SOLIRIS® (ECULIZUMAB) FOR PNH

SOLIRIS® (ECULIZUMAB) OVERVIEW

Soliris is a terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is approved in nearly 50 countries for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.[1] PNH is a serious and life-threatening ultra-rare disease characterized by complement-mediated hemolysis (destruction of red blood cells).[2,3]

Soliris has earned some of the pharmaceutical industry's highest honors, including the 2008 Prix Galien USA Award for Best Biotechnology Product and the 2009 Prix Galien France Award in the category of Drugs for Rare Diseases.

SOLIRIS IN PNH

Soliris is the first and only treatment approved to address the underlying cause of PNH, complement-mediated hemolysis. In healthy individuals, complement—a part of the immune system—attacks foreign particles. Patients with PNH, however, generate abnormal red blood cells (RBCs) that lack protective proteins, known as GPI-anchor proteins or complement regulatory proteins, on the surface of the cells. This makes RBCs susceptible to complement activation, leading to chronic hemolysis.[4] Chronic, complement-mediated hemolysis is the underlying cause of progressive morbidities and premature mortality in patients with PNH. Chronic hemolysis can cause patients with PNH to experience anemia, extreme fatigue that can impair functioning and health-related quality of life (QoL), dark urine and shortness of breath.[5,6,7] The most devastating consequence of hemolysis is thrombosis (blood clots), which can damage vital organs and cause premature death.[8]

Soliris works by selectively targeting and blocking the terminal complement cascade to significantly reduce hemolysis in patients with PNH, resulting in fewer thrombotic events (TEs), reduced need for transfusions, and improvements in fatigue and health-related QoL.[1,8,9,10]

CLINICAL TRIAL DATA

The safety and efficacy of Soliris to treat patients with PNH experiencing hemolysis were assessed in a randomized, double-blind, multi-center placebo-controlled 26 week study (TRIUMPH Study). The study comprised 87 transfusion-dependent patients with PNH receiving Soliris (n=43) or placebo (n=44). Patients were also treated in a single-arm multi-center study comprising 97 patients with PNH treated with Soliris over 52 weeks (SHEPHERD Study). An extension study consisted of 187 patients with PNH initially enrolled in one of 3 parent trials (N=195) who continued to receive Soliris for a range of 10 to 54 months.[1,11]

Data from the trials demonstrated that patients treated with Soliris experienced significantly reduced hemolysis, leading to an improvement in symptoms and a reduction of thrombotic events, a major health problem associated with the disease.[1,8,12]

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ALEXION®

- Patients treated with Soliris had an 87% reduction in hemolysis (as demonstrated by LDH) at 36 months. A reduction in hemolysis began with the first dose, was significant within the first week, and was sustained long term.[8-11]
- Patients treated with Soliris had a 92% reduction in thrombotic events over the course of 12 months compared to the same length of time pretreatment (3 TEs on Soliris treatment vs. 39 TEs before treatment).[8]
  - The majority of patients (63%) received concomitant anticoagulant therapy. The effect of anticoagulant withdrawal during Soliris treatment has not been studied.*[1]
- 51% of patients treated with Soliris achieved transfusion independence at 26 weeks compared to 0% of patients receiving placebo.[10,13]
- 78% of patients treated with Soliris experienced clinically meaningful improvements in fatigue which were sustained over time.[1,14] Patients also experienced sustained improvement in a range of health-related QoL measures.[9,10]
- The most frequently reported adverse reactions in the PNH randomized trial (≥10% overall and greater than placebo) are: headache, nasopharyngitis, back pain and nausea.[1]

ACCESS TO SOLIRIS

At Alexion, our objective is that every patient with PNH who can benefit from Soliris will have access to Soliris. As part of our commitment to the PNH community in the United States and Canada, Alexion offers OneSource™, a personalized program that provides disease education, assistance with access to Soliris, and treatment support for patients and their caregivers. OneSource is staffed by Alexion Nurse Case Managers, all of whom are registered nurses with extensive clinical experience and backgrounds in reimbursement. An Alexion Nurse Case Manager is assigned to each patient and his or her healthcare team to help coordinate care and provide information about reimbursement.

Patients, caregivers and healthcare providers can call 1.888.765.4747 to speak with an Alexion Nurse Case Manager.

In addition to the OneSource program, the Alexion Access Foundation was established by Alexion to help patients who do not have insurance, access to insurance, or any other means for obtaining Alexion medicines. We also support Patient Assistance Programs that are administered by non-profit, charitable organizations to help cover disease- and treatment-related costs for eligible patients.

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 [see *Warnings and Precautions (5.1)*].

- 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 *Warnings and Precautions (5.1)* 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 [see *Warnings and Precautions (5.2)*]. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at solirisrems.com.

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

Soliris is contraindicated in:

- Patients with unresolved serious *Neisseria meningitidis* infection
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection

* Soliris PI, page 4 "Study 2 and Extension Study"

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WARNINGS AND PRECAUTIONS

Other Infections

Soliris blocks terminal complement activation; therefore patients may have increased susceptibility to infections, especially with encapsulated bacteria. Additionally, Aspergillus infections have occurred in immunocompromised and neutropenic patients. Children treated with Soliris may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib) infections according to ACIP guidelines. Use caution when administering Soliris to patients with any systemic infection.

Monitoring Disease Manifestations After Soliris Discontinuation

Treatment Discontinuation for PNH

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

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.

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 patients experienced an infusion reaction which required discontinuation of Soliris. Interrupt Soliris infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

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.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

References

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