The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Soliris is a complement inhibitor indicated for:

• The treatment of adult patients with generalized Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AchR) antibody positive (1.3).

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).

For intravenous infusion only
PNH Dosage Regimen: (2.1)
aHUS Dosage Regimen: (2.2)
gMG Dosage Regimen (2.3)

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

CONTRAINDICATIONS
Soliris is contraindicated in:
• Patients with unresolved serious Neisseria meningitidis infection (4).
• Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection (5.1).

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, pyrosis (6.5).

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.

USE IN SPECIFIC POPULATIONS
Pregnancy: Based on animal data, Soliris may cause fetal harm (8.1).

See 17 PATIENT COUNSELING INFORMATION and Medication Guide.

<table>
<thead>
<tr>
<th>INDICATIONS AND USAGE</th>
<th>TABLE 1: Dosing Recommendations in Patients Less Than 18 Years of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Paroxysmal Nocturnal Hemoglobinuria (PNH)</td>
<td>Patient Body Weight</td>
</tr>
<tr>
<td>1.2 Atypical Hemolytic Uremic Syndrome (aHUS)</td>
<td>Induction</td>
</tr>
<tr>
<td>1.3 Generalized Myasthenia Gravis (gMG)</td>
<td>Maintenance</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td></td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td>40 kg and over</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td>30 mg to less than 40 kg</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td>20 kg to less than 40 kg</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td>10 kg to less than 20 kg</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td>5 kg to less than 10 kg</td>
</tr>
<tr>
<td>2.2 Recommended Dosage Regimen - aHUS</td>
<td></td>
</tr>
</tbody>
</table>
Administer Soliris at the recommended dosage regimen time points, or within two days of these time points.

### 2.3 Recommended Dosage Regimen – gMG
For patients with generalized Myasthenia Gravis, 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.

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

### 2.4 Dose Adjustment in Case of Plasmapheresis, Plasma Exchange, or Fresh Frozen Plasma Infusion
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 Interventions</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></td>
<td>≥600 mg</td>
<td>600 mg per each plasmapheresis or plasma exchange session</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 admixture concentration of 5 mg/mL using the following steps:
- Withdraw the required amount of Soliris from the vial into a sterile syringe.
- Transfer the recommended dose to an infusion bag.
- 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 Injection, 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. Admised solutions of Soliris are stable for 24 h at 2-8°C (36-46°F) and at room temperature.

If an adverse reaction occurs during the administration of Soliris, the infusion may be slowed or stopped at the discretion of the physician. If the infusion is slowed, the total infusion time should not exceed two hours in adults. Monitor the patient for at least one hour following completion of the infusion for signs or symptoms of an infusion reaction.

### 3 DOSAGE FORMS AND STRENGTHS
Injection: 300 mg single-dose vials containing each 30 mL of 10 mg/mL sterile, colorless, preservative-free eclizumab 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 (5.1)].

### 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).

Vaccination for meningococcal disease according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with complement deficiencies. Recommmendations of patients in accordance with ACIP recommendations, considering the duration of Soliris therapy. Immunize 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 against 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 (6.7)]. 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-SOLIRIS (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 an increased risk of developing serious infections due to Streptococcus pneumoniae and Haemophilus influenza type b (Hib). Administer vaccinations for the prevention of Streptococcus pneumoniae and Haemophilus influenza 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.

#### 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 (5.1)]
- 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 summarizes the adverse reactions that occurred at a numerically higher rate in the Soliris group than the placebo group and at a rate of 5% or more among patients treated with Soliris.

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

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Soliris</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>19 (44)</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>10 (23)</td>
<td>8 (18)</td>
</tr>
<tr>
<td>Back pain</td>
<td>8 (19)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (16)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (12)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Cough</td>
<td>5 (12)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Herpes simplex infections</td>
<td>3 (7)</td>
<td>0</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>3 (7)</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Constipation</td>
<td>3 (7)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>3 (7)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>2 (5)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>
In the placebo-controlled clinical study, serious adverse reactions occurred among 4 (6%) patients receiving Soliris and 9 (21%) patients receiving placebo. The serious reactions included infections and progression of PNH. No deaths occurred in the study and no patients receiving Soliris experienced a thrombotic event; one thrombotic event occurred in a patient receiving placebo.

Among 153 patients with PNH treated with Soliris in the single arm, clinical study or the follow-up study, the adverse reactions were similar to those reported in the placebo-controlled clinical study. Serious adverse reactions occurred among 16% of the patients in these studies. The most common serious adverse reactions were: viral infection (2%), headache (2%), anemia (2%), and pyrexia (2%).

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).

The data described below were derived from 78 adult and adolescent patients with Studies C08-002A/B, C08-003A/B, and C10-004 and all patients received the dosage regimen and 63 patients received placebo. Patients were 19 to 79 years of age, and 66% were female. Table 6 displays the most common adverse reactions from gMG Study 1 that occurred in ≥5% of Soliris-treated patients and at a greater frequency than placebo.

Infections and Infestations
Bronchitis 10 (59) 9 (45) 7 (17) 26 (33)
Nasopharyngitis 3 (18) 2 (10) 4 (10) 9 (12)
Gastroenteritis 3 (18) 11 (55) 7 (17) 21 (27)
Upper respiratory tract infection 5 (29) 8 (40) 2 (5) 15 (19)
Urinary tract infection 6 (35.3) 3 (15) 8 (20) 17 (22)
Gastrointestinal Disorders
Diarrhea 8 (47) 8 (40) 12 (33) 29 (37)
Vomiting 8 (47) 9 (45) 6 (15) 23 (30)
Nausea 5 (29) 8 (40) 5 (12) 18 (23)
Abdominal pain 3 (18) 6 (30) 6 (15) 15 (19)
Nervous System Disorders
Headache 7 (41) 10 (50) 15 (37) 32 (41)
Blood and Lymphatic System Disorders
Anemia 6 (33) 7 (35) 7 (17) 20 (26)
Leukopenia 4 (22) 3 (15) 5 (12) 12 (15)
Psychiatric Disorders
Insomnia 4 (24) 2 (10) 5 (12) 11 (14)
Renal and Urinary Disorders
Renal Impairment 5 (29) 3 (15) 6 (15) 14 (18)
Proteinuria 2 (12) 1 (5) 5 (12) 8 (10)
Respiratory, Thoracic and Mediastinal Disorders
Cough 4 (24) 6 (30) 8 (20) 18 (23)
General Disorders and Administration Site Conditions
Fatigue 3 (18) 4 (20) 3 (7) 10 (13)
Peripheral edema 5 (29) 4 (20) 9 (22) 18 (23)
Pyrexia 4 (24) 5 (25) 7 (17) 16 (21)
Anesthesia 3 (18) 4 (20) 6 (15) 13 (17)
Eye Disorder
5 (29) 2 (10) 8 (20) 15 (19)
Metabolism and Nutrition Disorders
Hypokalemia 3 (18) 2 (10) 4 (10) 9 (12)
Neoplasms benign, malignant, and unspecified (including cysts and polyps) 1 (6) 6 (30) 1 (20) 8 (10)
Skin and Subcutaneous Tissue Disorders
Rash 2 (12) 3 (15) 6 (15) 11 (14)
Pruritus 1 (6) 3 (15) 4 (10) 8 (10)
Musculoskeletal and Connective Tissue Disorders
Arthritis 1 (6) 2 (10) 7 (17) 10 (13)
Back pain 3 (18) 3 (15) 2 (5) 8 (10)

Infections and Infestations
Bronchitis 4 (22) 4 (18)
Nasopharyngitis 3 (18) 6 (27)
Rhinitis 4 (22) 4 (18)
Upper respiratory tract infection 3 (17) 4 (18)
Urinary tract infection 3 (17) 3 (14)
Musculoskeletal and Connective Tissue Disorders
Rheumatoid arthritis 2 (11) 3 (14)
Nervous System Disorders
Headache 3 (17) 4 (18)
Renal and Urinary Disorders
3 (17) 4 (18)
Respiratory, Thoracic and Mediastinal Disorders
Cough 7 (39) 8 (26)
Oral pharyngeal pain 1 (6) 3 (14)
Skin and Subcutaneous Tissue Disorders
Rash 4 (22) 4 (18)
Vascular Disorders
Hypertension 4 (22) 4 (18)

In Study C10-003, 59% (13/22) of patients experienced a serious adverse event (SAE). The most commonly reported SAEs were hypertension (9%), viral gastroenteritis (9%), pyrexia (9%), and upper respiratory infection (8%). One patient discontinued Soliris due to an adverse event (severe agitation).

Analysis of retrospectively collected adverse event data from pediatric and adult patients enrolled in Study C09-001r (N=30) revealed a safety profile that was similar to that which was observed in the two prospective studies. Study C09-001r included 19 pediatric patients less than 12 years of age. Overall, the safety of Soliris in pediatric patients with aHUS enrolled in Study C010-001 appeared similar to that observed in adult patients. The most common (≥15%) adverse events occurring in pediatric patients are presented in Table 7.

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>Reaction</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Rash</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Back pain</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (28)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (22)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 6: Per Patient Incidence of Adverse Reactions in 10% or More Patients Enrolled in StudyC010-003

<table>
<thead>
<tr>
<th>Reaction</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Rash</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Back pain</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (28)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (22)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0 (0)</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>Reaction</th>
<th>Soliris (N=62) n (%)</th>
<th>Placebo (N=63) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>4 (60)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1 (20)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (40)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection*</td>
<td>2 (40)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>3 (60)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>2 (40)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Tachycardia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (40)</td>
<td>2 (20)</td>
</tr>
</tbody>
</table>

General Myasthenia Gravis (gMG)
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 6 displays the most common adverse reactions from gMG Study 1 that occurred in ≥5% of Soliris-treated patients and at a greater frequency than placebo.

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>Reaction</th>
<th>Soliris (N=62) n (%)</th>
<th>Placebo (N=63) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5 (8)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>5 (8)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>4 (7)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex virus infections</td>
<td>5 (8)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Injury, Poisoning, and Procedural Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contusion</td>
<td>5 (8)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>9 (15)</td>
<td>5 (8)</td>
</tr>
</tbody>
</table>

The most common adverse reactions (≥10%) that occurred in Soliris-treated patients in the long-term extension to gMG Study 1, Study ECO1-MG-302, that are not included in Table 8 were headache (26%), nasopharyngitis (24%), diarrhea (16%), arthralgia (12%), upper respiratory tract infection (11%), and nausea (10%).

6.2 Immunogenicity
As with all proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to eculizumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.
The immunogenicity of Soliris has been evaluated using two different immunooassays 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 PHiN indication; and an electro-chemiluminescence (ECL) bridging assay using the ECL bridging assay as target was used for the aHUS indication, as well as for additional patients with PHiN. In the PHiN population, antibodies to Soliris were detected in 3/196 (2%) patients using the ELISA assay and in 5/161 (3%) patients using the ECL assay. In the aHUS population, antibodies to Soliris were detected in 5/301 (2%) patients using the ECL assay. An ECL-based neutralizing 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 PHiN with positive samples using the ECL assay. Two of 161 patients with PHiN (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.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Soliris. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Cases of serious or fatal meningoencephalitis have been reported.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

Alexion's PHiN and aHUS disease registries collect pregnancy outcomes in women exposed to Soliris during pregnancy. To enroll or to obtain information, contact www.pregnancyregistry.com or www.ahusregistry.com, or call (215)-616-3556.

Risk Summary

There are no available data on Soliris use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. Soliris, a recombinant IgG molecule (humanized anti-C5 antibody), is expected to cross the placenta. Animal studies using a mouse analogue of the Soliris molecule (murine anti-C5 antibody) showed increased rates of developmental abnormalities and an increased rate of death and moribund offspring at doses 2-8 times the human dose. Advise pregnant women of the potential risk to a fetus. Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively.

Data

Animal Data

Animal reproduction studies were conducted in mice using doses of a murine anti-C5 antibody that approximated 2.4-3 times (low dose) and 4.8-4 times (high dose) the recommended human Soliris dose, based on a body weight comparison. When animal exposure to the antibody occurred in the time period from before mating until early gestation, no decrease in fertility or reproductive performance was observed. When maternal exposure to the antibody occurred during organogenesis, two cases of retinal dysplasia and one case of umbilical hernia were observed among 250 offspring born to mothers exposed to the higher antibody dose; however, the exposure did not increase fetal loss or neonatal death. When maternal exposure to the antibody occurred in the time period from implantation through weaning, a higher number of male offspring became moribund or died (125 controls, 225 low dose group, 525 high dose group). Surviving offspring had normal development and reproductive function.

8.2 Lactation

Risk Summary

There is no information regarding the presence of ecuzlimab in human milk, the effects on the breastfed infant, or the effects on milk production. IgG is excreted in human milk, so it is expected that ecuzlimab will be present in human milk. However, published data suggest that antibodies in human milk do not enter the neonatal and infant circulation in substantial amounts. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Soliris and any potential adverse effects on the breastfed child from Soliris or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of Soliris for the treatment of PHiN in pediatric patients have not been established. The safety and effectiveness of Soliris for the treatment of aHUS have been established in pediatric patients. Use of Soliris in pediatric patients for this indication is supported by evidence from four adequate and well-controlled clinical studies assessing the safety and effectiveness of Soliris for the treatment of aHUS. The studies included a total of 47 pediatric patients (ages 2 months to 17 years). The safety and effectiveness of Soliris for the treatment of aHUS appear similar in pediatric and adult patients [see Adverse Reactions (6.1) and Clinical Studies (14.2)]. The safety and effectiveness of Soliris for the treatment of generalized Myasthenia Gravis in pediatric patients have not been established.

Administer vaccinations for the prevention of infection due to Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenza type b (Hib) according to ACP guidelines [see Warnings and Precautions (5.1, 5.2, 5.3)].

8.5 Geriatric Use

Fifty-four patients 65 years of age or older (15 with PHiN, 4 with aHUS, and 26 with gMG) were treated with Soliris in clinical trials in the approved indications. Although there were no apparent age-related differences observed in these studies, the number of patients aged 65 or over is not sufficient to determine whether they respond differently from younger patients.

11 DESCRIPTION

Soliris, a complement inhibitor, is a formulation of eculizumab which is a recombinant humanized monoclonal IgG2A, antibody produced by murine myeloma cell culture and purified by standard bioprocess technology. Eculizumab contains a κ heavy-chain variable region and gMG patients had antibodies to Soliris detected immediately following the 26-week active treatment.

The precise mechanism by which ecuzlimab 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 2200 ± 1034 U/L (mean ± SD) at baseline to 700 ± 388 U/L by week one and maintained the effect through the end of the study at week 26 [327 ± 433 U/L in patients with PHiN. In the single arm clinical study (PNH Study 2), the effect was maintained through week 52 [see Clinical Studies (14)].

In patients with eculizumab (ECL), and gMG, free C5 concentrations of < 0.5 mcg/mL was correlated with blockade of terminal complement activity.

12.3 Pharmacokinetics

Following intravenous maintenance doses of 900 mcg once every 2 weeks in patients with PHiN, the weekly dose = 30 mcg serum albumin maximum concentration (Cmax) was 104 ± 76 mcg/mL and the trough concentration (C trough) was 97 ± 60 mcg/mL. Following intravenous maintenance doses of 1200 mcg 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 mcg once every 2 weeks in patients with gMG, the week 26 observed mean ± SD Cmax was 763 ± 288 mcg/mL and the C trough was 341 ± 172 mcg/mL. Steady state was achieved 4 weeks after starting ecuzlimab treatment, with accumulation ratio of approximately 2-fold in all studied indications. Population pharmacokinetic analyses showed that ecuzlimab pharmacokinetics were dose- linear and time-independent over the 600 mcg to 1200 mg dose range, with inter-individual variability of 21% to 38%.

Distribution

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

Elimination

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

Plasma exchange or 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 ecuzlimab were not affected by age (2 months to 85 years), sex, or race.

Renal Impairment

Renal function did not affect the pharmacokinetics of ecuzlimab in PHiN (creatinine clearance of 8 mL/min calculated using Cockcroft-Gault formula), aHUS (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).
Table 10: PHN Study 1 Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>Soliris</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>44</td>
<td>43</td>
</tr>
<tr>
<td>Percentage of patients with stabilized hemoglobin levels</td>
<td>0</td>
<td>49</td>
</tr>
<tr>
<td>Packed RBC units transfused per patient (median) (range)</td>
<td>10 (2-21)</td>
<td>0 (0-16)</td>
</tr>
<tr>
<td>Transfusion avoidance (%)</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>LDH levels at end of study (median, U/L)</td>
<td>2,167</td>
<td>239</td>
</tr>
<tr>
<td>Free hemoglobin at end of study (median, mg/dL)</td>
<td>62</td>
<td>5</td>
</tr>
</tbody>
</table>

PHN Study 2 and Extension Study:

PHN patients with at least one transfusion in the prior 24 months and at least 30,000 platelets/microliter received Soliris over a 52-week period. Concomitant medications included anti-thrombotic agents in 63% of the patients and systemic corticosteroids in 40% of the patients. Overall, 96 of the 97 enrolled patients completed the study (one patient died following a thrombotic event). A reduction in intravascular hemolysis as measured by serum LDH levels was sustained for the treatment period and resulted in a reduced need for RBC transfusion and less fatigue. 187 Soliris-treated PHN patients were enrolled in a long-term extension study. All patients sustained a reduction in intravascular hemolysis over a total Soliris exposure time ranging from 10 to 54 months. There were fewer thrombotic events with Soliris treatment than during the same period of time prior to treatment. However, the majority of patients who received concomitant antiaggregants saw an improvement in adverse events during Soliris withdrawal for therapy was not studied [see Warnings and Precautions (5.4)].

14.2 Atypical Hemolytic Uremic Syndrome (aHUS)

Five single-arm studies [four prospective: C08-002A/B (NCT00844545 and NCT00844444), C08-003A/B (NCT00835813 and NCT00844428), C10-003 (NCT01193348), and C10-004 (NCT01194973); and one retrospective: C09-001r (NCT17770951)] evaluated the safety and efficacy of Soliris for the treatment of aHUS. Patients with aHUS received monoclonal antibody treatment prior to receipt of Soliris or received prophylactic treatment with antibiotics until 2 weeks after vaccination. In all studies, the dose of Soliris in adult and adolescent patients was 100 mg every 7-2 days for 4 weeks, followed by 1200 mg every 7-2 days later, then 1200 mg every 14-2 days thereafter. The dosage regimen for pediatric patients was less than 60 kg enrolled in Study C09-003r and Study C10-003 was based on body weight (see Dosage and Administration (2.2)). Efficacy endpoints were based on thrombotic microangiopathy (TMA) endpoints related to TMA included the following:

- platelet count change from baseline
- hematologic normalization (maintenance of normal platelet counts and LDH levels for at least four weeks)
- complete TMA response (hematologic normalization plus at least a 25% reduction in serum creatinine for a minimum of four weeks)
- TMA-event free status (absence of at least 12 weeks of a decrease in platelet count of >25% from baseline, plasma exchange or plasma infusion, and new dialysis requirement)
- Daily TMA intervention rate defined as the number of plasma exchange or plasma infusion interventions and the number of new dialyses required per patient per day.

The Table 11 of the baseline characteristics of patients enrolled in Study C08-002A/B.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>C08-002A/B N = 20</th>
<th>C08-003A/B N = 20</th>
<th>C08-003A/B N = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from aHUS diagnosis until screening in months, median (min, max)</td>
<td>10 (8, 26)</td>
<td>10 (8, 26)</td>
<td>10 (8, 26)</td>
</tr>
<tr>
<td>Time from current clinic TMA manifestation until screening in months, median (min, max)</td>
<td>&lt;1 (&lt;1, 4)</td>
<td>&lt;1 (&lt;1, 4)</td>
<td>&lt;1 (&lt;1, 4)</td>
</tr>
<tr>
<td>Baseline platelet count (× 10^9/L), median (range)</td>
<td>118 (62, 161)</td>
<td>118 (62, 161)</td>
<td>118 (62, 161)</td>
</tr>
<tr>
<td>Baseline LDH (U/L), median (range)</td>
<td>269 (124, 634)</td>
<td>269 (124, 634)</td>
<td>269 (124, 634)</td>
</tr>
</tbody>
</table>

Patients in Study C08-002A/B received Soliris for a minimum of 26 weeks. In Study C08-002A/B, the median duration of Soliris therapy was approximately 100 weeks (range: 2 weeks to 154 weeks).

Renal function, as measured by eGFR, was maintained during Soliris therapy. The mean eGFR (± SD) was 68 (± 30) mL/min/1.73m2 at baseline and was maintained through 26 weeks (67 ± 21 mL/min/1.73m2) and 2 patients (40 ± 18 mL/min/1.73m2). No patient required new dialysis with Soliris.

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

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 ± 53 x10^9/L at baseline to 233 ± 109 x10^9/L after one week of therapy. This effect was maintained through 26 weeks (mean platelet count (± SD) at week 26: 254 ± 79 x10^9/L).

A total of 19 pediatric patients (ages 2 months to 17 years) received Soliris in Study C09-001r. The median duration of Soliris therapy was 16 weeks (range 4 to 70 weeks) for children <2 years of age (n=5), 31 weeks (range 19 to 63 weeks) for children 2 to 12 years of age (n=10), and 38 weeks (range 1 to 69 weeks) for patients 12 to 18 years of age (n=4). Fifty three percent of pediatric patients had an identified complement regulatory factor mutation or auto-antibody. Overall, the efficacy results for these pediatric patients appeared consistent with what was observed in patients enrolled in Studies C08-002A/B and C08-003A/B (Table 15). No pediatric patient required new dialysis during treatment with Soliris.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C08-002A/B</th>
<th>Study C08-003A/B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete TMA response, n (%)</td>
<td>9 (45)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Median duration of complete TMA response, weeks (range)</td>
<td>10 (50)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>eGFR improvement ≥ 15 mL/min/1.73 m², n (%)</td>
<td>4 (20)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Hematologic normalization, n (%)</td>
<td>2 (10)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Daily TMA intervention rate, median (range)</td>
<td>0 (0, 0.01)</td>
<td>0 (0, 0.01)</td>
</tr>
<tr>
<td>Before eculizumab</td>
<td>0.23 (0.05, 1.07)</td>
<td>0.23 (0.05, 1.07)</td>
</tr>
<tr>
<td>On eculizumab treatment</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

1. Platelet count normalization was defined as a platelet count of at least 250,000 x10^9/L at baseline, and maintained through 26 weeks (≥ 75 mL/min/1.73m²) and 2 patients (40 ± 18 mL/min/1.73m²). No patient required new dialysis with Soliris.
2. Of the 9 patients who experienced an eGFR improvement of at least 15 mL/min/1.73 m², one received dialysis throughout the study period and another received Soliris as prophylaxis following renal allograft transplantation.
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 17 summarizes the efficacy results for Study C10-004. Reduction in terminal complement activity was observed in all patients 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. Twenty of the 24 patients who required dialysis at study baseline were able to discontinue dialysis during Soliris treatment.

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

Study C10-003 enrolled patients who were required to have a platelet count < lower limit of normal range (LLN), evidence of hemolysis such as an elevation in serum LDH, and serum creatinine above the upper limits of normal, without the need for chronic dialysis. The median patient age was 33 years (18 to 80 years). All patients enrolled in Study C10-003 were required to have ADAMD513 activity level > 50% observed value of the trial values 22%-31%. Fifty percent of patients had an identified complement regulatory factor proteins or auto-antibodies to factor H. A total of 62 patients were randomized to receive Soliris treatment and 63 were randomized to receive placebo. Baseline characteristics were similar between treatment groups, including age at diagnosis (38 years in each group), group with >65% female patients, and group with >65% female patients.

Table 18: Baseline Characteristics of Patients Enrolled in aHUS Study 5

Pediatric and Adolescent Patients with aHUS (Study C10-003)

Study C10-003 enrolled patients who were required to have a platelet count < lower limit of normal range (LLN), evidence of hemolysis such as an elevation in serum LDH above the upper limits of normal, serum creatinine level ≥ 37% patient decline for age without the need for chronic dialysis. The median patient age was 0.5-17 years. Patients enrolled in Study C10-003 were required to have ADAMD513 activity level >50% observed value of the trial values 38%-121%. Fifty percent of patients had an identified complement regulatory factor proteins or auto-antibodies. A total of 10 patients received PE/PI prior to eculizumab. Table 18 summarizes the key baseline clinical and disease-related characteristics of patients enrolled in Study C10-003.

Table 19: Efficacy Results for Study C10-003

P19.06 Soliris for Treatment in Adult Patients with aHUS (Study C10-004)

Study C10-004 enrolled patients who displayed signs of thrombotic microangiopathy (TMA). In order to qualify for enrollment, patients were required to have a platelet count < lower limit of normal range (LLN), evidence of hemolysis such as an elevation in serum LDH, and serum creatinine above the upper limits of normal, without the need for chronic dialysis. The median patient age was 33 years (18 to 80 years). All patients enrolled in Study C10-004 were required to have ADAMTS13 activity level > 50% observed value of the trial values 22%-31%. Fifty percent of patients had an identified complement regulatory factor proteins or auto-antibodies to auto-antibodies to factor H. A total of 35 patients received PE/PI prior to eculizumab. Table 19 summarizes the key baseline clinical and disease-related characteristics of patients enrolled in Study C10-004.

Table 19: Efficacy Results for Study C10-003

P19.06 Soliris for Treatment in Adult Patients with aHUS (Study C10-004)

Table 19 summarizes the efficacy results for Study C10-003. 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).

Table 19: Efficacy Results for Study C10-003

Table 19 summarizes the efficacy results for Study C10-003. 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).

Table 19: Efficacy Results for Study C10-003

Table 19 summarizes the efficacy results for Study C10-003. 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).

Table 19: Efficacy Results for Study C10-003

Table 19 summarizes the efficacy results for Study C10-003. 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).

Table 19: Efficacy Results for Study C10-003

Table 19 summarizes the efficacy results for Study C10-003. 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).
• 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.
- 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.
- 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 breakdown of your red blood cells due to aHUS.

Symptoms or problems that can happen due to abnormal clotting 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