



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EPAR summary for the public

Soliris

eculizumab

This is a summary of the European public assessment report (EPAR) for Soliris. It explains how the Agency assessed the medicine to recommend its authorisation and its conditions of use. It is not intended to provide practical advice on how to use Soliris.

For practical information about using Soliris, patients should read the package leaflet or contact their doctor or pharmacist.

What is Soliris and what is it used for?

Soliris is a medicine used to treat adults and children with:

- paroxysmal nocturnal haemoglobinuria (PNH);
- atypical haemolytic uraemic syndrome (aHUS).

These are rare, life-threatening genetic diseases that cause the breakdown of red blood cells resulting in various medical complications. PNH results in anaemia (low red blood cell counts), thrombosis (blood clots in the blood vessels), pancytopenia (low counts of blood cells) and dark urine, while aHUS results in anaemia, thrombocytopenia (a decrease in the number of platelets, components that help the blood to clot) and kidney failure.

Soliris can also be used for adults with myasthenia gravis (another rare disease where the immune system attacks and damages muscle cells causing muscle weakness), in whom other medicines do not work and who have a specific antibody in their body called AChR antibody.

Soliris contains the active substance eculizumab.

Because the numbers of patients with these medical conditions are low, the diseases are considered 'rare', and Soliris was designated an 'orphan medicine' (a medicine used in rare diseases) for PNH on 17 October 2003, for aHUS on 24 July 2009 and for myasthenia gravis on 29 July 2014.



How is Soliris used?

The medicine can only be obtained with a prescription and must be given under the supervision of a doctor who has experience in the management of patients with kidney disorders and disorders affecting the nervous system or the blood.

Soliris is given as an infusion (drip) into a vein and the recommended dose depends on what it is used for, and for patients under 18 years of age, on their bodyweight. Soliris is given once a week for the first four weeks, followed by a higher dose the next week, which is repeated every two weeks.

Patients are monitored for any reactions during the infusion and for at least one hour afterwards. In case of any infusion-related reactions, the doctor may slow down or stop the infusion.

In patients who receive plasma exchange (the removal, treatment, and return of their own blood plasma) or infusion of plasma, additional doses of Soliris are required.

For the treatment of aHUS and PNH, Soliris should be given for life unless the patient develops serious side effects. For myasthenia gravis, Soliris should be given for 12 weeks initially and if the patient's condition improves, Soliris treatment should continue.

How does Soliris work?

The active substance in Soliris, eculizumab, is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognise and attach to a specific structure (called an antigen) in the body. Eculizumab has been designed to attach to the C5 complement protein, which is a part of the body's defence system called the 'complement system'.

In patients with PNH and aHUS the complement proteins are over-active and damage the patients' own blood cells. In patients with myasthenia gravis, over-active complement proteins damage the junction between the nerves and muscles (neuromuscular junction). By blocking the C5 complement protein, eculizumab prevents complement proteins from damaging blood cells and the neuromuscular junction, thereby helping to relieve the symptoms of these diseases.

What benefits of Soliris have been shown in studies?

PNH

For PNH, Soliris was compared with placebo (a dummy treatment) in one main study involving 87 adults with PNH who had had at least four blood transfusions for anaemia in the previous year. Treatment with Soliris over 26 weeks led to stable haemoglobin levels in 49% of the patients (21 out of 43), without the need for transfusions of red blood cells. In comparison, none of the 44 patients receiving placebo had stable haemoglobin levels, and they needed an average of 10 transfusions.

In a study in 7 children with PNH who had had at least one transfusion in the previous two years, all patients received Soliris. Six out of seven patients did not need any transfusion of red blood cells, and haemoglobin levels improved during 12 weeks of treatment with Soliris.

A registry study of patients with PNH who had never had a blood transfusion looked at the blood levels of the enzyme lactate dehydrogenase (LDH). (Levels of LDH rise as breakdown of red blood cells increases). The study found that treatment with Soliris for 6 months led to clinically meaningful reductions in levels of LDH, indicating reduced breakdown of red blood cells.

aHUS

For aHUS, Soliris was studied in three main studies involving 67 patients. The first study involved 17 patients with aHUS who did not respond to or could not be treated with plasma exchange or infusion. Treatment with Soliris increased platelet counts in 82% of the patients, and platelet counts rose to normal levels in 87% (13 out of 15 patients) who had low platelet counts at the start. In addition, 76% achieved 'haematological normalisation' (levels of platelets and LDH within normal levels).

The second study, involving 20 patients with aHUS who were already receiving plasma exchange or infusion, measured the numbers of patients who achieved 'thrombotic microangiopathy event-free' status (they did not have a decrease of over 25% in platelet count after starting Soliris and did not require plasma exchange or infusion, or dialysis) and the number of patients who achieved haematological normalisation while receiving Soliris. Overall, 80% of the patients achieved 'thrombotic microangiopathy event-free' status and 90% achieved haematological normalisation.

The third study involved 30 patients with aHUS who had received at least one dose of Soliris. Treatment increased platelet counts to normal levels in 83% of the patients, while the platelet count rose to normal levels in 77% (10 out of 13 patients) who initially had low platelet counts.

Myasthenia gravis

For myasthenia gravis, Soliris was compared with placebo in one main study involving 126 adults with myasthenia gravis who had previously received standard treatment which had failed. Treatment with Soliris improved patients' symptoms and their ability to undertake daily activities based on a standard scoring system. A reduction in the score by 2 points indicates a clinically significant improvement of the patient's condition. Soliris led to a reduction of 4.7 points on the scale whereas placebo led to 2.8 point reduction after 26 weeks.

What are the risks associated with Soliris?

The most common side effect with Soliris (seen in more than 1 patient in 10) is headache. For the full list of all side effects reported with Soliris, see the package leaflet.

Because of an increased risk of developing a severe form of meningococcal disease (meningococcal sepsis), Soliris must not be given to people who have an infection caused by *Neisseria meningitides*; it must also not be given to patients who have not been vaccinated against this bacterium, unless they have the vaccination and take appropriate antibiotics to reduce the risk of infection for two weeks after vaccination. For the full list of restrictions, see the package leaflet.

Why is Soliris approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that the benefits of Soliris are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Soliris?

The company that markets Soliris will ensure that distribution of the medicine occurs only after checking that the patient has been vaccinated appropriately. The company will also provide prescribers and patients with information on the safety of the medicine, and will send reminders to prescribers and pharmacists to check if any further vaccination is needed for patients taking Soliris. Patients will also

be given a special card that explains the symptoms of certain types of infection, instructing patients to seek medical care immediately if they experience them.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Soliris have also been included in the summary of product characteristics and the package leaflet.

Other information about Soliris

The European Commission granted a marketing authorisation valid throughout the European Union for Soliris on 20 June 2007.

The full EPAR for Soliris can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports. For more information about treatment with Soliris, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Soliris can be found on the Agency's website:

- PNH: ema.europa.eu/Find_medicine/Human_medicines/Rare_disease_designations
- aHUS: ema.europa.eu/Find_medicine/Human_medicines/Rare_disease_designations
- myasthenia gravis: ema.europa.eu/Find_medicine/Human_medicines/Rare_disease_designations

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