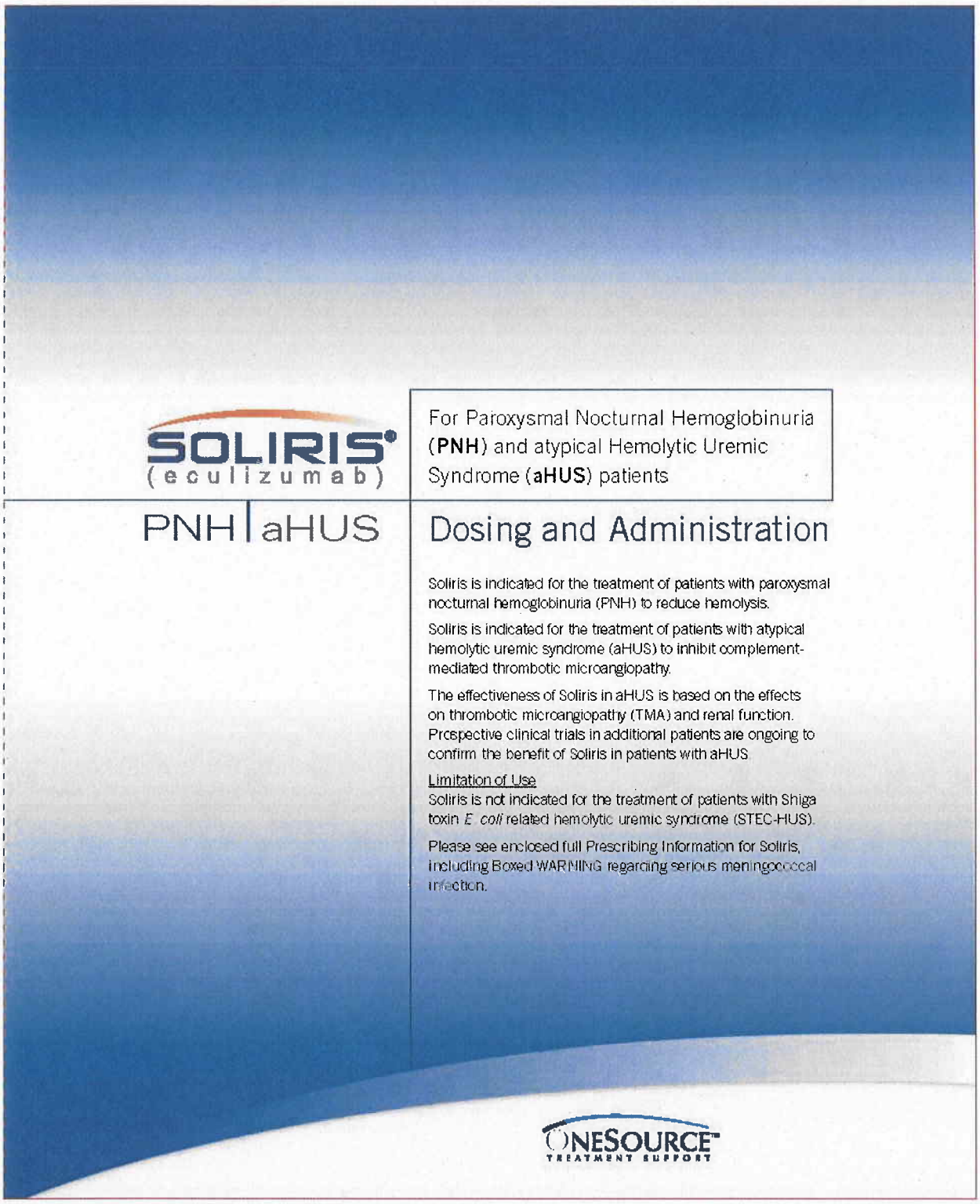

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See *Serious Meningococcal Infections* for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

Indications and usage

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

Soliris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

The effectiveness of Soliris in aHUS is based on the effects on thrombotic microangiopathy (TMA) and renal function. Prospective clinical trials in additional patients are ongoing to confirm the benefit of Soliris in patients with aHUS.

Limitation of Use

Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS).

Adverse reactions

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

The most frequently reported adverse reactions in aHUS single arm prospective trials (≥15% combined per patient incidence) are: hypertension, upper respiratory tract infection, diarrhea, headache, anemia, vomiting, nausea, urinary tract infection, and leukopenia.

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

PNH Clients

For patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)

Soliris® (eculizumab) PNH Dosing Guide

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.[1]

Soliris: a chronic therapy for a chronic disease[1,2]

Soliris should be administered at the recommended dosing interval or within 2 days before or after these time points.

- Fixed dose on time is critical to control chronic, complement-mediated hemolysis; for breakthrough hemolysis, dosing may be adjusted to every 12 days instead of 14 days[1]
- No dosing adjustments recommended based on age, gender, race, or renal insufficiency[1]
- Premedications are not routinely required

Monitoring After Discontinuation

Monitor patients after discontinuing Soliris for at least 8 weeks to detect hemolysis.

Important Administration Information

Soliris must be diluted to a final admixture concentration of 5 mg/mL prior to administration.

The diluted solution is a clear, colorless liquid and should be practically free of any particles.

DO NOT ADMINISTER AS AN IV PUSH OR BOLUS INJECTION.

- If diluted solution is refrigerated, warm to room temperature (18°C-25°C (64°F-77°F)) only by exposure to ambient air
- Administer as an IV infusion over 35 minutes via gravity feed, a syringe-type pump, or an infusion pump
- It is not necessary to protect diluted solution from light during administration

To learn more about Soliris, please call 1.888.SOLIRIS (1.888.765.4747) or visit www.Soliris.net.

SOLIRIS® (eculizumab)

For patients with atypical Hemolytic Uremic Syndrome (aHUS)

Soliris® (eculizumab) aHUS Dosing Guide

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.[1]

Soliris is a therapy for aHUS—a chronic disease needing chronic treatment[1]

Pretreatment		Induction Phase				Maintenance Phase				
≥2 weeks before induction	Week	1	2	3	4	5	6	7	8	9+
Meningococcal vaccination	Soliris dose	900 mg	900 mg	900 mg	900 mg	1200 mg	—	1200 mg	—	1200 mg every 14 (±2) days

Body Weight	Induction Phase	Maintenance Phase
40 kg and over	900 mg weekly × 4 doses	1200 mg at week 5; then 1200 mg every 2 weeks
30 kg to less than 40 kg	600 mg weekly × 2 doses	900 mg at week 3; then 900 mg every 2 weeks
20 kg to less than 30 kg	600 mg weekly × 2 doses	600 mg at week 3; then 600 mg every 2 weeks
10 kg to less than 20 kg	600 mg weekly × 1 dose	300 mg at week 2; then 300 mg every 2 weeks
5 kg to less than 10 kg	300 mg weekly × 1 dose	300 mg at week 2; then 300 mg every 3 weeks

→ **Soliris should be administered at the recommended dosing interval or within 2 days before or after these time points.**

Supplemental dosing of Soliris is required for patients undergoing concomitant plasma therapy[1]

Type of Intervention	Most Recent Soliris Dose	Supplemental Soliris Dose With Each PE/PI* Intervention	Timing of Supplemental Soliris Dose
Plasmapheresis or plasma exchange	300 mg	300 mg per each plasmapheresis or plasma exchange session	Within 60 minutes after each plasmapheresis or plasma exchange
	600 mg or more	600 mg per each plasmapheresis or plasma exchange session	
Fresh frozen plasma infusion	300 mg or more	300 mg per each unit of fresh frozen plasma	60 minutes prior to each unit of fresh frozen plasma infusion

*PE/PI = plasmapheresis or plasma exchange or fresh frozen plasma infusion.

Monitoring After Discontinuation

Thrombotic microangiopathy (TMA) complications after discontinuation were observed in the aHUS clinical studies.[1]

aHUS patients who discontinue treatment with Soliris should be monitored closely for at least 12 weeks for signs and symptoms of TMA complications. If TMA complications occur after Soliris discontinuation, consider reinstitution of Soliris treatment, plasma therapy,† or appropriate organ-specific supportive measures.[1]

DO NOT ADMINISTER AS AN IV PUSH OR BOLUS INJECTION.

- If diluted solution is refrigerated, warm to room temperature (18°C-25°C [64°F-77°F]) only by exposure to ambient air
- Administer as an IV infusion over 35 minutes via gravity feed, a syringe-type pump, or an infusion pump
- It is not necessary to protect diluted solution from light during administration

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†Plasma therapy = plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI).

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

SOLIRIS® (eculizumab)

aHUS Dosing

For PNH and aHUS

Preparation of Soliris® (eculizumab) for Administration[1]

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.[1]

Soliris Dose	Diluent Volume	Final Volume
300 mg	30 mL	60 mL
600 mg	60 mL	120 mL
900 mg	90 mL	180 mL
1200 mg	120 mL	240 mL

1. Withdraw the required amount of Soliris from the vial into a sterile syringe and transfer the recommended dose to an infusion bag
2. Dilute Soliris to a final concentration of 5 mg/mL using the above table as a guideline. The volume of diluent should be equivalent to the drug volume
3. Gently invert the infusion bag containing the diluted solution to ensure thorough mixture of the product and the diluent
   - Discard any unused portion left in the vial, as the product contains no preservatives
4. Inspect visually for particulate matter and discoloration prior to administration
   - The diluted solution is a clear colorless liquid and should be practically free of any particles
5. Allow the admixture to adjust to room temperature prior to administration (18°C-25°C, 64°F-77°F). **It must not be heated in a microwave or with any heat source other than ambient air temperature**
6. Admixed solution of Soliris is stable for 24 hours at 2°C-8°C (36°F-46°F) and at room temperature

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

How Supplied/Storage and Distribution[1]

- Vial—30 mL, liquid
- Product strength—10 mg/mL
- Product count—300 mg/30 mL (vial)
- Product physical specs—1 vial per carton
  - Shipped just in time for infusion
  - Weight: <1 lb
  - Dimensions: 1.625" x 1.625" x 3.125"
- Must be stored in the original carton until time of use under conditions at 2°C-8°C (36°F-46°F)
- Protect from light
- DO NOT FREEZE; DO NOT SHAKE
- Do not infuse beyond the expiration date stamped on the carton
- NDC 25682-001-01: Each single-unit carton contains one 30-mL vial of Soliris (10 mg/mL)

To enroll in the Soliris REMS and order Soliris, please call 1.888.SOLIRIS (1.888.765.4747)

Diagnosis code: XXXXXX

J code: J1300

Procedure code: XXXXXXX

ONESOURCE™ TREATMENT SUPPORT

Contact Soliris OneSource at 1.888.SOLIRIS (1.888.765.4747)

- All Alexion Nurse Case Managers are registered nurses and have extensive insurance and clinical experience. An Alexion Nurse Care Manager will partner with each patient and his or her healthcare team
- Fast and convenient same-day shipping that meets the needs of PNH and aHUS patients

SOLIRIS® (eculizumab)

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Please see enclosed full Prescribing Information for Soliris® (eculizumab), including Boxed WARNING regarding serious meningococcal infection.

References: 1. Soliris® [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc; 2011. 2. Helley D, de Latour RP, Porcher R, et al; French Society of Hematology. Evaluation of hemostasis and endothelial function in patients with paroxysmal nocturnal hemoglobinuria receiving eculizumab. *Haematologica*. 2010;95:574-581.

ALEXION