

SOLIRIS® (ECULIZUMAB) FOR aHUS



SOLIRIS® (ECULIZUMAB) OVERVIEW

Soliris is a terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is approved in the United States and more than 40 countries for the treatment of adult and pediatric patients with atypical hemolytic uremic syndrome (aHUS).¹ aHUS is a chronic, ultra-rare, and life-threatening disease in which a genetic mutation in one or more complement regulatory genes causes chronic uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA)—the formation of blood clots in small blood vessels throughout the body.^{2,3,4}

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 aHUS

Soliris is the first and only treatment approved to address the underlying cause of aHUS, complement-mediated TMA.^{1,2} In healthy individuals, complement—a part of the immune system—is used to attack foreign particles, and the system is highly regulated to prevent it from causing damage to tissues and organs. In patients with aHUS, genetic changes in, and autoantibodies to, proteins that regulate the complement system disrupt the delicate balance of the complement pathway, and the body is unable to control the activation of complement.³⁻⁶ This causes a lifelong risk for TMA, which can lead to progressive, catastrophic, and life-threatening damage to vital organs and premature death.^{2,3,4,7}

Soliris works by selectively targeting and blocking the terminal complement cascade. Soliris is indicated for the treatment of patients with aHUS to inhibit complement-mediated TMA.¹

CLINICAL TRIAL DATA

The safety and efficacy of Soliris for the treatment of aHUS has been demonstrated in 4 multinational, prospective studies (N=100). Baseline characteristics of these 4 studies are outlined on the next page.¹

DEMOGRAPHICS AND BASELINE VALUES IN aHUS PROSPECTIVE CLINICAL STUDIES¹

Study 1 Progressing TMA N=17	Study 2 Long duration of aHUS N=20		Study 4 Adult/earlier treatment N=41	Study 5 Pediatric/earlier treatment N=22
28 (17-68 yrs)	28 (13-63 yrs)	Median age (range)	35 (18-80 yrs)	6.5 (5 mo-17 yrs)
10 (0.26-236)	48 (0.66-286)	Time from aHUS diagnosis until Soliris initiation in months, median (range)	0.79 (0.03-311)	0.56 (0.03-191)
<1 (<1-4) 9 (1-45)	218 (105-421)	Time from current clinical TMA manifestation until Soliris initiation in months, median (range)	0.52 (0.03-19)	0.2 (0.03-4)
118 (62-161)	218 (105-421)	Baseline platelet count (x 10 ⁹ /L), median (range)	125 (16-332)	91 (19-146)
269 (134-634)	200 (151-391)	Baseline LDH (U/L), median (range)	375 (131-3318)	1244 (282-7164)

CLINICAL TRIALS RESULTS AT 26 WEEKS¹

Study 1 Progressing TMA N=17	Study 2 Long duration of aHUS N=20		Study 4 Adult/earlier treatment N=41	Study 5 Pediatric/earlier treatment N=22
76% (13)	90% (18)	Patients achieving hematological normalization*	88% (36)	82% (18)
65% (11)	25% (5)	Patients achieving complete TMA response**	56% (23)	64% (14)
88% (15)	80% (16)	Patients achieving TMA event-free status***	90% (37)	95% (21)
53% (9)	5% (1)	Patients with eGFR improvement ≥ 15 mL/min/1.73 m ²	54% (22)	86% (19)

*Hematologic normalization: normal platelet count (≥150 x 10⁹/L) and lactate dehydrogenase (LDH) levels ≤ upper limit of normal for ≥2 consecutive measurements taken ≥4 weeks apart

**Complete TMA response defined as hematologic normalization and ≥25% improvement in serum creatinine

***TMA-event free status defined as absence for at least 12 weeks of a decrease in platelet count of >25% from baseline, plasma exchange or plasma infusion, and new dialysis requirement

Ongoing Soliris treatment resulted in sustained improvement in hematologic markers of complement-mediated TMA, including platelet counts and lactate dehydrogenase (LDH) levels.^{1,8,9,10} Patients treated with Soliris also had improvements in renal function as measured by estimated glomerular filtration rate (eGFR).^{1,8,9,10}

The most frequently reported adverse reactions in aHUS single-arm prospective trials (≥20%) were: headache, diarrhea, hypertension, upper respiratory tract infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia.¹

ACCESS TO SOLIRIS

At Alexion, our objective is that every patient with aHUS who can benefit from Soliris will have access to Soliris. As part of our commitment to the aHUS 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

Atypical Hemolytic Uremic Syndrome (aHUS)

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

Limitation of Use

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

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

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 influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* 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 aHUS

After discontinuing Soliris, monitor patients with aHUS for signs and symptoms of thrombotic microangiopathy (TMA) complications for at least 12 weeks. In aHUS clinical trials, 18 patients (5 in the prospective studies) discontinued Soliris treatment. TMA complications occurred following a missed dose in 5 patients, and Soliris was reinitiated in 4 of these 5 patients.

Clinical signs and symptoms of TMA include changes in mental status, seizures, angina, dyspnea, or thrombosis. In addition, the following changes in laboratory parameters may identify a TMA complication: occurrence of two, or repeated measurement of any one of the following: a decrease in platelet count by 25% or more compared to baseline or the peak platelet count during Soliris treatment; an increase in serum creatinine by 25% or more compared to baseline or nadir during Soliris treatment; or, an increase in serum LDH by 25% or more over baseline or nadir during Soliris treatment.

If TMA complications occur after Soliris discontinuation, consider reinstatement of Soliris treatment, plasma therapy [plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI)], or appropriate organ-specific supportive measures.

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 aHUS single arm prospective trials ($\geq 20\%$) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia.

Please see full [prescribing information for Soliris](#), including boxed WARNING regarding serious meningococcal infection.

References

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