24 patients who required dialysis at study baseline were able to discontinue dialysis during Soliris treatment.

Before eculizumab

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median duration of complete TMA response, weeks (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>36 (14, 77)</td>
</tr>
<tr>
<td>On eculizumab</td>
<td>41 (14, 77)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median of complete TMA response with range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>40 (14, 77)</td>
</tr>
<tr>
<td>On eculizumab</td>
<td>41 (14, 77)</td>
</tr>
</tbody>
</table>

Table 14: Efficacy Results for Study C08-003A/B in Study C10-004.

Patients enrolled in Study C10-004 were required to have ADAMTS13 activity level above 5%; observed 22 (40) patients with complete TMA response (median duration of 36 weeks).

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

Table 19: Efficacy Results for Study C10-003

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Efficacy Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR improvement ≥15 mL/min/1.73 m2, n (%)</td>
<td>16 (89)</td>
</tr>
<tr>
<td>Hematologic Normalization, n (%)</td>
<td>22 (40)</td>
</tr>
</tbody>
</table>

MTA: Meningococcal Infection

Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 8 represents severe weakness.

Signs and Symptoms of Meningococcal Infection

• fever
• muscle aches with flu-like symptoms
• headache
• rash
• disorientation and confusion

Vaccination reduces, but does not eliminate, the risk of meningococcal infections. Monitor patients that vaccination may not prevent meningococcal infections such as:

• Haemophilus influenzae type b (Hib) according to current ACIP guidelines.
• Meningococcal (A, C, Y, W-135) conjugate vaccine.
• Pneumococcal 23-valent polysaccharide vaccine.

Soliris change

10% (95% CI)

LSMean-Difference (95% CI) = Difference in least square mean with 95% confidence interval;

10% (95% CI)

Revised: 07/2018
To the infusion bag.

the following schedule (Table 1):

Soliris treatment outweigh the risks of developing a meningococcal infection.

Infusion

| 900 mg | 90 mL |
| 300 mg | 300 mg per each plasmapheresis |
| 300 mg | 300 mg per each infusion of fresh |

discontinued Soliris treatment. TMA complications occurred following a missed dose in 5 patients, and

Treatment Discontinuation for aHUS

• Other Infections

[after meningococcal vaccination and 64 of these 75 patients received antibiotics for prophylaxis of

accordance with ACIP recommendations, considering the duration of Soliris therapy.

Clinical signs and symptoms of TMA include changes in mental status, seizures, angina,

infections, especially with encapsulated bacteria. Additionally,

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in

the general U.S. population annual rate (0.14 per 100,000 population in 2015).

5.3  Monitoring Disease Manifestations after Soliris Discontinuation

Haemophilus influenzae type b (Hib).

In clinical studies among non-PNH patients, one in pediatric and adolescent patients (Study C10-003), and one retrospective study (Study C09-001r).

Abdominal pain 3 (18) 6 (30) 6 (15) 15 (19)

Nervous System Disorders

Psychiatric Disorders

Blood and Lymphatic System Disorders

Infections and Infestations

Rash 2 (12) 3 (15) 6 (15) 11 (14)

Neoplasms benign, malignant, and unspecified

Eye Disorders

Musculoskeletal and Connective Tissue Disorders

Surviving offspring had normal development and reproductive function.

Injury, Poisoning, and Procedural Complications

in 2-4 times (low dose) and 4-8 times (high dose) the recommended human Soliris dose, based

study, the adverse reactions were similar to those reported in the placebo-controlled clinical study.

Number (%) of Patients

2  to  12

| 2 to 12 | 12 to 30 |
| 2  to  12 | 12  to  30 |

Endpoints related to TMA included the following:

Previous 12 months (median (Q1,Q3)) 17 (14, 25) 18 (12, 24)

Concomitant steroids/immunosuppressant treatments (%) 16 (36) 14 (33)

Major baseline characteristics were balanced (see Table 9).

Table 9: PNH Study1 Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>PNH Study1 Patient Baseline Characteristics</th>
<th>PNH Study1 Patient Baseline Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of patients with stabilized hemoglobin levels 0</td>
<td>49</td>
</tr>
<tr>
<td>Median duration of Soliris therapy was approximately 114 weeks (range: 26 to 129 weeks).</td>
<td></td>
</tr>
<tr>
<td>Median Duration of complete TMA response, weeks (range)</td>
<td>9 (53) 251</td>
</tr>
</tbody>
</table>

No apparent correlation of antibody development to clinical response was observed.

Table 11 summarizes the key baseline characteristics of peritoneal dialysis (PD) patients and one case of umbilical hernia were observed among 230 offspring born to mothers exposed to the

aHUS population, and one of 100 patients with aHUS (1%) had low positive values for neutralizing antibodies. None of 62 patients with

and one case of umbilical hernia were observed among 230 offspring born to mothers exposed to the

inhibitors (FCRn) recycling mechanism of monoclonal antibodies such as eculizumab and thereby decrease serum

[see Warnings and Precautions (5.1, 5.2, 5.3)]

[see Dosage and Administration (2.3)
Administer the Soliris admixture by intravenous infusion over 35 minutes in adults and 1 to 4 hours in pediatric patients.

Dilute Soliris to a final admixture concentration of 5 mg/mL using the following steps:

1. Mix gently to ensure a homogeneous admixture.
2. Use within 24 hours of preparation.
3. Discard any admixture not used within 24 hours.

Avoid extravasation.

**Side Effects and Adverse Reactions**

- **Systemic Infections:**
  - Sinusitis: 3 (7)
  - Pneumonia: 3 (7)
  - Meningitis: 2 (4)
  - Bacterial infections: 2 (4)
  - Fungal infection: 1 (2)
- **Vascular Disorders:**
  - Nervous System Disorders:
    - Migraine: 3 (7)
    - Headache: 3 (7)
    - Nervousness: 3 (7)
- **Infections and Infestations:**
  - Staphylococcal infections: 3 (7)
  -ii (1)
  - Bacterial infections: 3 (7)
- **Respiratory, Thoracic and Mediastinal Disorders:**
  - Nasal congestion: 2 (40)
  - Sinusitis: 3 (7)
  - Pneumonia: 3 (7)
- **Eye Disorders:**
  - Conjunctivitis: 2 (40)
  - Uveitis: 2 (40)
- **Blood and Lymphatic System Disorders:**
  - Anemia: 6 (35)
  - Thrombocytopenia: 5 (11)
  - Leukopenia: 5 (11)
  - Lymphadenopathy: 5 (11)
  - Hemolytic anemia: 5 (11)
- **Skin and Appendage Disorders:**
  - Pruritus: 4 (21)
  - Rash: 4 (21)
  - Erythema: 4 (21)
  - Urticaria: 4 (21)
  - Maculopapular rash: 4 (21)
  - Pityriasis: 4 (21)
  - Acne: 4 (21)
- **Musculoskeletal and Connective Tissue Disorders:**
  - Myalgia: 3 (7)
  - Arthritis: 3 (7)
- **Gastrointestinal Disorders:**
  - Diarrhea: 3 (7)
  - Nausea: 7 (16)
  - Abdominal pain: 13.1
  - Anorexia: 3 (7)
  - Vomiting: 3 (7)
- **General Disorders and Administration Site Reactions:**
  - Fatigue: 3 (7)
  - Hypersensitivity: 3 (7)
  - Hypotension: 3 (7)
  - Hypertension: 3 (7)
  - Palpitations: 3 (7)
  - Local injection site reactions: 3 (7)
- **Nervous System Disorders:**
  - Dizziness: 3 (7)
  - Tremor: 3 (7)
  - Somnolence: 3 (7)
  - Insomnia: 3 (7)
  - Anxiety: 3 (7)
  - Neuropathy: 3 (7)
  - Paresthesia: 3 (7)
  - Seizure: 3 (7)
- **Respiratory, Thoracic and Mediastinal Disorders:**
  - Shortness of breath: 3 (7)
  - Cough: 3 (7)
  - Wheezing: 3 (7)
  - Bronchospasm: 3 (7)
- **Cardiac Disorders:**
  - Tachycardia: 3 (7)
  - Cardiac failure: 3 (7)
  - Arrhythmia: 3 (7)
  - ECG changes: 3 (7)
- **Metabolism and Nutrition Disorders:**
  - Hypothyroidism: 3 (7)
  - Hypoglycemia: 3 (7)
  - Hyperglycemia: 3 (7)
- **Hepatobiliary Disorders:**
  - Hepatitis: 3 (7)
  - Ascites: 3 (7)
  - Jaundice: 3 (7)
  - Cholestasis: 3 (7)
- **Hypersensitivity Reactions:**
  - Anaphylaxis: 3 (7)
  - Urticaria: 3 (7)
  - Photosensitivity: 3 (7)
- **Neoplasms:**
  - Malignant lymphoma: 3 (7)
  - Carcinoma: 3 (7)
- **Other Events:**
  - Death: 3 (7)
  - CPR: 3 (7)
  - Prostration: 3 (7)
  -昏睡: 3 (7)
  -昏厥: 3 (7)

**Warnings and Precautions**

- **Anaphylaxis:**
  - Patients with a history of anaphylaxis should be monitored closely. Administration should be delayed or withheld in patients with a history of anaphylaxis to solirug or components of the admixture.

**Contraindications:**

- **Thrombocytopenia:**
  - Patients with severe thrombocytopenia should not receive Soliris.

**Precautions:**

- **Infusion Reactions:**
  - Monitor for signs of infusion reactions and discontinue infusions if necessary.

**Adverse Events Reporting:**

- Adverse events should be reported to the appropriate regulatory authorities.

**Pharmacokinetics:**

- Eculizumab is eliminated by renal excretion.

**Nursing Considerations:**

- Monitor patients for signs of anemia and adjust doses accordingly.

**Patient Counseling:**

- Inform patients about the need for vaccination before starting treatment.

**References:**

- Clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the frequency of adverse reactions observed in the clinical trials of another drug.

**Table 1:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinusitis</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Fungal infection</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td>11</td>
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<tr>
<td>Infections and Infestations</td>
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<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
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</tr>
<tr>
<td>Eye Disorders</td>
<td>2</td>
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</tr>
<tr>
<td>Blood and Lymphatic System Disorders</td>
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<tr>
<td>Skin and Appendage Disorders</td>
<td>4</td>
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<td>Musculoskeletal and Connective Tissue Disorders</td>
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<td>Gastrointestinal Disorders</td>
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<tr>
<td>General Disorders and Administration Site Reactions</td>
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<tr>
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<td></td>
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<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
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<td></td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
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<tr>
<td>Hepatobiliary Disorders</td>
<td>3</td>
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<tr>
<td>Hypersensitivity Reactions</td>
<td>3</td>
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<td>Neoplasms</td>
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<td></td>
</tr>
<tr>
<td>Other Events</td>
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</table>

**Table 2:**

<table>
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<th>Number</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Fungal infection</td>
<td>1</td>
<td></td>
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<tr>
<td>Nervous System Disorders</td>
<td>8</td>
<td></td>
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<tr>
<td>Vascular Disorders</td>
<td>11</td>
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<tr>
<td>Infections and Infestations</td>
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<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
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<td>Eye Disorders</td>
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<td>Blood and Lymphatic System Disorders</td>
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<td>Skin and Appendage Disorders</td>
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<td>Musculoskeletal and Connective Tissue Disorders</td>
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<tr>
<td>Gastrointestinal Disorders</td>
<td>3</td>
<td></td>
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<tr>
<td>General Disorders and Administration Site Reactions</td>
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<tr>
<td>Nervous System Disorders</td>
<td>3</td>
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</tr>
<tr>
<td>Cardiac Disorders</td>
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</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
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</tr>
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<td>Hepatobiliary Disorders</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity Reactions</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Neoplasms</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Other Events</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
**Precautions (5.1)**

Because of the risk of meningococcal infections, Soliris is available only through a restricted program.

Infections due to encapsulated bacteria can be prevented by vaccination. Vaccination reduces, but does not eliminate, the risk of meningococcal infections. In clinical studies, 2 out of 400 vaccine recipients developed confirmed meningococcal disease. People with an immune deficiency or an allergy to polysorbate 80 or neomycin are at increased risk of meningococcal infection.

Vaccination is recommended for all patients receiving eculizumab. The current licensed meningococcal conjugate vaccines may not provide complete protection for patients treated with eculizumab. It is recommended that children at least 2 years of age or adolescents and adults who lack adequate immunity to Neisseria meningitidis receive a licensed meningococcal conjugate vaccine. If the meningococcal vaccine administered is only 4-component meningococcal vaccine, a 23-valent meningococcal polysaccharide vaccine should be considered.

**INDICATIONS AND USAGE**

Soliris is indicated for the treatment of thrombotic microangiopathy (TMA) associated with atypical hemolytic uremic syndrome (aHUS) in adult and adolescent patients 18 years of age and older. Soliris was studied in patients with or without a recognized genetic predisposition to aHUS.

**DOSING AND ADMINISTRATION**

**Table 1: Dosing Recommendations in Patients Less Than 18 Years of Age**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6</td>
<td>600 mg every 2 weeks</td>
</tr>
<tr>
<td>7-12</td>
<td>900 mg every 2 weeks</td>
</tr>
<tr>
<td>≥13</td>
<td>900 mg every 2 weeks</td>
</tr>
</tbody>
</table>

**Table 2: Daily TMA Intervention Rate**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study C08-003A/B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 78</td>
</tr>
<tr>
<td></td>
<td>N = 17</td>
</tr>
<tr>
<td>Daily TMA intervention rate, median (range)</td>
<td>38 (25, 56)</td>
</tr>
<tr>
<td>On eculizumab treatment</td>
<td>99 (25, 145)</td>
</tr>
</tbody>
</table>

**Table 3: Preparation and Reconstitution of Soliris**

- Transfer the recommended dose to an infusion bag.
- Gently invert the infusion bag containing the diluted Soliris solution to ensure thorough mixing of the contents.
- Administer the reconstituted solution via intravenous infusion over 30 to 60 minutes.

**Table 4: Safety Data**

**Table 5: Per Patient Incidence of Adverse Reactions in 10% or More Patients Enrolled in Study C10-003**

- **Injection Site Reactions:**
  - Inflammation: 4 (24)
  - Pain: 4 (24)
  - Redness: 4 (24)
- **Gastrointestinal Disorders:**
  - Diarrhea: 8 (47)
  - Nausea: 8 (40)
  - Vomiting: 12 (32)
  - Upper abdominal pain: 29 (37)
- **General Disorders and Administration Site Conditions:**
  - Diarrhea: 6 (32)
  - Nausea: 6 (32)
  - Vomiting: 10 (59)
- **Infections and Infestations:**
  - Pyrexia: 4 (24)
  - Upper respiratory tract infection: 4 (24)
- **Neoplasms benign, malignant, and unspecified:**
  - Cancer: 2 (11)
  - Malignant neoplasm: 2 (11)
- **Injury, poisoning and procedural complications:**
  - Hypertension: 9 (59)
- **Laboratory Abnormalities:**
  - Ecotocytosis: 9 (59)
  - Hemoglobin: 9 (59)
  - Platelet count: 9 (59)
  - White blood cell count: 9 (59)

**Table 6: Adverse Reactions in 10% or More Patients Enrolled in Study C10-003**

- **Common Adverse Reactions:**
  - Hematological: Ecotocytosis, Hemoglobin reduction, Platelet count reduction
  - Oncological: Cancer, Malignant neoplasm
  - Infection: Upper respiratory tract infection, Pyrexia
  - Metabolic: Hypertension
  - Gastrointestinal: Diarrhea, Nausea, Vomiting, Upper abdominal pain
  - General Disorders: Diarrhea, Nausea, Vomiting
  - Injury, poisoning and procedural complications: Hypertension
  - Laboratory abnormalities: Ecotocytosis, Hemoglobin reduction, Platelet count reduction, White blood cell count reduction

**Table 7: Adverse Reactions in Pediatric Patients**

The safety of Soliris therapy in patients with aHUS was evaluated in four prospective, single-arm studies. The adverse reactions were similar to those reported in the placebo-controlled clinical study. The most common (≥15%) adverse events occurring in pediatric patients are presented in Table 7.

**Table 8: Clinical Studies**

- **Study C08-002A/B**
  - Treatment: Soliris
  - Results: The adverse reactions were similar to those reported in the placebo-controlled clinical study.
- **Study C08-003A/B**
  - Treatment: Soliris
  - Results: The adverse reactions were similar to those reported in the placebo-controlled clinical study.

**Table 9: Safety Data**

- **Injection Site Reactions:**
  - Inflammation: 4 (24)
  - Pain: 4 (24)
  - Redness: 4 (24)
- **Gastrointestinal Disorders:**
  - Diarrhea: 8 (47)
  - Nausea: 8 (40)
  - Vomiting: 12 (32)
  - Upper abdominal pain: 29 (37)
- **General Disorders and Administration Site Conditions:**
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  - Nausea: 6 (32)
  - Vomiting: 10 (59)
- **Infections and Infestations:**
  - Pyrexia: 4 (24)
  - Upper respiratory tract infection: 4 (24)
- **Neoplasms benign, malignant, and unspecified:**
  - Cancer: 2 (11)
  - Malignant neoplasm: 2 (11)
- **Injury, poisoning and procedural complications:**
  - Hypertension: 9 (59)
- **Laboratory Abnormalities:**
  - Ecotocytosis: 9 (59)
  - Hemoglobin: 9 (59)
  - Platelet count: 9 (59)
  - White blood cell count: 9 (59)

**Table 10: Adverse Reactions in Pediatric Patients**

The safety of Soliris therapy in patients with aHUS was evaluated in four prospective, single-arm studies. The adverse reactions were similar to those reported in the placebo-controlled clinical study. The most common (≥15%) adverse events occurring in pediatric patients are presented in Table 7.

**Table 11: Clinical Studies**

- **Study C08-002A/B**
  - Treatment: Soliris
  - Results: The adverse reactions were similar to those reported in the placebo-controlled clinical study.
- **Study C08-003A/B**
  - Treatment: Soliris
  - Results: The adverse reactions were similar to those reported in the placebo-controlled clinical study.

**Table 12: Safety Data**

- **Injection Site Reactions:**
  - Inflammation: 4 (24)
  - Pain: 4 (24)
  - Redness: 4 (24)
- **Gastrointestinal Disorders:**
  - Diarrhea: 8 (47)
  - Nausea: 8 (40)
  - Vomiting: 12 (32)
  - Upper abdominal pain: 29 (37)
- **General Disorders and Administration Site Conditions:**
  - Diarrhea: 6 (32)
  - Nausea: 6 (32)
  - Vomiting: 10 (59)
- **Infections and Infestations:**
  - Pyrexia: 4 (24)
  - Upper respiratory tract infection: 4 (24)
- **Neoplasms benign, malignant, and unspecified:**
  - Cancer: 2 (11)
  - Malignant neoplasm: 2 (11)
- **Injury, poisoning and procedural complications:**
  - Hypertension: 9 (59)
- **Laboratory Abnormalities:**
  - Ecotocytosis: 9 (59)
  - Hemoglobin: 9 (59)
  - Platelet count: 9 (59)
  - White blood cell count: 9 (59)
Soliris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA). The efficacy of Soliris was evaluated in two placebo-controlled, randomized, double-blind, 26-week trials (Study C08-003A/B and Study C10-004) in adult patients (≥18 years of age) and pediatric patients (≥12 to <18 years of age) with aHUS. The median duration of hematologic normalization for adult patients treated with Soliris was 46 weeks (range 10, 75 weeks). Fifty-one percent of patients had an identified complement regulatory factor mutation or auto-antibody. A total of 35 patients received PE/PI prior to eculizumab.

Table 17 summarizes the efficacy results for Study C10-004.

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Study C08-003A/B 26 wks</th>
<th>Study C10-004 24 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete TMA response, n (%)</td>
<td>2 (40)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Patients with eGFR improvement</td>
<td>4 (80)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Platelet count normalization, n (%)</td>
<td>4 (80)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Median duration of hematologic normalization, weeks (range)</td>
<td>28 (10, 67)</td>
<td>116 (10, 240)</td>
</tr>
</tbody>
</table>

Reduction in terminal complement activity and an increase in platelet count relative to baseline were observed in the Soliris-treated group. The mean change from baseline to Week 26 in QMG total scores was -4.6 points in the Soliris-treated group (p=0.006) compared to -1.6 points in the placebo-treated group. The proportion of clinical responders at Week 26 was higher in the Soliris arm (54%) than in the placebo arm (21%).

Other side effects observed in clinical trials included:
- Nausea (≥10% in the placebo group)
- Vomiting (≥10% in the placebo group)
- Fever (≥10% in the placebo group)
- Headache (≥10% in the placebo group)
- Cough (≥10% in the placebo group)
- Asthma (≥10% in the placebo group)

Soliris is supplied as a single-use vial containing 300 mg of eculizumab for injection, for intravenous use. It is recommended that patients receive a course of antibiotics before starting Soliris treatment.

Soliris and the vaccine against meningococcal disease should be administered at least two weeks apart to ensure appropriate immune response.

CAUTION: Do not administer to patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). Soliris can cause serious side effects including:
- Fever
- Rash
- Muscle aches
- Congestive heart failure
- Cardiac arrest
- Respiratory distress
- Stroke
- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Vomiting

Soliris can cause serious side effects including:
- Meningococcal infection
- Fungal infections (Aspergillus)
- Pneumonia
- Staphylococcal infections
- Lymphoma
- Necrotizing fasciitis
- Stomatitis
- Azithromycin-resistant Mycobacteria

Inform patients that there may be an increased risk of other types of infections, particularly those due to Pseudomonas aeruginosa, in patients treated with Soliris.

Prophylactic antibiotics are recommended for vertebral infections in patients with complement deficiencies.

Soliris is not for use in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) or meningococcal disease. The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) is:
- Diarrhea

Additional precautions include:
- Counsel patients about the risk of meningococcal infection
- Regular testing for fungal infections
- Long-term use of corticosteroids
- Cardiac arrest
- Respiratory distress
- Nausea
- Vomiting

The most common laboratory abnormality associated with Soliris treatment is anemia. Other laboratory abnormalities include decreased white blood cell count, increased alkaline phosphatase, increased creatinine, increased aspartate aminotransferase, and increased alanine aminotransferase.

See 17 PATIENT COUNSELING INFORMATION and Medication Guide.

To report SUSARs, contact PHERex at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
A total of 19 pediatric patients (ages 2 months to 17 years) received Soliris in Study C09-001r. The median platelet count from baseline to week 26 was 171 ± 83 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: 252 ± 70 x10^9/L). In Study C10-004, patients were required to have ADAMTS13 activity level above 5%; observed evidence of hemolysis such as an elevation in serum LDH, and serum creatinine above the upper limits of normal.

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

### Table 19: Efficacy Results for Study C10-003

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Patients with eGFR improvement ≥ 15 mL/min/1.73 m², n (%), Total</th>
<th>Patients treated with Soliris, n (%)</th>
<th>Patients treated with placebo, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 yr</td>
<td>22 (54)</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>3 yr</td>
<td>14 (78)</td>
<td>14</td>
<td>10</td>
</tr>
</tbody>
</table>

**Median duration of complete TMA response, weeks (range):**

- Soliris: 2 (0, 10)
- Placebo: 0 (0, <1)

**Median duration of hematologic normalization, weeks (range):**

- Soliris: 4 (0, 7)
- Placebo: 0 (0, <1)

### Clinical Trial Experience

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

- Total: 10
- Median (range) for duration of complete TMA response: 2 (1, 7)
- Median (range) for duration of complete hematologic normalization: 4 (2, 6)

**Kidney Transplantation:**

- Eight patients received a kidney transplant during the study.
- One patient died due to complications of kidney transplantation.

**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 count from baseline to week 26 in the Soliris group compared to the placebo group.**