SAMSUNG BIOEPIS

Epysqli™
(eculizumab)

Physician's Guide

Drug substance eculizumab

▼ 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.

This guide is intended to increase the prescriber's awareness of the risks associated with the use of eculizumab which include meningococcal infection, serious infections, immunogenicity, malignancies and haematological abnormalities in PNH patients and use in pregnant and breast-feeding women. It is also intended to increase the prescriber's awareness of the risks associated with discontinuation of eculizumab.
This guide must be used in combination with the eculizumab Summary of Product Characteristics (SmPC).

This document is approved by The Executive Directorate of Pharmacovigilance, at Saudi Food and Drug Authority (SFDA).

Please see SmPC for eculizumab, including information regarding serious meningococcal infection.

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TABLE OF CONTENTS

1. INTRODUCTION

Epysqli is indicated

- in the treatment of adult and paediatric patients with a body weight of 5 kg or above with paroxysmal nocturnal hemoglobinuria (PNH):
  - in patients with hemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history

You will be provided with the following material to be given to each patient treated with eculizumab:

- Patient Card
  - To inform the patients and healthcare providers about the risk of meningococcal infection associated with eculizumab
- Patient/Parent Guide
  - To educate patients, parents/legal guardians of infants and children and healthcare providers about the safety considerations associated with eculizumab treatment.
- Patient Information leaflet

Read these materials ahead of prescribing eculizumab to your patients.

2. IMPORTANT SAFETY INFORMATION[1]

Serious Meningococcal infection

- Due to its mechanism of action, the use of eculizumab increases the risk of meningococcal infection/sepsis *(Neisseria meningitidis)* for the patient.
- Cases of serious or fatal meningococcal infection/sepsis have been reported in eculizumab treated patients and with other terminal complement inhibitors. Meningococcal infections in patients treated with eculizumab 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 eculizumab:

- Vaccinate your patients with a meningococcal vaccine at least 2 weeks prior to initiating eculizumab, unless the risk of delaying eculizumab 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.

Please see SmPC for eculizumab, including information regarding serious meningococcal infection.

- For patients who initiate eculizumab treatment less than 2 weeks after receiving a meningococcal vaccine, in young children for whom there is no vaccine recommended or available for use, and in patients for whom the vaccine is contraindicated, treat with appropriate prophylactic antibiotics for at least 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.
- 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 eculizumab:

- Monitor your patients for early signs of meningococcal infections and sepsis, 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.

Other Systemic Serious Infections

- Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infection, have been reported with eculizumab. Advise 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 eculizumab therapy with caution to patients with active systemic infections (particularly due to *Neisseria* and encapsulated bacteria).

Immunogenicity

- Treatment with any therapeutic protein may induce an immune response (e.g. development of anti-drug antibodies).
- Monitor the patients for any signs and symptoms associated with positive antidrug antibodies

Haematologic Abnormality and Malignancy

- Due to the natural evolution of the disease, there is a risk for patients with PNH to develop haematologic abnormalities or malignancies, such as aplastic anaemia or myelodysplastic syndrome. The potential role of eculizumab in such abnormalities or malignancies has not been studied.
- Patients with PNH should be monitored for haematological changes.

Pregnancy and Lactation

- For eculizumab, no clinical data on exposed pregnancies are available. Eculizumab can be given to a pregnant woman only after risk benefit analysis.
- Women of childbearing potential must use effective contraception during treatment and up to 5 months after last dose of treatment with eculizumab.

Please see SmPC for eculizumab, including information regarding serious meningococcal infection.

Infusion Reactions

- Administration of eculizumab 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 eculizumab, 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.
- Eculizumab administration should be interrupted in all patients experiencing severe infusion reactions and appropriate medical therapy should be administered.

3. WHAT YOU NEED TO INFORM TO PATIENTS AND PARENTS/LEGAL GUARDIANS?

- As you have a chronic disease, eculizumab is intended to be an ongoing therapy.

- Do not stop treatment without first discussion with your doctor.

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
- 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

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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 to carry the patient card at all times throughout the duration eculizumab therapy and for 3 months after the last dose of eculizumab and show it to any healthcare professionals they see.

4. TREATMENT DISCONTINUATION

Treatment discontinuation for PNH:

Closely monitor patients with PNH who discontinue eculizumab for signs and symptoms of haemolysis and other reactions for at least 8 weeks.

These are identified by:

1. Serum lactate dehydrogenase (LDH) greater than pre-treatment LDH

AND

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

If serious haemolysis 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 eculizumab.

FURTHER INFORMATION

For more information about eculizumab, please contact +XXX XXXX XXXXX.

To report any side effect(s), please contact:

The National Pharmacovigilance Centre (NPC) - Saudi Food and Drug Authority (SFDA):
SFDA Call Center: 19999

E-mail: npc.drug@sfda.gov.sa

Website: https://ade.sfda.gov.sa

Or

PharmaKnowl Consulting

Email: qppv-saudi@pharmaknowl.com

Phone: +966112777729 / +966112404409

REFERENCES

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3. 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: 24 August 2023).

4. Meningitis symptoms in children. Meningitis Now website. Available at: https://www.meningitisnow.org/meningitis-explained/signs-and-symptoms/signs-and-symptoms-children/ (Accessed: 24 August 2023)

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