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.

It must be used in combination with the ULTOMIRIS (ravulizumab) Israeli Prescribing Information.

The guide describes:

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

WHAT IS ULTOMIRIS?

ULTOMIRIS is indicated for the treatment of:

Adult and pediatric patients with a body weight of 10 kg or above with paroxysmal nocturnal hemoglobinuria (PNH):

- In patients with haemolysis with clinical symptom(s) indicative of high disease activity.
- In patients who are clinically stable after having been treated with eculizumab for at least the past 6 months.

Patients with a body weight of 10 kg or above with atypical hemolytic uremic syndrome (aHUS) who are complement inhibitor treatment naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab.

Adult patients with generalized myasthenia gravis (gMG) who are antiacetylcholine receptor (AChR) antibody-positive.

Adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive.

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.
- Ultomiris is contraindicated in patients who are not currently vaccinated against Neisseria meningitidis unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination.

Key Actions Required

- You will be provided with the following materials to be given to each patient treated with ULTOMIRIS. **Please read these materials ahead of prescribing ULTOMIRIS to your patients.**
  - **Patient Card**
    To inform patients and healthcare providers about the risk of meningococcal infection associated with ULTOMIRIS.

- **Guide for Patients/parents/caregivers**
  To educate patients/parents/caregivers about the risk of meningococcal infection associated with ULTOMIRIS treatment and the need for vaccination.

- **Patient Information leaflet**
  To provide comprehensive information to patients/parents/caregivers about ULTOMIRIS.

▶ **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 – MoH: https://www.gov.il/he/pages/vaccine-guidelines-main. Vaccines against serogroups A, B, C, Y, W135, 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.

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- **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.
  - In addition, instruct the parents/legal guardians not to stop the treatment without consulting with their treating physician.
  - 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 that they 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.

To minimise the risk of other systemic infections

Patients below the age of 18 years old must be vaccinated against haemophilus influenzae and pneumococcal infections, and strictly need to adhere to the national vaccination recommendations for each age group.

REPORTING OF ADVERSE EVENTS

Side effects can be reported to the Israeli Ministry of Health by clicking on the link “report side effects of drug treatment” that appears on the homepage of the Israeli Ministry of Health’s website (www.health.gov.il) which links to a portal, or by the following link: https://sideeffects.health.gov.il/ and by emailing the registration holder's patient safety unit at: drugsafety@neopharmgroup.com, Tel: 1-800-250-255.

CONTACT INFORMATION

For more information about ULTOMIRIS, email: drugsafety@neopharmgroup.com

REFERENCES

ULTOMIRIS® (ravulizumab) Prescribing Information as approved by the Israeli MOH.

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