TMA complications due to aHUS when Soliris is discontinued and that they will be monitored by their healthcare professional for at least 12 weeks following Soliris discontinuation.
Inform patients who discontinue Soliris to keep the Soliris Patient Safety Information Card with them for three months after the last Soliris dose, because the increased risk of meningococcal infection persists for several weeks following discontinuation of Soliris.

Manufactured by:
Alexion Pharmaceuticals, Inc.
100 College Street
New Haven, CT 06510 USA
US License Number 1743

This product, or its use, may be covered by one or more US patents, including US Patent No. 6,355,245 in addition to others including patents pending.
MEDICATION GUIDE
SOLIRIS® (so-leer-is) (eculizumab)

injection, for intravenous use

What is the most important information I should know about SOLIRIS?
SOLIRIS is a medicine that affects your immune system. SOLIRIS can lower the ability of your immune system to fight infections.

- SOLIRIS increases your chance of getting serious and life-threatening meningococcal infections. Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

1. You must receive meningococcal vaccines at least 2 weeks before your first dose of SOLIRIS unless you have already had this vaccine. If your doctor decided that urgent treatment with SOLIRIS is needed, you should receive meningococcal vaccination as soon as possible.

2. If you had a meningococcal vaccine in the past, you might need additional vaccination before starting SOLIRIS. Your doctor will decide if you need additional meningococcal vaccination.

3. Meningococcal vaccines do not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection:
   - headache with nausea or vomiting
   - headache and a fever
   - headache with a stiff neck or stiff back
   - fever
   - fever and a rash
   - confusion
   - muscle aches with flu-like symptoms
   - eyes sensitive to light

Your doctor will give you a Patient Safety Card about the risk of meningococcal infection. Carry it with you at all times during treatment and for 3 months after your last SOLIRIS dose. Your risk of meningococcal infection may continue for several weeks after your last dose of SOLIRIS. It is important to show this card to any doctor or nurse who treats you. This will help them diagnose and treat you quickly.

SOLIRIS is only available through a program called the SOLIRIS REMS. Before you can receive SOLIRIS, your doctor must:
- enroll in the SOLIRIS REMS program
- counsel you about the risk of meningococcal infection
- give you information about the symptoms of meningococcal infection
- give you a Patient Safety Card about your risk of meningococcal infection, as discussed above
- make sure that you are vaccinated with a meningococcal vaccine

SOLIRIS may also increase the risk of other types of serious infections. If your child is treated with SOLIRIS, make sure that your child receives vaccinations against Streptococcus pneumoniae and Haemophilus influenza type b (Hib).

What is SOLIRIS?
SOLIRIS is a prescription medicine called a monoclonal antibody. SOLIRIS is used to treat:
- adults with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH)
- adults and children with a disease called atypical Hemolytic Uremic Syndrome (aHUS)
- adults with a disease called generalized Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AchR) antibody positive

It is not known if SOLIRIS is safe and effective in children with PNH or gMG.

Who should not receive SOLIRIS?
Do not receive SOLIRIS if you:
- have a meningococcal infection.
- have not been vaccinated against meningitis infection unless your doctor decides that urgent treatment with SOLIRIS is needed. See “What is the most important information I should know about SOLIRIS?”

Before you receive SOLIRIS, tell your doctor about all of your medical conditions, including if you:
- have an infection or fever.
- are pregnant or plan to become pregnant. It is not known if SOLIRIS will harm your unborn baby.

- are breastfeeding or plan to breastfeed. It is not known if SOLIRIS passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SOLIRIS and other medicines can affect each other causing side effects.

It is important that you:
- have all recommended vaccinations before you start SOLIRIS.
- stay up-to-date with all recommended vaccinations during treatment with SOLIRIS.

Know the medications you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I receive SOLIRIS?
- SOLIRIS is given through a vein (I.V. or intravenous infusion) usually over 35 minutes in adults and 1 to 4 hours in pediatric patients. If you have an allergic reaction during your SOLIRIS infusion, your doctor may decide to give SOLIRIS more slowly or stop your infusion.
- If you are an adult, you will usually receive a SOLIRIS infusion by your doctor:
  - weekly for five weeks, then
  - every 2 weeks
- If you are less than 18 years of age, your doctor will decide how often you will receive SOLIRIS depending on your age and body weight
- After each infusion, you should be monitored for one hour for allergic reactions. See “What are the possible side effects of SOLIRIS?”
- If you forget or miss a SOLIRIS infusion, call your doctor right away.
- If you have PNH, your doctor will need to monitor you closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS may cause breakdown of your red blood cells due to PNH.

Symptoms or problems that can happen due to red blood cell breakdown include:
- drop in the number of your red blood cell count
- drop in your platelet count
- confusion
- difficulty breathing
- chest pain
- kidney problems
- blood clots

- If you have aHUS, your doctor will need to monitor you closely during and for at least 12 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS may cause symptoms or problems related to abnormal clotting (thrombotic microangiopathy).

Symptoms or problems that can happen due to abnormal clotting may include:
- stroke
- confusion
- seizures
- chest pain (angina)
- difficulty breathing
- kidney problems
- swelling in arms or legs
- a drop in your platelet count

What are the possible side effects of SOLIRIS?
SOLIRIS can cause serious side effects including:
- See “What is the most important information I should know about SOLIRIS?”
- Serious allergic reactions. Serious allergic reactions can happen during your SOLIRIS infusion. Tell your doctor or nurse right away if you get any of these symptoms during your SOLIRIS infusion:
  - chest pain
  - trouble breathing or shortness of breath
  - swelling of your face, tongue, or throat
  - feel faint or pass out

If you have an allergic reaction to SOLIRIS, your doctor may need to infuse SOLIRIS more slowly, or stop SOLIRIS. See “How will I receive SOLIRIS?”
The most common side effects in people with PNH treated with SOLIRIS include:

- headache
- pain or swelling of your nose or throat (nasopharyngitis)
- back pain
- nausea

The most common side effects in people with aHUS treated with SOLIRIS include:

- headache
- abdominal pain
- cough
- fever
- diarrhea
- vomiting
- swelling of legs or feet (peripheral edema)
- hypertension
- pain or swelling of your nose or throat (nasopharyngitis)
- nausea
- common cold (upper respiratory infection)
- anemia
- urinary tract infections

The most common side effects in people with gMG treated with SOLIRIS include:

- muscle and joint (musculoskeletal) pain

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of SOLIRIS. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of SOLIRIS.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SOLIRIS for a condition for which it was not prescribed. Do not give SOLIRIS to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or doctor for information about SOLIRIS that is written for health professionals.

What are the ingredients in SOLIRIS?

Active ingredient: eculizumab

Inactive ingredients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 (vegetable origin) and Water for Injection

Manufactured by Alexion Pharmaceuticals, Inc., 100 College Street, New Haven, CT 06510 USA.

Medication Guide has been approved by the U.S. Food and Drug Administration

Revised: 10/2017