ULTOMIRIS® ▼ (ravulizumab)

Patient Guide

Important safety information to minimise the risk of serious side effects

▼ This medicine is subject to additional monitoring.
This will allow quick identification of new safety information.
You can help by reporting any side effects you may get.

ALEXION®
AstraZeneca Rare Disease

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This guide is for adult patients diagnosed with paroxysmal nocturnal haemoglobinuria (PNH), adult patients diagnosed with Generalised Myasthenia Gravis (gMG), adult and adolescent patients suffering from atypical haemolytic uraemic syndrome (aHUS).
It gives you important safety information that you must be aware of. In addition, separate Parent/ Guardian Guide for parents/legal guardians of young patients has been developed, which your doctor will be able to give you.

GLOSSARY OF TERMS

Atypical haemolytic uremic syndrome (aHUS)
A rare disorder caused by chronic and excessive activation of the complement system, a part of your normal immune system. The overactive complement system damages small blood vessels and causes TMA, which can damage vital organs such as the kidneys.

Anaemia
A condition in which your body does not have enough red blood cells; this may lead to fatigue and other symptoms.

Blood clots
When many platelets in the blood stick together, they form a blood clot. These clots can block blood flow in the veins and arteries, depending on their size and location (see Thrombosis).

Chronic haemolysis
The destruction of red blood cells (haemolysis) over a long period of time (chronic).

Complement system (also known as the complement cascade or just complement)
Part of your immune system that destroys bacteria and other foreign cells. In PNH, complement is responsible for the destruction of red blood cells that lack specific protective proteins.

Generalised Myasthenia Gravis (gMG)
Myasthenia gravis (MG) is a rare, debilitating, neurological disorder in which the body's immune system initiates an attack on the neuromuscular junction. This attack causes tissue damage and impaired neuromuscular transmission, which can manifest in patients as debilitating weakness and/or fatigue.

Gonococcal infection
Infection sexually transmitted and caused by the bacterium *Neisseria gonorrhoeae* (also named gonorrhoea). Can disseminate and cause widespread blood infection (See Sepsis).

Haemoglobin
The brownish-red substance in red blood cells that carries oxygen throughout your body. Responsible for the characteristic dark urine seen in PNH.

Haemoglobinuria
Haemoglobin in the urine. This is the technical term for the dark "cola- coloured" urine which is sometimes seen in PNH. When the red blood cells are lysed or destroyed, as they are in PNH, haemoglobin is released from the red blood cells. When it is not all processed by the body's system, it is sent out as waste and colours the urine a characteristic cola-brown colour.

Kidney injury or impairment
A condition in which the kidneys stop working and are unable to remove waste products or regulate the amount of water and essential substances in the body.

Lactate dehydrogenase (LDH) levels
Lactate dehydrogenase is an enzyme that is found in most cells, but is particularly abundant in red blood cells. During the destruction of red blood cells (haemolysis) that occurs as part of the disease process of aHUS or PNH, LDH is released into the blood stream. When a blood test demonstrates an elevation in LDH levels this provides an indication that the haemolysis process is ongoing.

Meningococcal infection
Infection caused by the bacterium *Neisseria meningitidis* (also named meningococcus). Can cause meningitis or widespread blood infection (See Sepsis).

Paroxysmal nocturnal haemoglobinuria (PNH)
A rare blood disorder in which red blood cells are chronically destroyed or haemolysed by the complement system. This can lead to severe problems including anaemia, fatigue and thrombosis.

Platelets
Smallest blood cells whose function is to help stop bleeding by forming blood clots.

Red blood cells
Blood cells that carry oxygen using a protein complex called haemoglobin. PNH red blood cells are continually attacked and destroyed by the complement system because they are missing important protective proteins.

Sepsis
The presence of bacteria (bacteraemia), other infectious organisms, or toxins created by infectious organisms in the bloodstream that spread throughout the body.

Thrombocytopenia
A condition used to describe unusually low levels of platelets (small blood cells used to stop bleeding) in the blood.

Thrombosis (thrombotic events)
The formation or development of a blood clot that often blocks blood from flowing through a vessel. In PNH, blood clots can occur in common places, but can also occur in unusual sites, such as in vessels in the abdomen (see Blood clots).

Thrombotic microangiopathy (TMA)
TMA is a condition that causes small blood clots in vessels throughout the body. It is characterised by a triad of kidney injury, red blood cell destruction and low platelets. TMA is identified through laboratory tests with your doctor. TMA universally occurs in patients with aHUS and also occurs in many other diseases.

FREQUENTLY ASKED QUESTIONS

WHAT ARE THE SAFETY CONSIDERATIONS RELATED TO RAVULIZUMAB?

Important Safety Information: Risk of Meningococcal Infection

As ravulizumab blocks a part of your immune system it increases the risk of severe infection and sepsis, especially by a type of bacteria called *Neisseria meningitidis*. This can cause cases of meningitis which is a major brain inflammation or a severe infection of the blood.

These infections require urgent and appropriate care as it may become rapidly fatal or life-threatening or lead to major disabilities.

It is important to understand the precautions to take to reduce the risk of these infections and what to do if you are worried you may have an infection (see below).

As a safety precaution:

YOU/YOUR CHILD MUST BE VACCINATED against meningococcal infection before starting ravulizumab. If you initiate ravulizumab treatment less than 2 weeks after receiving a meningococcal vaccine, you/your child must receive antibiotic(s) until 2 weeks after vaccination to reduce the risk of infection with *Neisseria meningitidis*.

Vaccination reduces the risk of developing meningococcal infection, but it does not eliminate the risk completely.

If no vaccine is available or if the vaccine is contraindicated for you, you will be given an antibiotic throughout the treatment period or until 2 weeks after the vaccine can be given.

YOU MUST CARRY YOUR PATIENT ALERT CARD AT ALL TIMES WHILE ON RAVULIZUMAB AND FOR 8 MONTHS AFTER YOU STOP TAKING IT AND PRESENT IT TO ANY HEALTHCARE PROVIDERS YOU MAY SEE.

WHAT ARE THE SYMPTOMS THAT SHOULD ALERT ME DURING TREATMENT?

YOU WILL NEED TO BE AWARE OF THE SIGNS AND SYMPTOMS OF MENINGOCOCCAL INFECTION AND NOTIFY YOUR DOCTOR IMMEDIATELY IF ANY OF THE FOLLOWING SYMPTOMS OCCUR.

- 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

Symptoms of meningitis can appear in any order. Some may not appear at all. In the early stages, there may not be a rash, or the rash may fade on pressure.

For parents/legal guardians of newborns and infants, please be aware that the typical symptoms of headache, fever and neck stiffness may be hard to detect, so other symptoms in babies to be aware of include inactivity, irritability, vomiting, and poor feeding.

Refer to the Parent Guide for additional information on signs and symptoms of meningococcal infections in infants and children.

IF YOU CANNOT REACH YOUR DOCTOR, GO TO AN EMERGENCY DEPARTMENT. SHOW THEM YOUR PATIENT ALERT CARD.

ARE THERE STEPS I SHOULD TAKE BEFORE STARTING THERAPY?

Prior to commencing treatment, your doctor will discuss with you the importance of:

- Receiving vaccines against meningitis and in some cases specific antibiotic(s) to reduce the risk of infection with a type of bacteria called *Neisseria meningitidis.*
- Paediatric patients: Other vaccinations, such as *Haemophilus influenza* and pneumococcal vaccines.

Your doctor or nurse will make sure you receive a vaccine against meningococcal infection at least 2 weeks before the first infusion. If you initiate ravulizumab treatment less than 2 weeks after receiving a meningococcal vaccine, your doctor or nurse will make sure you receive antibiotic(s) until 2 weeks after vaccination to reduce the risk of infection with *Neisseria meningitidis*.

- Understanding the symptoms associated with infections listed in your Patient Alert Card and what to do if you experience those symptoms.
- Being carefully monitored by your doctor following any discontinuation of ravulizumab treatment.

In addition, you will be closely monitored for meningococcal and other infections during the course of your treatment.

ARE THERE OTHER SAFETY CONSIDERATIONS WHILE I AM ON RAVULIZUMAB?

Risk of Serious Infections: Due to its mechanism of action, ravulizumab should be administered with caution to patients with active systemic infections. You should monitor your symptoms and report any changes to your doctor. You may also be at risk of other infections with bacteria called *Neisseria gonorrhoeae*, including disseminated gonococcal infection. If you are at risk of gonorrhoea, ask your doctor or pharmacist for advice before using this medicine. There is also a potential risk of non-neisserial infections during ravulizumab therapy.

Haematological Abnormalities and Malignancies: As a PNH patient, you will be monitored for haematological changes. The PNH laboratory monitoring may potentially alert your physician to haematological abnormalities and malignancies. The PNH laboratory monitoring continues during ravulizumab treatment and for a period not less than 16 weeks after ravulizumab discontinuation.

Infusion/Allergic Reactions: You may experience reactions to the infusion (drip) as ravulizumab contains a protein and proteins that may cause immune or hypersensitivity reactions in some people, and sometimes an anaphylactic reaction. Anaphylaxis is a serious allergic reaction which causes difficulty breathing or dizziness. If you experience any signs or symptoms after receiving ravulizumab, you should consult your doctor.

Pregnancy: Ravulizumab is not recommended during pregnancy. Tell your doctor before starting treatment with ravulizumab if you are pregnant or plan to become pregnant.

Women of childbearing potential should use adequate contraception methods during treatment and up to 8 months after treatment.

Male patients on ravulizumab should not father a child or donate sperm up to 8 months after treatment.

Breast-feeding: Ravulizumab is not recommended during breastfeeding as it may pass into the breast milk to your baby. Therefore, you should not breast-feed during ravulizumab treatment and up to 8 months after treatment.

Elderly: There are no special precautions for treated patients aged 65 years and older.

HOW DO I GET STARTED ON RAVULIZUMAB THERAPY?

Ravulizumab must be prescribed by a doctor. You will also be given a starter kit containing:

- **Patient Alert Card**

It is very important to rapidly identify and treat certain types of infection in patients who receive ravulizumab; therefore, you will be given a Patient Alert Card that lists the specific symptoms you should always look for. You should carry this card at all times while on ravulizumab and for 8 months after the final dose, and show it to any healthcare professional you see.

- **Patient Guide**
- **Parent Guide will be given to parents/legal guardians of young children with PNH or aHUS**
- **Patient Information Leaflet for Ultomiris® (containing ravulizumab)**

PNH and aHUS REGISTRIES

To ensure that the care of people with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome (aHUS) continues to improve, it is important we have detailed information on the state of health and treatment of as many people with these conditions as possible. The aim of the **PNH and aHUS Registries** is to collect data to characterise and provide a better understanding of these diseases. Your physician will provide you with further details about these registries.

Your doctor may also ask you if you would like to participate in the **PNH or aHUS Registr**y and will register you if you agree. If this happens you will receive more detailed information about the registry and be asked to sign a consent form to participate. You will be asked to complete a simple questionnaire about your health and well-being at the beginning and then every 6 months for the duration of the Registry. Your doctor will provide the Registry with some of your medical information such as diagnosis, treatment and medical history.

To include your data in the **PNH or aHUS Registry** your written permission is required. Your participation is entirely voluntary and any information that would allow you to be identified directly or indirectly will be removed so that it cannot be linked to you. Also, you can withdraw your permission at any time. **These registries are only open to patients in Great Britain.**

HOW LONG WILL I NEED TO TAKE RAVULIZUMAB?

As you have a chronic disease, ravulizumab is intended to be an ongoing therapy. Patients who start ravulizumab should continue receiving ravulizumab, even if they feel better.

Risk of serious haemolysis after drug discontinuation in PNH patients

Interrupting or ending treatment with ravulizumab may cause your PNH symptoms to come back more severely soon after stopping ravulizumab treatment. Your doctor will closely monitor for signs and symptoms of serious haemolysis.

Risk of recurrence of symptoms after drug discontinuation in patients with aHUS or gMG

Interrupting or ending treatment with ravulizumab may cause your gMG symptoms to come back or for aHUS patients your TMA symptoms to come back.

YOU MUST NOT STOP THE TREATMENT WITHOUT MEDICAL SUPERVISION

If you plan to stop treatment with ravulizumab, to better understand if this is appropriate for your situation you need to discuss beforehand with your doctor the possible side effects and risks of discontinuation, that may include:

In patients with PNH:

- An increase in your lactate dehydrogenase (LDH) levels, a laboratory marker of destruction of red blood cells
- A significant fall in red blood cell count (anaemia)
- Confusion or change in how alert you are
- Dark urine
- Fatigue
- Abdominal pain
- Shortness of breath
- Difficulty swallowing
- Erectile dysfunction (impotence)
- Chest pain or angina
- Problems with the kidneys (increase in serum creatinine level)
- Blood clotting (thrombosis)

In patients with aHUS:

- A significant fall in your platelets (thrombocytopenia)
- A significant rise in destruction of your red blood cells
- An increase in your lactate dehydrogenase (LDH) levels, a laboratory marker of destruction of red blood cells
- Decreased urination (problems with your kidneys)
- Problems with your kidneys (increase in your serum creatinine level)
- Confusion or change in how alert you are
- Change in your vision
- Chest pain, or angina
- Shortness of breath
- Abdominal pain, diarrhoea
- Blood clotting (thrombosis)

IF YOU HAVE ANY OF THESE SYMPTOMS CONTACT YOUR DOCTOR

REPORTING SIDE EFFECTS

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the patient information leaflet or this guide.

United Kingdom (Great Britain and Northern Ireland)

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme. You can report via:

- the Yellow Card website www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Ireland

In Ireland via HPRA Pharmacovigilance
Website: www.hpra.ie

REPORTING SIDE EFFECTS TO THE MANUFACTURER

By reporting side effects, you can help provide more information on the safety of this medicine.
You can report side effects to Alexion, please email: uk.adverseevents@alexion.com or, call:
UK: 0800 321 3902. Ireland: 1800 936 544

MORE INFORMATION

If you require further information on ravulizumab, please call or email Alexion Medical Information.
Email: medinfo.EMEA@alexion.com Tel: UK: 0800 028 4394 / Ireland: 1800 882 840

HOME HEALTHCARE SERVICE

Alexion funds a Home Healthcare service, which is available to all patients prescribed with ravulizumab.
For more details, please ask your physician about this service and availability.

REFERENCES

1. ULTOMIRIS® (ravulizumab) Current Patient Information Leaflet, available here: https://www.medicines.org.uk/emc/, https://www.emcmedicines.com/en-GB/northernireland/ or https://www.medicines.ie/

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