## HIGHLIGHTS OF PRESCRIBING INFORMATION

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

**Soliris™ (eculizumab),**

**Concentrated solution for intravenous infusion**
**Initial U.S. Approval: 2007**

**WARNING: SERIOUS MENINGOCOCCAL INFECTIONS**

***See full prescribing information for complete boxed warning***

**Soliris increases the risk of meningococcal infections (5.1)**

- **Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of Soliris; revaccinate according to current medical guidelines for vaccine use**
- **Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary.**

**----------INDICATIONS AND USAGE----------**

Soliris is a complement inhibitor indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis (1).

**----------DOSAGE AND ADMINISTRATION----------**

Dosage Regimen: (2.1)

- 600 mg via 35 minute intravenous infusion every 7 days for the first 4 weeks, followed by
- 900 mg for the fifth dose 7 days later, then
- 900 mg every 14 days thereafter

Administration: (2.2, 2.3)

- Do not administer as an intravenous push or bolus.
- Dilute to a final concentration of 5 mg/mL prior to administration.
- Administer by intravenous infusion over 35 minutes.

**----------DOSAGE FORMS AND STRENGTHS----------**

300 mg single-use vials each containing 30 mL of 10 mg/mL sterile, preservative-free solution (3).

**----------CONTRAINDICATIONS----------**

Do not initiate Soliris therapy in patients:

- with unresolved serious *Neisseria meningitidis* infection (4).
- who are not currently vaccinated against *Neisseria meningitidis* (4).

**----------WARNINGS AND PRECAUTIONS----------**

- Other Infections: Use caution when administering Soliris to patients with any systemic infection (5.2).
- Monitoring After Soliris Discontinuation: Soliris increases the number of PNH red blood cells (RBCs). All patients who discontinue Soliris therapy should be monitored for signs and symptoms of intravascular hemolysis, including evaluation of serum lactate dehydrogenase (LDH) levels (5.3).

**----------ADVERSE REACTIONS----------**

The most frequently reported adverse reactions (≥10% overall and greater than placebo) are: headache, nasopharyngitis, back pain and nausea (6).

**To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-888-SOLIRIS (1-888-765-4747) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**See 17 PATIENT COUNSELING INFORMATION AND MEDICATION GUIDE**

**Revised: 3/2007**

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**FULL PRESCRIBING INFORMATION: CONTENTS***


**WARNING: SERIOUS MENINGOCOCCAL INFECTIONS**

**1 INDICATIONS AND USAGE**
**2 DOSAGE AND ADMINISTRATION**
2.1 Recommended Dosage Regimen
2.2 Preparation for Administration
2.3 Administration
**3 DOSAGE FORMS AND STRENGTHS**
**4 CONTRAINDICATIONS**
**5 WARNINGS AND PRECAUTIONS**
5.1 Serious Meningococcal Infections
5.2 Other Infections
5.3 Monitoring After Soliris Discontinuation
5.4 Thrombosis Prevention and Management
5.5 Laboratory Monitoring
5.6 Infusion Reactions
**6 ADVERSE REACTIONS**
6.1 Clinical Trial Experience
6.2 Immunogenicity
**7 DRUG INTERACTIONS**
**8 USE IN SPECIFIC POPULATIONS**
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
**10 OVERDOSAGE**
**11 DESCRIPTION**
**12 CLINICAL PHARMACOLOGY**
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
**13 NONCLINICAL TOXICOLOGY**
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
**14 CLINICAL STUDIES**
**16 HOW SUPPLIED/STORAGE AND HANDLING**
**17 PATIENT COUNSELING INFORMATION**


*Sections or subsections omitted from the full prescribing information are not listed.

**FULL PRESCRIBING INFORMATION**

**WARNING: SERIOUS MENINGOCOCCAL INFECTION**

**Soliris increases the risk of meningococcal infections (5.1)**

- **Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of Soliris; revaccinate according to current medical guidelines for vaccine use**
- **Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary.**

## 1 INDICATIONS AND USAGE

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

## 2 DOSAGE AND ADMINISTRATION

Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of Soliris therapy and revaccinated according to current medical guidelines for vaccine use. [*see Warnings and Precautions (5.1)*].

### 2.1 Recommended Dosage Regimen

Soliris therapy consists of:

- 600 mg every 7 days for the first 4 weeks, followed by
- 900 mg for the fifth dose 7 days later, then
- 900 mg every 14 days thereafter.

Soliris should be administered at the recommended dosage regimen time points, or within two days of these time points. [*see Warnings and Precautions (5.5)*]

### 2.2 Preparation for Administration

Soliris must be diluted 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 120 mL for 600 mg doses or 180 mL for 900 mg doses. 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 heated in a microwave or with any heat source other than ambient air temperature. The Soliris admixture should be inspected visually for particulate matter and discoloration prior to administration.

### 2.3 Administration

*Do Not Administer As An Intravenous Push Or Bolus Injection*

The Soliris admixture should be administered by intravenous infusion over 35 minutes via gravity feed, a syringe-type pump, or an infusion pump. Admixed solutions of Soliris are stable for 24 hours 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. 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

Soliris is supplied as 300 mg single-use vials each containing 30 mL of 10 mg/mL sterile, preservative-free eculizumab solution.

## 4 CONTRAINDICATIONS

Do not initiate Soliris therapy in patients:

- with unresolved serious *Neisseria meningitidis* infection.
- who are not currently vaccinated against *Neisseria meningitidis*.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Serious Meningococcal Infections

The use of Soliris increases a patient's susceptibility to serious meningococcal infections (septicemia and/or meningitis). All patients without a history of prior meningococcal vaccination must receive the meningococcal vaccine at least 2 weeks prior to receiving the first dose of Soliris and revaccinated according to current medical guidelines for vaccine use. Quadravalent, conjugated meningococcal vaccines are strongly recommended. Vaccination may not prevent meningococcal infections.

All patients must be monitored for early signs and symptoms of meningococcal infections and evaluated immediately if an infection is suspected. Physicians should strongly consider discontinuation of Soliris during the treatment of serious 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)*].

### 5.2 Other Infections

Soliris blocks terminal complement; therefore patients may have increased susceptibility to infections, especially with encapsulated bacteria. Use caution when administering Soliris to patients with any systemic infection.

### 5.3 Monitoring After Soliris Discontinuation

Since Soliris therapy increases the number of PNH cells [in study 1, the proportion of PNH RBCs increased among Soliris-treated patients by a median of 28% from baseline (range from -25% to 69%)], patients who discontinue treatment with Soliris may be at increased risk for serious hemolysis. Serious hemolysis is identified by serum LDH levels greater than the pre-treatment level, along with any of the following: greater than 25% absolute decrease in PNH clone size (in the absence of dilution due to transfusion) in one week or less; a hemoglobin level of <5 gm/dL or a decrease of >4 gm/dL in one week or less; angina; change in mental status; a 50% increase in serum creatinine level; or thrombosis. Monitor any patient who discontinues Soliris for at least 8 weeks to detect serious hemolysis and other reactions.

If serious hemolysis occurs after Soliris discontinuation, consider the following procedures/treatments: blood transfusion (packed RBCs), or exchange transfusion if the PNH RBCs are >50% of the total RBCs by flow cytometry; anticoagulation; corticosteroids; or reinstitution of Soliris.

In clinical studies, 16 of 196 PNH patients discontinued treatment with Soliris. Patients were followed for evidence of worsening hemolysis and no serious hemolysis was observed.

### 5.4 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.

### 5.5 Laboratory Monitoring

Serum LDH levels increase during hemolysis and may assist in monitoring Soliris effects, including the response to discontinuation of therapy. In clinical studies, six patients achieved a reduction in serum LDH levels only after a decrease in the Soliris dosing interval from 14 to 12 days. All other patients achieved a reduction in serum LDH levels with the 14 day dosing interval [*see Clinical Pharmacology (12.2) and Clinical Studies (14)*].

### 5.6 Infusion Reactions

As with all protein products, administration of Soliris may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no PNH patients experienced an infusion reaction which required discontinuation of Soliris. Soliris administration should be interrupted in all patients experiencing severe infusion reactions and appropriate medical therapy administered.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trial Experience

Meningococcal infections are the most important adverse reactions experienced by patients receiving Soliris therapy. 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 an unvaccinated patient [*see Warnings and Precautions (5.1)*].

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 (in which 43 patients received Soliris and 44, placebo); a single arm clinical study and a long term extension study. 182 patients were exposed for greater than one year. All patients received the recommended Soliris dose regimen.

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. Table 1 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 1

ADVERSE REACTIONS REPORTED IN 5% OR MORE OF SOLIRIS TREATED PATIENTS AND GREATER THAN PLACEBO IN THE CONTROLLED CLINICAL STUDY

| Reaction | Soliris<br>N = 43<br>N (%) | Placebo<br>N = 44<br>N (%) |
|---|---|---|
| Headache | 19 (44) | 12 (27) |
| Nasopharyngitis | 10 (23) | 8 (18) |
| Back pain | 8 (19) | 4 (9) |
| Nausea | 7 (16) | 5 (11) |
| Fatigue | 5 (12) | 1 (2) |
| Cough | 5 (12) | 4 (9) |
| Herpes simplex infections | 3 (7) | 0 |
| Sinusitis | 3 (7) | 0 |
| Respiratory tract infection | 3 (7) | 1 (2) |
| Constipation | 3 (7) | 2 (5) |
| Myalgia | 3 (7) | 1 (2) |
| Pain in extremity | 3 (7) | 1 (2) |
| Influenza-like illness | 2 (5) | 1 (2) |

In the placebo-controlled clinical study, serious adverse reactions occurred among 4 (9%) 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 193 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%).

### 6.2 Immunogenicity

As with all proteins there is a potential for immunogenicity. Low titers of antibodies to Soliris were detected in 3/196 (2%) of all PNH patients treated with Soliris. No apparent correlation of antibody development to clinical response was observed. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to Soliris in an enzyme linked immunosorbent assay (ELISA) and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in the assay may be influenced by several factors including sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of the incidence of antibodies to Soliris with the incidence of antibodies to other products may be misleading.

## 7 DRUG INTERACTIONS

Drug interaction studies have not been performed with Soliris.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Pregnancy Category C:

PNH is a serious illness. Pregnant women with PNH and their fetuses have high rates of morbidity and mortality during pregnancy and the postpartum period. There are no adequate and well-controlled studies of Soliris in pregnant women. 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 dead and moribund offspring at doses 2-8 times the human dose. Soliris should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal reproduction studies were conducted in mice using doses of a murine anti-C5 antibody that approximated 2-4 times (low dose) and 4-8 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 230 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 (1/25 controls, 2/25 low dose group, 5/25 high dose group). Surviving offspring had normal development and reproductive performance.

### 8.2 Labor and Delivery

No information is available on the effects of Soliris during labor and delivery.

### 8.3 Nursing Mothers

It is not known whether Soliris is secreted into human milk. IgG is excreted in human milk, so it is expected that Soliris will be present in human milk. However, published data suggest that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts. Caution should be exercised when Soliris is administered to a nursing woman. The unknown risks to the infant from gastrointestinal or limited systemic exposure to Soliris should be weighed against the known benefits of breastfeeding.

### 8.4 Pediatric Use

The safety and effectiveness of Soliris therapy in pediatric patients below the age of 18 have not been established.

### 8.5 Geriatric Use

In PNH studies, 15 patients 65 years of age or older were treated with Soliris. Although there were no apparent age-related differences observed in these studies, the number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger patients.

## 10 OVERDOSAGE

No cases of Soliris overdose have been reported during clinical studies.

## 11 DESCRIPTION

Soliris is a formulation of eculizumab which is a recombinant humanized monoclonal $IgG_{2/4}\kappa$ antibody produced by murine myeloma cell culture and purified by standard bioprocess technology. Eculizumab contains human constant regions from human IgG2 sequences and human IgG4 sequences and murine complementarity-determining regions grafted onto the human framework light- and heavy-chain variable regions. Eculizumab is composed of two 448 amino acid heavy chains and two 214 amino acid light chains and has a molecular weight of approximately 148 kDa.

Soliris is a sterile, clear, colorless, preservative-free 10 mg/mL solution for intravenous infusion and is supplied in 30-mL single-use vials. The product is formulated at pH 7 and each vial contains 300 mg of eculizumab, 13.8 mg sodium phosphate monobasic, 53.4 mg sodium phosphate dibasic, 263.1 mg sodium chloride, 6.6 mg polysorbate 80 (vegetable origin) and Water for Injection, USP.

## 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.

A genetic mutation in PNH patients leads to the generation of populations of abnormal RBCs (known as PNH cells) that are deficient in terminal complement inhibitors, rendering PNH RBCs sensitive to persistent terminal complement-mediated destruction. The destruction and loss of these PNH cells (intravascular hemolysis) results in low RBC counts (anemia), and also fatigue, difficulty in functioning, pain, dark urine, shortness of breath, and blood clots.

### 12.2 Pharmacodynamics

In the placebo-controlled clinical study, Soliris when administered as recommended reduced hemolysis as shown by the reduction of 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 the single arm clinical study, Soliris maintained this effect through 52 weeks [*see Clinical Studies (14)*].

### 12.3 Pharmacokinetics

A population PK analysis with a standard 1-compartmental model was conducted on the multiple dose PK data from 40 PNH patients receiving the recommended Soliris regimen [*see Dosage and Administration (2.1)*]. In this model, the clearance of Soliris for a typical PNH patient weighing 70 kg was 22 mL/hr and the volume of distribution was 7.7 L. The half-life was 272 ± 82 hrs (mean ± SD). The mean observed peak and trough serum concentrations of Soliris by week 26 were 194 ± 76 mcg/mL and 97 ± 60 mcg/mL, respectively.

Studies have not been conducted to evaluate the PK of Soliris in special patient populations identified by gender, race, age (pediatric or geriatric), or the presence of renal or hepatic impairment.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic and genotoxic potential of Soliris. Effects of Soliris upon fertility have not been studied in animals. Intravenous injections of male and female mice with a murine anti-C5 antibody at up to 4-8 times the equivalent of the clinical dose of Soliris had no adverse effects on mating or fertility.

## 14 CLINICAL STUDIES

The safety and efficacy of Soliris in PNH patients with hemolysis were assessed in a randomized, double-blind, placebo-controlled 26 week study (Study 1); PNH patients were also treated with Soliris in a single arm 52 week study (Study 2); and in a long term extension study. Patients received meningococcal vaccination prior to receipt of Soliris. In all studies, the dose of Soliris was 600 mg study drug every 7 ± 2 days for 4 weeks, followed by 900 mg 7 ± 2 days later, then 900 mg every 14 ± 2 days for the study duration. Soliris was administered as an intravenous infusion over 25 - 45 minutes.

Study 1:

PNH patients with at least four transfusions in the prior 12 months, flow cytometric confirmation of at least 10% PNH cells and platelet counts of at least 100,000/microliter were randomized to either Soliris (n = 43) or placebo (n = 44). Prior to randomization, all patients underwent an initial observation period to confirm the need for RBC transfusion and to identify the hemoglobin concentration (the "set-point") which would define each patient's hemoglobin stabilization and transfusion outcomes. The hemoglobin set-point was less than or equal to 9 g/dL in patients with symptoms and was less than or equal to 7 g/dL in patients without symptoms. Endpoints related to hemolysis included the numbers of patients achieving hemoglobin stabilization, the number of RBC units transfused, fatigue, and health-related quality of life. To achieve a designation of hemoglobin stabilization, a patient had to maintain a hemoglobin concentration above the hemoglobin set-point and avoid any RBC transfusion for the entire 26 week period. Hemolysis was monitored mainly by the measurement of serum LDH levels, and the proportion of PNH RBCs was monitored by flow cytometry. Patients receiving anticoagulants and systemic corticosteroids at baseline continued these medications.

Major baseline characteristics were balanced (see table 2).

TABLE 2
STUDY 1 PATIENT BASELINE CHARACTERISTICS

| | Study 1 | |
|---|---|---|
| Parameter | Placebo N = 44 | Soliris N = 43 |
| Mean age (SD) | 38 (13) | 42 (16) |
| Gender - female (%) | 29 (66) | 23 (54) |
| History of aplastic anemia or myelodysplastic syndrome (%) | 12 (27) | 8 (19) |
| Patients with history of thrombosis (events) | 8 (11) | 9 (16) |
| Concomitant anticoagulants (%) | 20 (46) | 24 (56) |
| Concomitant steroids/immunosuppressant | 16 (36) | 14 (33) |

| Parameter | Study 1 Placebo N = 44 | Study 1 Soliris N = 43 |
|---|---|---|
| treatments (%) | | |
| Packed RBC units transfused per patient in previous 12 months (median (Q1,Q3)) | 17 (14, 25) | 18 (12, 24) |
| Mean hgb level (g/dL) at setpoint (SD) | 8 (1) | 8 (1) |
| Pre-treatment LDH levels (median, U/L) | 2,234 | 2,032 |
| Free hemoglobin at baseline (median, mg/dL) | 46 | 41 |

Patients treated with Soliris had significantly reduced ($p < 0.001$) hemolysis resulting in improvements in anemia as indicated by increased hemoglobin stabilization and reduced need for RBC transfusions compared to placebo treated patients (see table 3). 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 3
STUDY 1 RESULTS

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

Study 2 and Extension Study:
PNH 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 PNH 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 received concomitant anticoagulants; the effects of anticoagulant withdrawal during Soliris therapy was not studied [*see Warnings and Precautions (5.4)*].

## 16 HOW SUPPLIED / STORAGE AND HANDLING

Soliris (eculizumab) is supplied as 300 mg single-use vials containing 30 mL of 10 mg/mL sterile, preservative-free Soliris solution per vial.

Soliris vials must be stored in the original carton until time of use under refrigerated conditions at 2-8º C (36-46º F) and protected from light. Do not use beyond the expiration date stamped on the carton. Refer to *Dosage and Administration* (2) for information on the stability and storage of diluted solutions of Soliris.

*DO NOT FREEZE. DO NOT SHAKE.*

NDC 25682-001-01 Single unit 300 mg carton: Contains one (1) 30 mL vial of Soliris (10 mg/mL).

## 17 PATIENT COUNSELING INFORMATION

*See Medication Guide.*

Prior to treatment, patients should fully understand the risks and benefits of Soliris, in particular the risk of meningococcal infection. Ensure that patients receive the Medication Guide.

Patients should be informed that they are required to receive a meningococcal vaccination at least 2 weeks prior to receiving the first dose of Soliris, if they have not previously been vaccinated. They are required to be revaccinated according to current medical guidelines for meningococcal vaccine use while on Soliris therapy. Patients should also be informed that vaccination may not prevent meningococcal infection. Patients should be educated about any of the signs and symptoms of meningococcal infection, and strongly advised to seek immediate medical attention if these signs or symptoms occur. These signs and symptoms are as follows:

- moderate to severe headache with nausea or vomiting
- moderate to severe headache and a fever
- moderate to severe headache with a stiff neck or stiff back
- fever of 103° F (39.4° C) or higher
- fever and a rash
- confusion
- severe muscle aches with flu-like symptoms, and eyes sensitive to light

Patients should be informed that they would be provided with the Patient Safety 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.

Patients should be informed that there is a potential for serious hemolysis when Soliris is discontinued and that they will be monitored by their healthcare professional for at least 8 weeks following Soliris discontinuation.

Manufactured by:

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US License Number 1743

# MEDICATION GUIDE

Soliris (eculizumab)

(so-leer-is)

Read the Medication Guide before you start Soliris and before each dose (infusion). This Medication Guide does not take the place of talking with your doctor about your condition or your treatment. Talk to your doctor if you have any questions about your treatment with Soliris.

**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.**

  1. **You must receive a meningococcal vaccine at least 2 weeks before your first dose of Soliris unless you have already had this vaccine.**

  2. **If you had a meningococcal vaccine in the past, you might need a booster dose before starting Soliris.** Your doctor will decide if you need another dose of a meningococcal vaccine.

  3. **A meningococcal vaccine does not prevent all meningococcal infections. You must be aware of the following signs and symptoms of a meningococcal infection:**

     - **moderate to severe headache with nausea or vomiting**
     - **moderate to severe headache and a fever**
     - **moderate to severe headache with a stiff neck or stiff back**
     - **fever of 103° F (39.4° C) or higher**
     - **fever and a rash**
     - **confusion**
     - **severe muscle aches with flu-like symptoms, and eyes sensitive to light**

**Call your doctor or get emergency medical care right away if you have any of these symptoms.**

You will receive a Patient Safety Card that lists these symptoms and what to do if you have them. Carry it with you at all times. You will need to show the card to any healthcare provider that treats you.

**What Is Soliris?**

Soliris is a medicine called a monoclonal antibody. Soliris is used for the treatment of patients with a disease that affects red blood cells called Paroxysmal Nocturnal Hemoglobinuria (PNH).

Soliris works by blocking part of your immune system. This can help your PNH symptoms but it can also increase your chance for infection. **It is important that you:**

- have all recommended immunizations and vaccines before you start Soliris
- stay up-to-date with all recommended immunizations and vaccines during treatment with Soliris

**Who Should Not Receive Soliris?**

**Do not receive Soliris if you:**

- have a meningococcal infection
- have not been vaccinated with, or you are not up-to-date with a meningococcal vaccine. See "What is the most important information about Soliris?"

**Tell your doctor if you:**

- have an infection or fever
- are pregnant, become pregnant, or are breastfeeding. Soliris has not been studied in pregnant or nursing women.

**How Do I Receive Soliris?**

- Soliris is given through a vein (I.V. infusion) over 35 minutes.
- You will usually receive a Soliris infusion:
  - every 7 days for five weeks, then
  - every 14 days
- Following each infusion, you may be monitored for one hour for allergic reactions.

**What If I Miss a Dose or Stop Soliris Treatment?**

- If you forget or miss a Soliris infusion, call your doctor right away.
- Stopping treatment with Soliris may cause a sudden and serious breakdown of your red blood cells. Symptoms or problems from red blood cell breakdown include:
  - a large drop in your red blood cell count causing anemia
  - confusion
  - chest pain
  - kidney problems
  - blood clots
- Your doctor will need to monitor you closely for at least 8 weeks after stopping Soliris.

**What Are The Possible Side Effects With Soliris?**

**Serious side effects with Soliris include:**

- **serious and life-threatening infections.** See "What is the most imortant information I should know about Soliris?"

**Common side effects with Soliris include:**

- headaches
- runny nose and colds
- sore throat
- back pain
- nausea

Call your doctor if you have any of these side effects. These are not all the side effects with Soliris. Ask your doctor for more information.

**General Information About Soliris**

Medicines are sometimes prescribed for conditions other than those listed in a Medication Guide. If you have any concerns about Soliris, ask your doctor. Your doctor or pharmacist can give you information about Soliris that was written for health care professionals.

Soliris contains eculizumab in a solution of water, polysorbate, sodium phosphate and sodium chloride.

Manufactured by Alexion Pharmaceuticals, Inc., 352 Knotter Drive, Cheshire, CT 06410 USA.

Revised: March 2007

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