This is a summary of the European public assessment report (EPAR) for Soliris. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Soliris.

What is Soliris?

Soliris is a concentrate that is made up into a solution for infusion. It contains the active substance eculizumab.

What is Soliris used for?

Soliris is used to treat adults and children with:

- paroxysmal nocturnal haemoglobinuria (PNH);
- atypical haemolytic uremic 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.

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 and for aHUS on 24 July 2009.

The medicine can only be obtained with a prescription.
**How is Soliris used?**

Soliris must be given under the supervision of a doctor who has experience in the management of patients with blood and/or kidney disorders.

In PNH, treatment for patients aged 18 and over consists of an infusion (drip into a vein) of 600 mg over 25 to 45 minutes once a week, followed by 900 mg in the fifth week. After this, the dose should be maintained at 900 mg, given approximately every two weeks. At least two weeks before starting Soliris treatment, patients must be vaccinated against meningitis caused by the bacterium *Neisseria meningitidis* and revaccinated according to current guidelines.

In aHUS, patients aged 18 and over receive an infusion of 900 mg over 25 to 45 minutes once a week for four weeks, followed by 1,200 mg in the fifth week. After this, the dose should be maintained at 1,200 mg, given approximately every two weeks.

PNH and aHUS patients under 18 years old receive lower doses based on their body weight, administered over 1 to 4 hours.

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

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

**How does Soliris work?**

The active substance in Soliris, eculizumab, is a monoclonal antibody. A monoclonal antibody is an antibody (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-activated and cause damage to the patients’ own blood cells. By blocking the C5 complement protein, eculizumab prevents complement proteins from damaging the blood cells, thereby helping to relieve the symptoms of the disease.

**How has Soliris been studied?**

Soliris was studied in one main study involving 87 adults with PNH who had had at least four blood transfusions for anaemia in the previous year. Soliris was compared with placebo (a dummy treatment). The main measures of effectiveness were the number of patients whose level of haemoglobin (a protein found in red blood cells) remained above their individual target level, and the number of red blood cell transfusions that the patients needed during the first 26 weeks of treatment.

A study was also performed in seven children with PNH who had had at least one transfusion in the previous two years. All patients received Soliris and the study measured the number of red blood cell transfusions needed during the 12 weeks of treatment.

A registry study of patients with PNH who had never had a blood transfusion was also conducted. This study looked at the blood levels of the enzyme lactate dehydrogenase (LDH), which reflect the extent of the breakdown of red blood cells.

Soliris was studied in three main studies involving 67 patients with aHUS. The first study involved 17 patients with aHUS who did not respond to or could not be treated with plasma exchange or infusion. The main measures of effectiveness were the change in platelet count and the number of patients who
achieved ‘platelet count normalisation’ and ‘haematological normalisation’ (their levels of platelets and lactate dehydrogenase, an enzyme normally found in red blood cells, were within normal levels).

The second study involved 20 patients with aHUS who were already receiving plasma exchange or infusion. The main measures of effectiveness were 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.

The third study involved 30 patients with aHUS who had already received at least one dose of eculizumab. The effectiveness of Soliris treatment was assessed using a range of measurements, including the change in platelet count and other measures of effectiveness also used in the first two studies.

**What benefit has Soliris shown during the studies?**

Soliris was more effective than placebo in improving the symptoms of PNH. In the main study in PNH, 49% of the adult patients receiving Soliris had stable haemoglobin levels (21 out of 43), and, on average, they did not need any 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 the study in children, six out of seven patients did not need any transfusion of red blood cell and haemoglobin levels improved during treatment with Soliris.

In the registry study of patients with PNH who had never had a blood transfusion, patients treated with Soliris had clinically meaningful reductions in levels of lactate dehydrogenase (LDH) after 6 months of treatment, indicating reduced breakdown of red blood cells.

In the first study in aHUS, platelet counts increased and were within normal levels in 82% of the patients, while 87% (13 out of 15 patients) with initially low platelet counts achieved platelet count normalisation and 76% achieved haematological normalisation. In the second study in aHUS, 80% of the patients achieved ‘thrombotic microangiopathy event-free’ status and 90% achieved haematological normalisation. In the third study, platelet counts increased and were within normal levels in 83% of the patients, while 77% (10 out of 13 patients) with initially low platelet counts achieved platelet count normalisation.

**What is the risk 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 meningitis (meningococcal sepsis), Soliris must not be given to people who are infected with *Neisseria meningitidis*; it must also not be given to patients who have not been vaccinated against this bacterium, unless they take appropriate antibiotics to reduce the risk of infection until two weeks after vaccination. For the full list of restrictions, see the package leaflet.

**Why has Soliris been approved?**

The 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?

A risk management plan has been developed to ensure that Soliris is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Soliris, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, 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 a (re)-vaccination is needed for patients taking Soliris.

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

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