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Withdrawal of application for the marketing authorisation of Orblid (bevacizumab)

Laboratoires Delbert withdrew its application for a marketing authorisation of Orblid for the treatment of hereditary haemorrhagic telangiectasia, a genetic disease that causes abnormalities in the capillaries (small blood vessels that connect arteries with veins).

The company withdrew the application on 20 April 2026.

What is Orblid and what was it intended to be used for?

Orblid was developed as a medicine for treating adults with hereditary haemorrhagic telangiectasia who have:

- severe liver damage causing heart problems, such as high-flow strain on the heart leading to persistent shortness of breath despite adequate treatment;
- or a form of the disease that causes severe bleeding (with nosebleeds or digestive bleeding) that requires blood transfusions or iron given through a vein.

The most common symptoms of the disease are spontaneous and frequent nosebleeds, and red spots on the skin. Bleeding can also occur in the stomach, gut, brain, liver and lungs, and often leads to anaemia (low red blood cell counts).

Orblid contains the active substance bevacizumab and was to be available as an infusion (drip) given through a vein. Bevacizumab has been approved in the EU since 2005 in combination with other medicines to treat various cancer. Thus this application concerned the use of a well-known active substance in a new indication.

Orblid was designated an 'orphan medicine' (a medicine used in rare diseases) on 16 December 2014 for hereditary haemorrhagic telangiectasia. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/medicines/human/orphan-designations/eu-3-14-1390.

How does Orblid work?

Patients with hereditary haemorrhagic telangiectasia have a genetic mutation (defect) that leads to high levels of VEGF (vascular endothelial growth factor), a protein involved in the growth of blood

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vessels. This causes abnormal growth of blood vessels which results in direct connections between arteries and veins, increasing the risk of bleeding.

The active substance in Orblid, bevacizumab, is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to VEGF and block its action. By blocking VEGF, bevacizumab is expected to prevent the growth of abnormal blood vessels, thus relieving the symptoms of bleeding in hereditary haemorrhagic telangiectasia.

What did the company present to support its application?

The company presented the results from 2 main studies. The first one involved 25 adults with hereditary haemorrhagic telangiectasia with severe liver damage and heart problems who all received Orblid. The main measure of effectiveness was a reduction in cardiac index after 3 months, which may reflect an improvement in heart function.

The second main study involved 24 adults with a form of the disease that causes severe bleeding and who require transfusions or iron given through a vein. They received 6 infusions of either Orblid or placebo (a dummy treatment) every 2 weeks. The main measure of effectiveness was the proportion of patients with a decrease of at least 50% in the number of red blood cell transfusions in 3 to 6 months period after they began treatment, compared with the 3-month period before they started treatment.

The company also provided published literature data on the use of bevacizumab in patients with hereditary haemorrhagic telangiectasia.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared questions for the company. The company had not responded to the questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the data, at the time of the withdrawal, the Agency had concerns and its provisional opinion was that Orblid could not have been authorised for the treatment of hereditary haemorrhagic telangiectasia.

The main study that evaluated Orblid in patients with severe liver damage as well as the supportive studies did not compare the medicine with another treatment or placebo and had several scientific limitations, such as the use of other therapeutic interventions before or during the study, which made it difficult to conclude on the medicine’s effect. In addition, the main measure of effectiveness, cardiac index, is not considered to be an independent, reliable measure of treatment effect, as it may be influenced by other factors, including the patient’s overall state of health and natural variations of the disease.

The study in patients with a severe haemorrhagic form of the disease failed to show an effect of Orblid on the number of blood transfusions people required. Results from supportive studies did not provide evidence on the medicine’s effectiveness either.

In terms of safety, the active substance bevacizumab is known to be associated with serious side effects in the treatment of cancer and the data provided for Orblid were too limited to conclude on the medicine’s safety in patients with hereditary haemorrhagic telangiectasia, in particular in the long term.

Finally, there were uncertainties with the data provided regarding the most appropriate dose and dosing interval.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough data to support the application for Orblid.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of the application, the company stated that it withdrew its application due to Agency's identification of major clinical issues which could only be addressed by carrying out a new clinical study.

Does this withdrawal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no ongoing clinical trials or in compassionate use programmes with Orblid.