AstraZeneca

SOLIRIS® (eculizumab) PHYSICIAN'S GUIDE

Paroxysmal Nocturnal Hemoglobinuria (**PNH**)

Atypical Hemolytic Uremic Syndrome (**aHUS**)

Generalized Myasthenia Gravis (**gMG**)

Neuromyelitis Optica Spectrum Disorder (**NMOSD**)

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1 INTRODUCTION

SOLIRIS® is indicated in adults and children for the treatment of:

- Paroxysmal nocturnal hemoglobinuria **(PNH)**

  Evidence of clinical benefit is demonstrated in patients with hemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history.
- Atypical hemolytic uremic syndrome **(aHUS)**

SOLIRIS® is also indicated in adults for the treatment of:

- Refractory generalized myasthenia gravis (**gMG**) in patients who are anti-acetylcholine receptor (AChR) antibody-positive.
- Neuromyelitis optica spectrum disorder (**NMOSD**) in patients who are anti-aquaporin-4 (AQP4) antibody-positive.

This guide is intended to increase the prescriber's awareness of the risks associated with the use of SOLIRIS® which include meningococcal infections, serious infections (including sepsis), infusion reactions and immunogenicity. It is also intended to increase the prescriber's awareness of the risks associated with discontinuation of SOLIRIS®.

This guide must be used in combination with the SOLIRIS® (eculizumab) Singapore Package Insert (PI).

You will be provided with the following materials to be given to each patient treated with SOLIRIS®:

- **Patient Safety Information Card**

  To inform patients and healthcare providers about the risk of meningococcal infection associated with SOLIRIS®
- **Patient/Parent/Legal Guardian Guide**

  To educate patients and parents/legal guardians of infants and children about the safety considerations associated with SOLIRIS® treatment

Read these materials ahead of prescribing SOLIRIS® to your patients.

2 IMPORTANT SAFETY INFORMATION[1]

Serious Meningococcal Infection

- Due to its mechanism of action, the use of SOLIRIS® increases the risk of meningococcal infection (*Neisseria meningitidis*) for the patient.
- Cases of serious or fatal meningococcal infection have been reported in SOLIRIS® treated patients. Meningococcal infections in patients treated with SOLIRIS® have presented as meningococcal sepsis.

To minimise the risk of meningococcal infection and poor outcomes following infection:

Prior to starting treatment with SOLIRIS®:

- ▶ Vaccinate your patients with a meningococcal vaccine at least 2 weeks prior to initiating SOLIRIS® unless the risk of delaying SOLIRIS® therapy outweighs the risk of developing a meningococcal infection. Vaccines against serogroups A, C, Y, W135, are recommended in preventing the commonly pathogenic meningococcal serogroups. Vaccine against serogroup B where available is also recommended.
  - For patients who initiate SOLIRIS® treatment less than 2 weeks after receiving a meningococcal vaccine, treat with appropriate prophylactic antibiotics until 2 weeks after vaccination.
- ▶ Monitor patients closely for disease symptoms after recommended vaccination as vaccination may further activate complement. As a result, patients with complement-mediated diseases may experience increased signs and symptoms of their underlying disease, such as hemolysis (PNH), thrombotic microangiopathy (TMA) (aHUS), exacerbation of MG (refractory gMG), or relapse (NMOSD).
- ▶ Since vaccination may not be sufficient to prevent meningococcal infection, consider prophylactic use of antibiotics in addition to vaccination based on the official guidance on the appropriate use of antibacterial agents.

During treatment with SOLIRIS®:

- ▶ Monitor your patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary.
- ▶ Revaccinate according to current national vaccination guidelines for vaccine use in patients treated with complement inhibitors.

Do not initiate SOLIRIS® treatment in patients:

- with unresolved *Neisseria meningitidis* infection.
- who are not currently vaccinated against *Neisseria meningitidis* unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination.

Other Systemic Infections

- Patients may have increased susceptibility to infections, especially with *Neisseria* and encapsulated bacteria. Serious infections with Neisseria species (other than *Neisseria meningitidis*), including disseminated gonococcal infection, have been reported with SOLIRIS®. Counsel patients about gonorrhea prevention.
- Vaccinate patients less than 18 years of age against *Haemophilus influenzae* and pneumococcal infections. Strict adherence to the national vaccination recommendations for each age group is needed.
- Administer SOLIRIS® therapy with caution to patients with active systemic infections.

Infusion Reactions

- Administration of SOLIRIS® may result in infusion reactions that could cause allergic or hypersensitivity reactions (including anaphylaxis).
- Monitor patients for one hour following infusion. If an adverse event 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 may not exceed two hours in adults and adolescents (aged 12 years to under 18 years) and four hours in children aged less than 12 years.
- SOLIRIS® administration should be interrupted in all patients experiencing severe infusion reactions and appropriate medical therapy should be administered.

Immunogenicity

- Infrequent antibody responses have been detected in SOLIRIS® treated patients across clinical studies.
- Monitor the patients for any signs and symptoms associated with positive anti-drug antibodies.

3 INFORMATION THAT YOU SHOULD PROVIDE TO PATIENTS AND PARENTS/LEGAL GUARDIANS

Risk of meningococcal infection:

Inform and educate patients that if they suspect an infection, they should seek immediate medical attention.

The relevant signs and symptoms include:

- Headache with nausea or vomiting
- Headache and a fever
- Headache with a stiff neck or stiff back
- Fever
- Fever and a rash
- Confusion
- Muscle aches with flu-like symptoms
- Eyes sensitive to light

Common signs and symptoms in infants include[2]:

- Fever, cold hands and feet
- Fretful, dislike being handled
- Rapid breathing or grunting
- Unusual cry, moaning
- Stiff neck, dislike bright lights
- Refusing food and vomiting
- Drowsy, floppy, unresponsive
- Pale, blotchy skin spots/rash
- Tense, bulging fontanelle (soft spot)
- Convulsions/seizures

In children, additional signs and symptoms to those listed for infants may include[3]:

- Severe muscle pain
- Severe headache
- Confusion
- Irritability

Explain to the patient that he/she needs to carry the Patient Safety Information Card at all times throughout the duration of SOLIRIS® therapy and for 3 months after the last dose of SOLIRIS® and show it to any healthcare professionals they see.

4 TREATMENT DISCONTINUATION[1]

Treatment discontinuation in PNH

Closely monitor patients with PNH who discontinue SOLIRIS® for signs and symptoms of serious intravascular hemolysis and other reactions for at least 8 weeks.

Serious hemolysis is identified by:

1. serum lactate dehydrogenase (LDH) > pre-treatment LDH

AND

2. any of the following criteria:

- PNH clone size absolute↓ of > 25% (in the absence of dilution due to transfusion) in 1 week or less
- Hb < 5 g/dL OR Hb ↓ of > 4 g/dL in 1 week or less
- Angina
- Change in mental status
- Serum creatinine ↑ of 50%
- Thrombosis

If serious hemolysis occurs, consider the following procedures/treatment:

Blood transfusion (packed RBCs) OR Exchange transfusion if PNH RBCs>50% of total RBCs by flow cytometry + Anticoagulation + Corticosteroids OR Reinstitution of SOLIRIS®

Treatment discontinuation in aHUS

Severe thrombotic microangiopathy (TMA) complications were observed after SOLIRIS® discontinuation in the aHUS clinical studies.

Monitor aHUS patients who discontinue treatment with SOLIRIS® for signs and symptoms of TMA.

TMA complications following discontinuation can be identified by:

1. any two, or repeated measurement of any one, of the following:

- a decrease in platelet count of 25% or more as compared to either baseline or to peak platelet count during SOLIRIS® treatment;
- an increase in serum creatinine of 25% or more as compared to baseline or to nadir during SOLIRIS® treatment; or,
- an increase in serum LDH of 25% or more as compared to baseline or to nadir during SOLIRIS® treatment;

OR

2. any one of the following:

- a change in mental status or seizures;
- angina or dyspnea; or
- thrombosis.

If severe TMA complications occur after SOLIRIS® discontinuation, consider reinstitution of SOLIRIS® treatment, supportive care with PE/PI (plasmapheresis or plasma exchange, or fresh frozen plasma infusion), or appropriate organ-specific supportive measures including renal support with dialysis, respiratory support with mechanical ventilation or anticoagulation.

Treatment Discontinuation in gMG and NMOSD

Use of SOLIRIS® in refractory gMG and NMOSD treatment has been studied only in the setting of chronic administration. Carefully monitor patients who discontinue SOLIRIS® treatment for signs and symptoms of MG exacerbation (refractory gMG) or relapse (NMOSD).

FURTHER INFORMATION

For more information about SOLIRIS®, email: MedInfo.SG@astrazeneca.com.

Adverse events should be reported to: PatientSafety.SG@astrazeneca.com.

Company address: AstraZeneca Singapore Pte Ltd, 10 Kallang Avenue, #12-10, Aperia Tower 2, Singapore 339510.

This document has been approved by Singapore Health Sciences Authority (HSA) on 21/08/24

REFERENCES

1. SOLIRIS® (eculizumab) Singapore Package Insert (PI).
2. Signs and symptoms of meningitis in babies and toddlers. Meningitis Now website. Available at: https://www.meningitisnow.org/meningitis-explained/signs-and-symptoms/signs-and-symptoms-babies-and-toddlers/ (Accessed: 04 November 2022).
3. Meningitis symptoms in children. Meningitis Now website. Available at: https://www.meningitisnow.org/meningitis-explained/signs-and-symptoms/signs-and-symptoms-children/ (Accessed: 04 November 2022).

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