

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125166

LABELING

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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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. Quadrivalent, 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.

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.

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.

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

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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.

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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 IgG₂/4k 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
180 Soliris is a sterile, clear, colorless, preservative-free 10 mg/mL solution for intravenous infusion and is
181 supplied in 30-mL single-use vials. The product is formulated at pH 7 and each vial contains 300 mg of
182 eculizumab, 13.8 mg sodium phosphate monobasic, 53.4 mg sodium phosphate dibasic, 263.1 mg sodium
183 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 ± 1034 U/L (mean \pm SD) at baseline to 700 ± 388 U/L
 198 by week one and maintained the effect through the end of the study at week 26 (327 ± 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 ± 82 hrs (mean \pm SD). The mean observed peak and trough
 205 serum concentrations of Soliris by week 26 were 194 ± 76 mcg/mL and 97 ± 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 ± 2 days for 4 weeks,
 219 followed by 900 mg 7 ± 2 days later, then 900 mg every 14 ± 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

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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.

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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

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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)].

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16 HOW SUPPLIED / STORAGE AND HANDLING

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

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Soliris vials must be stored in the original carton until time of use under refrigerated conditions at 2-8° C (36-46° 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.

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.*

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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:

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- 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

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US License Number 1743

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MEDICATION GUIDE

Soliris (eculizumab)

(so-leer-is)

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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.

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

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

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

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

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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.

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

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- 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

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

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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.

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What Is Soliris?

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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).

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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:**

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

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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

Patients receiving Soliris treatment should carry this card at all times.

INFORMATION FOR THE PATIENT

You should call your doctor (# _____) right away if you have any of these symptoms:

- 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

If you cannot reach your doctor right away, go to an emergency room and show them this card.

INFORMATION FOR THE PHYSICIAN

This patient was prescribed Soliris (eculizumab) therapy. Soliris is an antibody that inhibits terminal complement activation and prevents the formation of C5b-9 complex. Before beginning treatment, this patient should have received a meningococcal vaccine, but may still be susceptible to meningococcal infections.

For more information about Soliris, see the full prescribing information available at www.soliris.net/soliris.pdf, or call 1-888-SOLIRIS (1-888-765-4747)