



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Orfadin (*nitisinone*)

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

What is Orfadin and what is it used for?

Orfadin is a medicine for the treatment of:

- hereditary tyrosinaemia type 1 (HT-1) in patients of all ages who also follow diet restrictions;
- alkaptonuria (AKU) in adults.

These diseases occur when the body cannot fully break down certain amino acids including tyrosine. As a result, harmful substances build up, which can cause serious liver problems and liver cancer in patients with HT-1 and joint problems in patients with AKU.

Orfadin contains the active substance nitisinone.

How is Orfadin used?

Orfadin can only be obtained with a prescription and treatment should be started and supervised by a doctor with experience in treating the disease for which Orfadin is used. It is available as capsules and as an oral suspension to take by mouth.

For patients with HT-1, the recommended starting dose of Orfadin is 1 mg per kilogram of body weight daily. The dose is then adjusted according to the patient's response and weight.

For adults with AKU, the recommended dose is 10 mg daily.

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

How does Orfadin work?

Patients with HT-1 and AKU lack enzymes to break down the amino acid tyrosine properly and, as a result, it is converted to harmful substances. The active substance in Orfadin, nitisinone, blocks the enzymes that convert tyrosine into harmful substances. Diet restrictions prevent excessive levels of amino acids such as tyrosine and of phenylalanine, which is converted into tyrosine in the body.

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What benefits of Orfadin have been shown in studies?

Hereditary tyrosinaemia type 1

The largest study of Orfadin involved 257 patients with HT-1. The study looked at the effect of Orfadin on how long patients lived ('survival'), and compared this with reports in medical journals describing survival in patients with HT-1 who were only receiving a modified diet. Orfadin greatly extended life expectancy. For example, a baby aged under 2 months with HT-1 would normally have a 28% chance of surviving for five years using a modified diet alone. With the addition of Orfadin treatment, the survival rate increased to 82%. The sooner treatment was started, the better the chances of survival.

Alkaptonuria

Orfadin was effective at reducing the harmful breakdown product of tyrosine called homogentisic acid (HGA). In a main study involving 138 adults with AKU the main measure of effectiveness was the amount of HGA appearing in the urine over 24 hours, which reflects the amount of HGA in the body. In patients taking Orfadin for 1 year, the level of HGA in the urine over 24 hours was 86 micromol/litre, compared with over 26,000 micromol/litre in patients who did not take the medicine. Moreover, patients taking Orfadin had fewer symptoms of the disease compared with those who did not take it.

What are the risks associated with Orfadin?

The most common side effect with Orfadin (which may affect more than 1 in 10 people) is high levels of tyrosine in the blood (because of the way the medicine works). Other common side effects (which may affect up to 1 in 10 people) are thrombocytopenia (low blood platelet counts), leucopenia (low white blood cell counts), granulocytopenia (low levels of granulocytes, a type of white blood cell), conjunctivitis (redness and discomfort in the eye), corneal opacity (clouding of the cornea, the transparent layer that covers the pupil), keratitis (inflammation of the cornea), photophobia (abnormal sensitivity of the eyes to light) and eye pain. Many of these side effects result from high tyrosine levels.

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

Why is Orfadin authorised in the EU?

Orfadin was effective treatment for HT-1, particularly if started early before the patient's liver is too damaged. Orfadin provides a better outcome for patients than that reported for patients eating a modified diet alone. In patients with AKU, Orfadin was effective in reducing levels of HGA in the urine and this was accompanied by a reduction in symptoms, particularly those affecting joints, bones and eyes. The European Medicines Agency considered that the pattern of Orfadin's side effects is well-established but noted that side effects on the eye occurred more often in patients with AKU and they also had new side effects such as infections. Overall, Orfadin's side effects are considered manageable.

Therefore, the Agency decided that Orfadin'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 Orfadin?

Recommendations and precautions for the safe and effective use of Orfadin have been included in the summary of product characteristics and the package leaflet.

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

Other information about Orfadin

Orfadin received a marketing authorisation valid throughout the EU on 21 February 2005.

Further information on Orfadin can be found on the Agency's website:

ema.europa.eu/medicines/human/EPAR/orfadin.

This overview was last updated in 11-2020.