ULTOMIRIS® (ravulizumab)

Guide for Healthcare Professionals

The aim of this guide is to help mitigate the risk of meningococcal infection associated with the use of ULTOMIRIS® and to increase awareness of the need for the required vaccinations. This guide also provides important safety information on the risks of other systemic serious infections, use in pregnant and breast-feeding women and the discontinuation of ULTOMIRIS®.

It must be used in combination with the ULTOMIRIS® (ravulizumab) Singapore Package Insert (PI).

The guide describes:

- What is ULTOMIRIS®?
- Important Safety Information
- Treatment Discontinuation
- Adverse Event Reporting
- Contact Information

WHAT IS ULTOMIRIS®?

ULTOMIRIS® is indicated for the treatment of adult and pediatric patients with:

- **Paroxysmal Nocturnal Hemoglobinuria (PNH):**
    - Who present with clinical symptom(s) indicative of high disease activity.
    - Who are clinically stable after having been treated with eculizumab for at least the past 6 months.
- **Atypical Hemolytic Uremic Syndrome (aHUS):**
    - To inhibit complement-mediated thrombotic microangiopathy (TMA).
    - **Limitations of Use:** ULTOMIRIS® is not indicated for the treatment of patients with Shiga toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS).

ULTOMIRIS® is also indicated for the treatment of adult patients with:

- **Generalized Myasthenia Gravis (gMG):**
    - Who are anti-acetylcholine receptor (AChR) antibody-positive, as an add-on to standard therapy.
- **Neuromyelitis Optica Spectrum Disorder:**
    - Who are anti-aquaporin-4 (AQP4) antibody positive.

You will be provided with the following materials to be given to each patient or parents/caregivers of pediatric patients treated with ULTOMIRIS®. **Please read these materials and the Singapore Package Insert ahead of prescribing ULTOMIRIS® to your patients.**

- **Patient Card**
  To inform patients and healthcare professionals about the risk of meningococcal infection associated with ULTOMIRIS®.
- **Guide for Patients/Parents/Caregivers**
  To educate patients/parents/caregivers about important safety information related to ULTOMIRIS®, including the risk of meningococcal infection and the need for vaccination.

IMPORTANT SAFETY INFORMATION

Serious Meningococcal Infection

- Due to its mechanism of action, the use of ULTOMIRIS® increases the patient's susceptibility to meningococcal infection/sepsis (*Neisseria meningitidis*).

- Cases of serious or fatal meningococcal infections/sepsis have been reported in ULTOMIRIS® treated patients and with other terminal complement inhibitors. Meningococcal infections in patients treated with ULTOMIRIS® have presented as meningococcal sepsis or meningococcal encephalitis.

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

Prior to starting treatment with ULTOMIRIS®:

- Ensure vaccination of patients with a meningococcal vaccine at least 2 weeks prior to initiating ULTOMIRIS®, unless the risk of delaying ULTOMIRIS® therapy outweighs the risk of developing a meningococcal infection.
  - For patients who initiate ULTOMIRIS® treatment less than 2 weeks after receiving a meningococcal vaccine, treat with appropriate prophylactic antibiotics until 2 weeks after vaccination.

- Patients must receive vaccination according to current national vaccination guidelines for vaccination use. Vaccines against serogroups A, C, Y, W135 and B, where available, are recommended in preventing the commonly pathogenic meningococcal serogroups.

- 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.

- 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 ULTOMIRIS®:

- Monitor patients for early signs of meningococcal infections and sepsis, evaluate immediately if infection is suspected, and treat with antibiotics.

- Revaccinate according to current national vaccination guidelines for vaccine use in patients treated with complement inhibitors.

Do not initiate ULTOMIRIS® therapy 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.

- **Inform patients and parents/caregivers about the 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 fever
    - Headache with a stiff neck or stiff back
    - Fever
    - Fever and rash
    - Confusion
    - Muscle aches with flu-like symptoms
    - Eyes sensitive to light

  - **Common signs and symptoms in infants include:**
    - 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:**

    - Severe muscle pain
    - Severe headache
    - Confusion
    - Irritability

  - Explain to the patient or parent/caregiver that he/she must carry the Patient Card at all times throughout the duration of ULTOMIRIS® therapy and for 8 months after the last dose of ULTOMIRIS® and show it to any healthcare professionals they see.

Other Systemic Serious Infections

To minimise the risk of other systemic infections:

- Advise patients about gonorrhea prevention. Serious infections with Neisseria species (other than *Neisseria meningitidis*), including disseminated gonococcal infection, have been reported with ULTOMIRIS®.
- Patients below the age of 18 years old must be vaccinated against *Haemophilus influenzae* and pneumococcal infections, and strictly adhere to the national vaccination recommendations for each age group.
- Administer ULTOMIRIS® therapy with caution to patients with active systemic infections.

Pregnancy and Lactation

- For ULTOMIRIS®, no clinical data on exposed pregnancies are available.
- Women of childbearing potential should use effective contraception during treatment and up to 8 months after treatment.
- Breastfeeding should be discontinued during treatment and up to 8 months after treatment.

TREATMENT DISCONTINUATION

Treatment discontinuation in PNH

Closely monitor patients with PNH who discontinue ULTOMIRIS® for signs and symptoms of hemolysis and other reactions for at least 16 weeks.

These are identified by:

1. Elevated LDH (lactate dehydrogenase)

   AND

2. any of the following

   sudden decrease in PNH clone size or hemoglobin

   OR

   re-appearance of symptoms such as

- fatigue
- hemoglobinuria

- abdominal pain
- shortness of breath (dyspnea)
- major adverse vascular event (including thrombosis)
- dysphagia
- erectile dysfunction

If signs and symptoms of hemolysis occur after discontinuation, including elevated LDH, consider restarting treatment with ULTOMIRIS®.

Treatment discontinuation in aHUS

Monitor aHUS patients who discontinue treatment with ULTOMIRIS® for signs and symptoms of thrombotic microangiopathy (TMA).

TMA complications following discontinuation can be identified by:

1. at least two of the following laboratory results observed concurrently:

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

  (results should be confirmed by a second measurement 28 days apart)

  OR

2. any one of the following symptoms of TMA:

- a change in mental status or seizures;
- other extra renal TMA manifestations including cardiovascular abnormalities, pericarditis, gastrointestinal symptoms/diarrhea; or,
- thrombosis.

If TMA complications occur after discontinuation, consider reinitiation of ULTOMIRIS® treatment beginning with the loading dose and maintenance dose.

Treatment discontinuation in gMG and NMOSD

Considering that gMG and NMOSD are chronic diseases, patients benefiting from ULTOMIRIS® treatment who discontinue treatment should be monitored for symptoms of the underlying disease. If symptoms of gMG or NMOSD occur after discontinuation, consider restarting treatment with ULTOMIRIS®.

REPORTING OF ADVERSE EVENTS

Adverse events should be reported to: https://contactazmedical.astrazeneca.com/

CONTACT INFORMATION

For more information about ULTOMIRIS®, email: MedInfo.SG@astrazeneca.com.
AstraZeneca Singapore Pte Ltd, 10 Kallang Avenue, #12-10, Aperia Tower 2, Singapore 339510.

REFERENCES

ULTOMIRIS® (ravulizumab) Singapore Package Insert (PI)

This document has been approved by HSA as of 19-05-2025.

Scan here for Ultomiris® (Ravulizumab) Full Prescribing Information
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