

Epysqli™ ▼
(Eculizumab)

Physician's Guide

Important information for patients about serious adverse events or reactions with eculizumab

▼ **This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspect adverse reactions.**

EPYSQLI™ is only approved for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uraemic syndrome (aHUS). It is not approved for and should not be used for the treatment of generalised myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD).

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The aim of this brochure is to educate and/or remind healthcare professionals about the selected prevention measures, detection, careful monitoring and/or proper management of selected safety concerns associated with EPYSQLI.



IMPORTANT INFORMATION

Prescriber Enrollment Form

In order to minimise the risk of inappropriate use of EPYSQLI (eculizumab), the Decision of the European Commission and the follow-up measures agreed by the CHMP require that drug distribution by Samsung Bioepis will only be possible after your written confirmation that you as prescriber have understood that every patient will receive meningococcal vaccination and/or antibiotic prophylaxis before Epysqli infusion. Please send the completed Prescriber Enrollment for:

For Ireland.

RMP-Ireland@iqvia.com

Samsung Bioepis will not be able to process any orders for prescribers for which we have not received a completed Prescriber Enrollment Form that would ensure that the prescriber will have his/her patient vaccinated.

We therefore ask you to enter the unique prescriber ID on any orders for Epysqli, in order to verify the correspondence with the Prescriber Enrollment Form.

ECULIZUMAB¹

Eculizumab, the active drug substance in EPYSQLI, is a recombinant humanised monoclonal antibody targeting the complement protein C5.

Eculizumab is a terminal complement inhibitor that prevents the generation of the terminal complement complex C5b-9. The early components of complement activation essential for opsonisation of microorganisms, initiation of immune response (both humoral and cellular) and clearance of immune complexes are preserved.

EPYSQLI INDICATIONS¹

Epysqli is indicated in:

- Adults and children for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history.
- Adults and children for the treatment of atypical haemolytic uraemic syndrome (aHUS).

IMPORTANT SAFETY INFORMATION¹

Risk of severe infection and sepsis

Due to its mechanism of action, the use of eculizumab increases the risk of severe infection and sepsis, especially meningococcal infection (*Neisseria meningitidis*) for the patient. Cases of serious or fatal meningococcal infections have been reported in eculizumab-treated patients.

The following steps must be taken to minimise the risk of infection and the risk of poor outcomes following infection:

***Neisseria meningitidis*: Vaccination and antibiotic prophylaxis**

- Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving eculizumab unless the risk of delaying eculizumab therapy outweighs the risks of developing a meningococcal infection.
- Vaccines against serogroups A, C, Y, W 135 and B (where available) are recommended.
- Vaccinate according to current national vaccination guidelines for vaccine use.²
- Vaccination may not be sufficient to prevent meningococcal infection. Consideration should be given to official guidance on the appropriate use of antibacterial agents.
- All patients should be monitored for early signs of meningococcal infection, evaluated immediately if infection is suspected, and treated with appropriate antibiotics if necessary.
- In young children for whom there is no vaccine recommended or available for use, in patients for whom the vaccine is contra-indicated and in patients treated with eculizumab less than 2 weeks after receiving a meningococcal vaccine, treat with antibiotic prophylaxis throughout the treatment period or until 2 weeks after the vaccination can be given.

***Haemophilus influenzae* and pneumococcal infections in children: Vaccination**

- **Patients receiving eculizumab for PNH and aHUS:** Vaccinate patients less than 18 years against *Haemophilus influenzae* and pneumococcal infections according to national vaccination guidelines at least 2 weeks prior to initiation of eculizumab therapy and strictly adhere to the national vaccination recommendations for each age group.

Impact of vaccination on underlying disease

Vaccination or revaccination may further activate complement and, as a result, patients with complement-mediated diseases, including PNH and aHUS may experience increased signs and symptoms of their underlying disease, such as haemolysis (PNH) or thrombotic microangiopathy (TMA), (aHUS). Therefore, patients should be closely monitored for disease symptoms after recommended vaccination.

SIGNS AND SYMPTOMS OF SEVERE INFECTION

Meningococcal infection

- **Sepsis** is a common presentation of meningococcal infections in patients treated with eculizumab.
- **Monitor** your patients for early signs of meningococcal infections.
- **Evaluate** immediately if infection is suspected, and treat with antibiotics if necessary.
- **Provide the Patient/Parent brochure. Explain the brochure** to patients or parents/caregivers of patients being treated with eculizumab in order to increase their awareness of potential serious infections and the relevant signs and symptoms which include:
 - Headache with nausea or vomiting
 - Headache with a stiff neck or back
 - Fever
 - Rash
 - Confusion
 - Severe muscle ache combined with flu-like symptoms
 - Sensitivity to light

In babies, additional signs and symptoms to those listed above may include:

- Rapid breathing
- Cold hands and feet
- Refusing food and/or vomiting
- Unusual crying or moaning
- Baby doesn't like being handled
- Baby is drowsy, floppy or unresponsive

In children, additional signs and symptoms to those listed above may include:

- Stiff neck
- Being drowsy or difficult to wake
- Irritability
- Shaking and leg pain



- **Provide a Patient Safety Card** to patients being treated with **EPYSQLI** and explain that they must carry it at all times and for 3 months after last dose and show it to healthcare professionals they see.
- Physicians must discuss the benefits and risks of eculizumab therapy with patients/parents.
- **Inform patients that if they suspect they may have an infection, they should seek urgent medical advice.**



Ensure that the parents/legal guardians of new-borns and infants are able to confidently identify typical symptoms of headache, fever, and neck stiffness, which may be hard to detect, so train them to be aware of other symptoms in babies including inactivity, irritability, vomiting, and poor feeding and to seek urgent medical attention.

Other systemic infections

Neisseria species infections

Due to its mechanism of action, eculizumab therapy should be administered with caution to patients with active systemic infections (particularly due to *Neisseria* and encapsulated bacteria). Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

Physicians should advise patients about gonorrhoea prevention, based on advice for prevention of other sexually transmitted infections that includes use of appropriate barrier contraception and condoms in sexually active patients.

Aspergillus infection

Cases of *Aspergillus* infections, some of them fatal, have been reported in eculizumab-treated patients.

Underlying risk factors such as, long term steroid use, immunosuppressive treatments, severe pancytopenia, exposure to construction or demolition sites, and pre-existing lung impairment or *Aspergillus* infection should be considered. If one of the above risk factors is identified before starting treatment with eculizumab, appropriate measures to mitigate the risk of *Aspergillus* infection are advisable.

OTHER SERIOUS ADVERSE REACTIONS¹

Infusion reactions including anaphylaxis

As with all therapeutic proteins, administration of EPYSQLI (eculizumab) may result in infusion reactions or immunogenicity that could cause allergic or hypersensitivity reactions (including anaphylaxis).

Patients should be monitored for one hour following infusion. If an adverse event occurs during the administration of EPYSQLI, 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 four hours in children aged less than 18 years.

Immunogenicity

Infrequent antibody responses have been detected in eculizumab-treated patients across clinical studies. There has been no observed correlation of antibody development to clinical response or adverse events.

RISKS ASSOCIATED WITH DISCONTINUATION OF ECUlizumab¹

Serious intravascular haemolysis in patients treated for PNH

Patients who start eculizumab as treatment for PNH should continue receiving eculizumab, even if they feel better.

However, patients who discontinue treatment with eculizumab should be monitored for signs and symptoms of serious intravascular haemolysis and other reactions for at least 8 weeks. Serious haemolysis is identified by serum LDH levels greater than the pre-treatment level, along with any of the following: greater than 25% absolute decrease in PNH clone size (in the absence of dilution due to transfusion) in one week or less; a haemoglobin level of <5 g/dL or a decrease of >4 g/dL in one week or less; angina; change in mental status; a 50% increase in serum creatinine level; or thrombosis.

If serious haemolysis occurs, consider the following procedures/treatments: blood transfusion (packed RBCs) or exchange transfusion if PNH RBCs >50% of total RBCs by flow cytometry; anticoagulation; corticosteroids, or reconstitution of eculizumab.

Thrombotic microangiopathy in patients treated for aHUS

Thrombotic microangiopathy (TMA) complications have been observed as early as 4 weeks and up to 127 weeks following discontinuation of eculizumab treatment in some aHUS patients. Discontinuation of treatment should only be considered if medically justified.

If aHUS patients discontinue treatment with eculizumab, they should be monitored closely for signs and symptoms of severe TMA complications. Monitoring may be insufficient to predict or prevent severe TMA complications in patients with aHUS after discontinuation of eculizumab.

Severe TMA complications post discontinuation can be identified by (i) 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 eculizumab treatment; an increase in serum creatinine of 25% or more as compared to baseline or to nadir during eculizumab treatment; or, an increase in serum LDH of 25% or more as compared to baseline or to nadir during eculizumab treatment; or (ii) any one of the following: a change in mental status or seizures; angina or dyspnea; or thrombosis.

If severe TMA complications occur after eculizumab discontinuation, consider reinstatement of eculizumab treatment, supportive care with PE/PI, or appropriate organ-specific supportive measures including renal support with dialysis, respiratory support with mechanical ventilation or anticoagulation.

HOME HEALTHCARE SERVICE

There is a Home Healthcare service, which is available to all patients prescribed with EPYSQLI. Home infusion may be considered for patients who have tolerated infusions well in the clinic. The decision of a patient to receive home infusions should be made after evaluation and recommendation from the treating physician.

For more details, please contact local Samsung Bioepis office via css.sbeu@samsung.com or Tel: 0800 208 1063

REFERENCES

1. EPYSQLI™ (eculizumab) Summary of Product Characteristics. Samsung Bioepis NL, B.V.

REPORTING ADVERSE DRUG REACTIONS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via contacting HPRA Pharmacovigilance website: www.hpra.ie.

Ireland

In Ireland via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2
Tel: +353 1676 4971 Fax: +353 1676 251

Website: www.hpra.ie

Email: medsafety@hpra.ie

Adverse events should also be reported to Samsung Bioepis on bioepis.mi@medinformation.co.uk. Freephone (Ireland): 1800 441 100

MORE INFORMATION

For more information about eculizumab contact: bioepis.mi@medinformation.co.uk
Tel: Ireland: 1800 441 100