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Aspaveli (*pegcetacoplan*)

An overview of Aspaveli and why it is authorised in the EU

What is Aspaveli and what is it used for?

Aspaveli is a medicine used in adults to treat paroxysmal nocturnal haemoglobinuria (PNH), an acquired disease in which there is excessive breakdown of red blood cells (haemolysis), leading to large amounts of haemoglobin (the protein in red blood cells that carries oxygen around the body) being released into the urine. Aspaveli is used in patients with PNH who have anaemia (low levels of red blood cells) due to haemolysis.

Paroxysmal nocturnal haemoglobinuria is rare, and Aspaveli was designated an 'orphan medicine' (a medicine used in rare diseases) on 22 May 2017. Further information on the orphan designation can be found here: ema.europa.eu/medicines/human/orphan-designations/eu3171873.

Aspaveli contains the active substance pegcetacoplan.

How is Aspaveli used?

The medicine can only be obtained with a prescription. Treatment should be started under the supervision of a healthcare professional experienced in the management of blood-related disorders.

Aspaveli is given as an infusion (drip) under the skin of the belly, thighs, hips or upper arms. It is given twice a week (on days 1 and 4). Patients may give themselves the drip if their doctor considers it appropriate and they have been trained to do so. Unless there is a clinical reason for stopping treatment, Aspaveli is continued for life.

For more information about using Aspaveli, see the package leaflet or contact your doctor or pharmacist.

How does Aspaveli work?

The active substance in Aspaveli, pegcetacoplan, is made of two synthetic peptides (short chains of amino acids) that are linked together. It attaches to the C3 complement protein, which is a part of the immune system (the body's natural defences) called the 'complement system'.

In patients with PNH, the complement proteins are overactive and damage the patients' own cells. By blocking the C3 complement protein, Aspaveli prevents complement proteins from damaging cells, thereby helping to relieve the symptoms of PNH.

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What benefits of Aspaveli have been shown in studies?

Aspaveli was shown to be effective at preventing breakdown of red blood cells and increasing blood levels of haemoglobin in a study involving patients with PNH who had been treated with eculizumab for at least 3 months but were still anaemic.

The study was conducted in 80 patients with PNH currently being treated with eculizumab, a medicine known as a complement inhibitor, but who were still anaemic (haemoglobin level <10.5 g/dL) despite this treatment. Patients were either switched to Aspaveli or continued their eculizumab treatment. After 16 weeks, haemoglobin levels in patients receiving Aspaveli increased on average by 2.37 g/dL while it decreased by 1.47 g/dL on average in patients who were still treated with eculizumab. During this period, 6 of 41 patients given Aspaveli needed a blood transfusion, compared with 33 of 39 treated with eculizumab.

A second study evaluated the use of Aspaveli in 53 patients with PNH who had not received a complement inhibitor in the 3 months leading up to the study. Aspaveli was more effective than supportive care (treatment to prevent or relieve the symptoms of the disease) in controlling the breakdown of red blood cells and stabilising haemoglobin levels. After 26 weeks of treatment, haemoglobin levels had stabilised (meaning they did not decrease by more than 1g/dL without the patient having a blood transfusion) in around 86% of patients treated with Aspaveli (30 out of 35) compared to none of those treated with supportive care (0 out of 18).

The study also evaluated the effect of treatment on blood levels of lactate dehydrogenase (LDH; a marker for tissue damage that is increased when red blood cells break down). After 26 weeks, patients treated with Aspaveli had an average decrease of 1,870 units/L in their LDH levels compared with an average decrease of 400 units/L in those treated with supportive care. During this period, around 91% of those given Aspaveli (32 out of 35) did not require a transfusion, compared with 6% given supportive care (1 out of 18).

What are the risks associated with Aspaveli?

For the full list of side effects and restrictions, see the package leaflet.

The most common side effects with Aspaveli (which may affect more than 1 in 10 people) include injection site reactions (reddening of the skin, itching, swelling, bruising and site pain), upper respiratory tract (nose and throat) infection, abdominal (belly) pain, diarrhoea, haemolysis, headache, tiredness, fever, cough, urinary tract infection, pain in extremity (arm or leg), dizziness, joint and back pain and complications with vaccination. The most serious side effects include haemolysis (which may affect more than 1 in 10 people) and sepsis (blood poisoning; which may affect up to 1 in 10 people).

Based on its mechanism of action, Aspaveli may increase the risk of infections. Aspaveli must not be used in patients with an ongoing infection caused by certain bacteria known as encapsulated bacteria including *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. It must also not be used in patients who are not currently vaccinated against these bacteria unless they take appropriate antibiotics to reduce the risk of infection for two weeks after vaccination.

Why is Aspaveli authorised in the EU?

Aspaveli is effective at increasing blood haemoglobin levels in patients with PNH who had been treated with eculizumab for at least 3 months but were still anaemic. Aspaveli was also more effective than supportive care for PNH at stabilising haemoglobin levels and controlling the breakdown of red blood cells in patients who had not been treated with complement inhibitors for at least 3 months. It also reduced the need for blood transfusions in patients with PNH. However, uncertainties related to the

design of the study in patients who had not been treated with complement inhibitors for at least 3 months limited the evaluation of the benefits and risks of Aspaveli in these patients.

In terms of safety, although the data on safety are limited due to the small number of patients included in the main studies, the side effects of Aspaveli are considered manageable, considering the measures in place to minimise its risk.

The European Medicines Agency therefore decided that Aspaveli's benefits are greater than its risks and it can be authorised for use in the EU.

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

The company that markets Aspaveli 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 Aspaveli. 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 Aspaveli have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Aspaveli are continuously monitored. Suspected side effects reported with Aspaveli are carefully evaluated and any necessary action taken to protect patients.

Other information about Aspaveli

Aspaveli received a marketing authorisation valid throughout the EU on 13 December 2021.

Further information on Aspaveli can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/aspaveli.

This overview was last updated in 02-2024.