Orfadin
nitisinone

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis for the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Orfadin?
Orfadin is a medicine that contains the active substance nitisinone. It is available as white capsules (2, 5 and 10 mg).

What is Orfadin used for?
Orfadin is used to treat hereditary tyrosinaemia type 1 (HT-1). This is a rare childhood disease in which the body is unable to completely break down the amino acid tyrosine. This causes harmful substances to be formed and to build up in the body, causing serious liver problems and liver cancer in young children. Orfadin is used with a diet that restricts the intake of the amino acids called tyrosine and phenylalanine. These amino acids are normally found in protein 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.
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. 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 the tyrosine in their body 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?
The most common side effects with Orfadin (seen in between 1 and 10 patients in 100) are 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. Many of these can be the result of high tyrosine levels caused by patients not eating the right foods. For the full list of all side effects reported with Orfadin, see the Package Leaflet.

Orfadin should not be used in people who may be hypersensitive (allergic) to nitisinone or any of the other ingredients.

Why has Orfadin been approved?
The Committee for Medicinal Products for Human Use (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.

Other information about Orfadin:
The European Commission granted a marketing authorisation valid throughout the European Union for Orfadin to Swedish Orphan International AB on 21 February 2005. The marketing authorisation is valid for an unlimited period.

The summary of the opinion of the Committee for Orphan Medicinal Products for Orfadin is available here.
The full EPAR for Orfadin can be found here.

This summary was last updated in 01-2010.