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EPAR summary for the public

Orfadin

nitisinone

This is a summary of the European public assessment report (EPAR) for Orfadin. 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 Orfadin.

What is Orfadin?

Orfadin is a medicine that contains the active substance nitisinone. It is available as capsules (2 mg, 5 mg, 10 mg and 20 mg) and as a suspension (4 mg/ml) to be taken by mouth.

What is Orfadin used for?

Orfadin is used to treat hereditary tyrosinaemia type 1 (HT-1). This is a rare disease in which the body is unable to completely break down the amino acid tyrosine, and harmful substances are formed, causing serious liver problems and liver cancer. Orfadin is used together with a diet that restricts the intake of the amino acids tyrosine and phenylalanine. These amino acids are normally found in proteins in foods and drinks.

Because the number of patients with HT-1 is low, the disease is considered 'rare', and Orfadin was designated an 'orphan medicine' (a medicine used in rare diseases) on 29 December 2000.

The medicine can only be obtained with a prescription.

How is Orfadin used?

Treatment with Orfadin should be started and monitored by doctors who have experience in the treatment of patients with HT-1. Treatment should be started as early as possible and the dose of Orfadin adjusted according to the patient's response and body weight.

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The recommended starting dose is 1 mg per kilogram body weight per day, divided into two doses. The capsules are usually swallowed whole, but they may be opened and their contents mixed into a small amount of water or formula just before swallowing. The oral suspension is for children who have difficulty swallowing capsules.

Orfadin is intended for long-term use. Patients should be monitored at least every six months.

How does Orfadin work?

Tyrosine is broken down in the body by a number of enzymes. Patients with HT-1 lack one of these enzymes, so tyrosine is not properly eliminated but is transformed into harmful substances. The active substance in Orfadin, nitisinone, blocks an enzyme that converts tyrosine into harmful substances. However, as tyrosine remains in the body during Orfadin treatment, patients need to eat a special diet low in tyrosine. The diet also needs to be low in phenylalanine, as this is converted into tyrosine in the body.

How has Orfadin been studied?

The largest study of Orfadin was carried out in 257 patients in 87 different hospitals in 25 countries, as part of a 'compassionate-use' programme. This is a programme through which doctors can request a medicine for one of their patients before the medicine is fully authorised. The study looked at the effect of Orfadin on survival, and compared this with reports published in medical journals describing survival in patients with HT-1 who were only receiving a modified diet.

What benefit has Orfadin shown during the studies?

The main benefit of Orfadin is to greatly extend life expectancy. For example, a baby less than two months old with HT-1 would normally have only a 28% chance of surviving for five years using a modified diet alone. With additional Orfadin treatment, the survival rate increases to 82%. The sooner treatment is started, the better the chances of survival.

What is the risk associated with Orfadin?

Treatment with Orfadin leads to high levels of tyrosine in the blood (due to the medicine's mode of action); this side effect is seen in more than 1 patient in 10. Thrombocytopenia (low blood platelet counts), leucopenia (low white blood cell counts), granulocytopenia (low levels of granulocytes, a type of white blood cell), conjunctivitis (inflammation of the membrane that lines the eyelid), corneal opacity (clouding of the cornea, the transparent layer in front of the pupil), keratitis (inflammation of the cornea), photophobia (increased sensitivity of the eyes to light) and eye pain are also common (seen in between 1 and 10 patients in 100). Many of these side effects can be the result of high tyrosine levels caused by patients not eating the right foods. For the full list of all side effects and restrictions with Orfadin, see the package leaflet.

Why has Orfadin been approved?

The CHMP noted that Orfadin seems to be an effective treatment for HT-1, particularly if it is started early, before the patient's liver is too damaged. Orfadin also provides a better outcome for patients than that reported in the literature in patients eating a modified diet alone. Therefore, the CHMP decided that Orfadin's benefits are greater than its risks and recommended that it be given marketing authorisation.

Orfadin was originally authorised under 'exceptional circumstances', because, as the disease is rare, limited information was available at the time of the approval. As the company had submitted the additional information requested, the 'exceptional circumstances' ended on 21 September 2009.

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

A risk management plan has been developed to ensure that Orfadin 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 Orfadin, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Orfadin

The European Commission granted a marketing authorisation valid throughout the European Union for Orfadin on 21 February 2005.

The full EPAR for Orfadin 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 Orfadin, 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 Orfadin can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 05-2015.