

## 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 ( $\geq 10\%$  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](http://www.fda.gov/medwatch).

See 17 PATIENT COUNSELING INFORMATION AND MEDICATION GUIDE

Revised: 3/2007

## 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.

# Soliris™ (eculizumab)

## 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*.

# Soliris™ (eculizumab)

## 52 5 WARNINGS AND PRECAUTIONS

### 53 5.1 Serious Meningococcal Infections

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

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

62 In clinical studies, 2 out of 196 PNH patients developed serious meningococcal infections while receiving  
63 treatment with Soliris; both had been vaccinated. [*see Adverse Reactions (6.1)*].

### 64 5.2 Other Infections

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

### 67 5.3 Monitoring After Soliris Discontinuation

68 Since Soliris therapy increases the number of PNH cells [in study 1, the proportion of PNH RBCs increased  
69 among Soliris-treated patients by a median of 28% from baseline (range from -25% to 69%)], patients who  
70 discontinue treatment with Soliris may be at increased risk for serious hemolysis. Serious hemolysis is identified  
71 by serum LDH levels greater than the pre-treatment level, along with any of the following: greater than 25%  
72 absolute decrease in PNH clone size (in the absence of dilution due to transfusion) in one week or less; a  
73 hemoglobin level of <5 gm/dL or a decrease of >4 gm/dL in one week or less; angina; change in mental status; a  
74 50% increase in serum creatinine level; or thrombosis. Monitor any patient who discontinues Soliris for at least 8  
75 weeks to detect serious hemolysis and other reactions.

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

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

### 81 82 5.4 Thrombosis Prevention and Management

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

### 85 86 5.5 Laboratory Monitoring

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

### 91 5.6 Infusion Reactions

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

## 96 97 6 ADVERSE REACTIONS

### 98 6.1 Clinical Trial Experience

99 Meningococcal infections are the most important adverse reactions experienced by patients receiving Soliris  
100 therapy. In PNH clinical studies, two patients experienced meningococcal sepsis. Both patients had previously  
101 received a meningococcal vaccine. In clinical studies among patients without PNH, meningococcal meningitis  
102 occurred in an unvaccinated patient [*see Warnings and Precautions (5.1)*].

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

108 Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the  
109 clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not  
110 reflect the rates observed in practice. Table 1 summarizes the adverse reactions that occurred at a numerically

# Soliris™ (eculizumab)

111 higher rate in the Soliris group than the placebo group and at a rate of 5% or more among patients treated with  
112 Soliris.

113 TABLE 1  
114 ADVERSE REACTIONS REPORTED IN 5% OR MORE OF SOLIRIS TREATED PATIENTS AND GREATER  
115 THAN PLACEBO IN THE CONTROLLED CLINICAL STUDY

Reaction	Soliris N = 43 N (%)	Placebo N = 44 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)

116 In the placebo-controlled clinical study, serious adverse reactions occurred among 4 (9%) patients receiving  
117 Soliris and 9 (21%) patients receiving placebo. The serious reactions included infections and progression of  
118 PNH. No deaths occurred in the study and no patients receiving Soliris experienced a thrombotic event; one  
119 thrombotic event occurred in a patient receiving placebo.

120 Among 193 patients with PNH treated with Soliris in the single arm, clinical study or the follow-up study, the  
121 adverse reactions were similar to those reported in the placebo-controlled clinical study. Serious adverse  
122 reactions occurred among 16% of the patients in these studies. The most common serious adverse reactions  
123 were: viral infection (2%), headache (2%), anemia (2%), and pyrexia (2%).

## 124 6.2 Immunogenicity

125 As with all proteins there is a potential for immunogenicity. Low titers of antibodies to Soliris were detected in  
126 3/196 (2%) of all PNH patients treated with Soliris. No apparent correlation of antibody development to  
127 clinical response was observed. The immunogenicity data reflect the percentage of patients whose test results  
128 were considered positive for antibodies to Soliris in an enzyme linked immunosorbent assay (ELISA) and are  
129 highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of  
130 antibody positivity in the assay may be influenced by several factors including sample handling, timing of  
131 sample collection, concomitant medications and underlying disease. For these reasons, comparison of the  
132 incidence of antibodies to Soliris with the incidence of antibodies to other products may be misleading.

## 133 7 DRUG INTERACTIONS

134 Drug interaction studies have not been performed with Soliris.

# Soliris™ (eculizumab)

## 135 8 USE IN SPECIFIC POPULATIONS

### 136 8.1 Pregnancy

137 Pregnancy Category C:

138 PNH is a serious illness. Pregnant women with PNH and their fetuses have high rates of morbidity and  
139 mortality during pregnancy and the postpartum period. There are no adequate and well-controlled studies of  
140 Soliris in pregnant women. Soliris, a recombinant IgG molecule (humanized anti-C5 antibody), is expected to  
141 cross the placenta. Animal studies using a mouse analogue of the Soliris molecule (murine anti-C5 antibody)  
142 showed increased rates of developmental abnormalities and an increased rate of dead and moribund offspring at  
143 doses 2-8 times the human dose. Soliris should be used during pregnancy only if the potential benefit justifies  
144 the potential risk to the fetus.

145 Animal reproduction studies were conducted in mice using doses of a murine anti-C5 antibody that  
146 approximated 2-4 times (low dose) and 4-8 times (high dose) the recommended human Soliris dose, based on a  
147 body weight comparison. When animal exposure to the antibody occurred in the time period from before  
148 mating until early gestation, no decrease in fertility or reproductive performance was observed. When maternal  
149 exposure to the antibody occurred during organogenesis, two cases of retinal dysplasia and one case of  
150 umbilical hernia were observed among 230 offspring born to mothers exposed to the higher antibody dose;  
151 however, the exposure did not increase fetal loss or neonatal death. When maternal exposure to the antibody  
152 occurred in the time period from implantation through weaning, a higher number of male offspring became  
153 moribund or died (1/25 controls, 2/25 low dose group, 5/25 high dose group). Surviving offspring had normal  
154 development and reproductive performance.

### 155 8.2 Labor and Delivery

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

### 157 8.3 Nursing Mothers

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

### 163 8.4 Pediatric Use

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

### 166 8.5 Geriatric Use

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

## 170 10 OVERDOSAGE

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

## 172 11 DESCRIPTION

173 Soliris is a formulation of eculizumab which is a recombinant humanized monoclonal IgG<sub>2/4</sub>κ antibody  
174 produced by murine myeloma cell culture and purified by standard bioprocess technology. Eculizumab  
175 contains human constant regions from human IgG2 sequences and human IgG4 sequences and murine  
176 complementarity-determining regions grafted onto the human framework light- and heavy-chain variable  
177 regions. Eculizumab is composed of two 448 amino acid heavy chains and two 214 amino acid light chains  
178 and has a molecular weight of approximately 148 kDa.

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

## 184 12 CLINICAL PHARMACOLOGY

### 185 12.1 Mechanism of Action

186 Eculizumab, the active ingredient in Soliris, is a monoclonal antibody that specifically binds to the  
187 complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the  
188 generation of the terminal complement complex C5b-9. Soliris inhibits terminal complement mediated  
189 intravascular hemolysis in PNH patients.

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

# Soliris™ (eculizumab)

## 195 12.2 Pharmacodynamics

196 In the placebo-controlled clinical study, Soliris when administered as recommended reduced hemolysis as  
197 shown by the reduction of serum LDH levels from  $2200 \pm 1034$  U/L (mean  $\pm$  SD) at baseline to  $700 \pm 388$  U/L  
198 by week one and maintained the effect through the end of the study at week 26 ( $327 \pm 433$  U/L). In the single  
199 arm clinical study, Soliris maintained this effect through 52 weeks [see *Clinical Studies (14)*].

## 200 12.3 Pharmacokinetics

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

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

## 208 13 NONCLINICAL TOXICOLOGY

### 209 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

## 214 14 CLINICAL STUDIES

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

### 221 Study 1:

222 PNH patients with at least four transfusions in the prior 12 months, flow cytometric confirmation of at least  
223 10% PNH cells and platelet counts of at least 100,000/microliter were randomized to either Soliris (n = 43) or  
224 placebo (n = 44). Prior to randomization, all patients underwent an initial observation period to confirm the  
225 need for RBC transfusion and to identify the hemoglobin concentration (the "set-point") which would define  
226 each patient's hemoglobin stabilization and transfusion outcomes. The hemoglobin set-point was less than or  
227 equal to 9 g/dL in patients with symptoms and was less than or equal to 7 g/dL in patients without symptoms.  
228 Endpoints related to hemolysis included the numbers of patients achieving hemoglobin stabilization, the number  
229 of RBC units transfused, fatigue, and health-related quality of life. To achieve a designation of hemoglobin  
230 stabilization, a patient had to maintain a hemoglobin concentration above the hemoglobin set-point and avoid  
231 any RBC transfusion for the entire 26 week period. Hemolysis was monitored mainly by the measurement of  
232 serum LDH levels, and the proportion of PNH RBCs was monitored by flow cytometry. Patients receiving  
233 anticoagulants and systemic corticosteroids at baseline continued these medications.

234 Major baseline characteristics were balanced (see table 2).

235 **TABLE 2**  
236 **STUDY 1 PATIENT BASELINE CHARACTERISTICS**

Parameter	Study 1	
	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)

# Soliris™ (eculizumab)

## Study 1

Parameter	Placebo N = 44	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

237

238 Patients treated with Soliris had significantly reduced ( $p < 0.001$ ) hemolysis resulting in improvements in anemia as  
 239 indicated by increased hemoglobin stabilization and reduced need for RBC transfusions compared to placebo treated  
 240 patients (see table 3). These effects were seen among patients within each of the three pre-study RBC transfusion  
 241 strata (4 - 14 units; 15 - 25 units; > 25 units). After 3 weeks of Soliris treatment, patients reported less fatigue and  
 242 improved health-related quality of life. Because of the study sample size and duration, the effects of Soliris on  
 243 thrombotic events could not be determined.

244

245

246

**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) (range)	10 (2 - 21)	0 (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

247

248

### Study 2 and Extension Study:

249

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

260

## **16 HOW SUPPLIED / STORAGE AND HANDLING**

261

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

263

Soliris vials must be stored in the original carton until time of use under refrigerated conditions at 2-8° C (36-  
 264 46° F) and protected from light. Do not use beyond the expiration date stamped on the carton. Refer to  
 265 *Dosage and Administration (2)* for information on the stability and storage of diluted solutions of Soliris.

# Soliris™ (eculizumab)

266 *DO NOT FREEZE. DO NOT SHAKE.*

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

268 **17 PATIENT COUNSELING INFORMATION**

269 *See Medication Guide.*

270

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

273

274 Patients should be informed that they are required to receive a meningococcal vaccination at least 2 weeks prior  
275 to receiving the first dose of Soliris, if they have not previously been vaccinated. They are required to be  
276 revaccinated according to current medical guidelines for meningococcal vaccine use while on Soliris therapy.

277 Patients should also be informed that vaccination may not prevent meningococcal infection. Patients should be  
278 educated about any of the signs and symptoms of meningococcal infection, and strongly advised to seek  
279 immediate medical attention if these signs or symptoms occur. These signs and symptoms are as follows:

280

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

288 Patients should be informed that they would be provided with the Patient Safety Card that they should carry with  
289 them at all times. This card describes symptoms which, if experienced, should prompt the patient to immediately seek  
290 medical evaluation.

291

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

294

Manufactured by:

Alexion Pharmaceuticals, Inc.

352 Knotter Drive

Cheshire, CT 06410 USA

US License Number 1743

295  
296  
297

## MEDICATION GUIDE

### Soliris (eculizumab)

(so-leer-is)

---

298  
299  
300  
301

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.

302

#### **What Is The Most Important Information I Should Know About Soliris?**

303  
304

**Soliris is a medicine that affects your immune system. Soliris can lower the ability of your immune system to fight infections.**

305  
306

- **Soliris increases your chance of getting serious and life-threatening meningococcal infections.**

307

308

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

309

310

311

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.

312

313

314

315

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

316

317

318

319

- **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**

320

321

322

323

324

325

326

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

327

328

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.

329

330

331

#### **What Is Soliris?**

332

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).

333

334

335

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:**

336

337

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

338

339

340

#### **Who Should Not Receive Soliris?**

341

**Do not receive Soliris if you:**

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

345 **Tell your doctor if you:**

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

349 **How Do I Receive Soliris?**

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

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

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

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

366 **Serious side effects with Soliris include:**

- 367 • **serious and life-threatening infections.** See “What is the most important information I  
368 should know about Soliris?”  
369

370 **Common side effects with Soliris include:**

- 371 • headaches  
372 • runny nose and colds  
373 • sore throat  
374 • back pain  
375 • nausea

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

378 **General Information About Soliris**

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

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

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

386 Revised: March 2007

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

---