

## Package leaflet: Information for the user

**Orfadin 2 mg hard capsules**  
**Orfadin 5 mg hard capsules**  
**Orfadin 10 mg hard capsules**  
**Orfadin 20 mg hard capsules**  
nitisinone

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

### What is in this leaflet

1. What Orfadin is and what it is used for
2. What you need to know before you take Orfadin
3. How to take Orfadin
4. Possible side effects
5. How to store Orfadin
6. Contents of the pack and other information

#### 1. What Orfadin is and what it is used for

Orfadin contains the active substance nitisinone. Orfadin is used to treat:

- a rare disease called hereditary tyrosinemia type 1 in adults, adolescents and children (in any age range)
- a rare disease called alkaptonuria (AKU) in adults

In these diseases your body is unable to completely break down the amino acid tyrosine (amino acids are building blocks of our proteins), forming harmful substances. These substances are accumulated in your body. Orfadin blocks the breakdown of tyrosine and the harmful substances are not formed.

For the treatment of hereditary tyrosinemia type 1, you must follow a special diet while you are taking this medicine, because tyrosine will remain in your body. This special diet is based on low tyrosine and phenylalanine (another amino acid) content.

For the treatment of AKU, your doctor may advise you to follow a special diet.

#### 2. What you need to know before you take Orfadin

##### Do not take Orfadin

- if you are allergic to nitisinone or any of the other ingredients of this medicine (listed in section 6).

Do not breast-feed while taking this medicine, see section "Pregnancy and breast-feeding".

### **Warnings and precautions**

Talk to your doctor or pharmacist before taking Orfadin.

- Your eyes will be checked by an ophthalmologist before and regularly during nitisinone treatment. If you get red eyes or any other signs of effects on the eyes, contact your doctor immediately for an eye examination. Eye problems could be a sign of inadequate dietary control (see section 4).

During the treatment, blood samples will be drawn in order for your doctor to check whether the treatment is adequate and to make sure that there are no possible side effects causing blood disorders.

If you receive Orfadin for treatment of hereditary tyrosinemia type 1, your liver will be checked at regular intervals because the disease affects the liver.

Follow-up by your doctor should be performed every 6 months. If you experience any side effects, shorter intervals are recommended.

### **Other medicines and Orfadin**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Orfadin may interfere with the effect of other medicines, such as:

- Medicines for epilepsy (such as phenytoin)
- Medicines against blood clotting (such as warfarin)

### **Orfadin with food**

If you start treatment by taking it with food, it is recommended that you carry on taking it with food throughout your course of treatment.

### **Pregnancy and breast-feeding**

The safety of this medicine has not been studied in pregnant and breast-feeding women.

Please contact your doctor if you plan to become pregnant. If you become pregnant you should contact your doctor immediately.

Do not breast-feed while taking this medicine, see section “Do not take Orfadin”.

### **Driving and using machines**

This medicine has minor influence on the ability to drive and use machines. However, if you experience side effects affecting your vision you should not drive or use machines until your vision is back to normal (see section 4 “Possible side effects”).

## **3. How to take Orfadin**

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

For hereditary tyrosinemia type 1, treatment with this medicine should be started and supervised by a doctor experienced in the treatment of the disease.

For hereditary tyrosinemia type 1, the recommended total daily dose is 1 mg/kg body weight administered orally. Your doctor will adjust the dose individually.

It is recommended to administer the dose once daily. However, due to the limited data in patients with body weight <20 kg, it is recommended to divide the total daily dose into two daily administrations in this patient population.

For AKU, the recommended dose is 10 mg once daily.

If you have problems with swallowing the capsules, you may open the capsule and mix the powder with a small amount of water or formula diet just before you take it.

#### **If you take more Orfadin than you should**

If you have taken more of this medicine than you should, contact your doctor or pharmacist as soon as possible.

#### **If you forget to take Orfadin**

Do not take a double dose to make up for a forgotten dose. If you forget to take a dose, contact your doctor or pharmacist.

#### **If you stop taking Orfadin**

If you have the impression that the medicine is not working properly, talk to your doctor. Do not change the dose or stop the treatment without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

## **4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice any side effects relating to the eyes, talk to your doctor immediately to have an eye examination. Treatment with nitisinone leads to higher levels of tyrosine in the blood which can cause eye related symptoms. In patients with hereditary tyrosinemia type 1, commonly reported eye related side effects (may affect more than 1 in 100 people) caused by higher tyrosine levels are inflammation in the eye (conjunctivitis), opacity and inflammation in the cornea (keratitis), sensitivity to light (photophobia) and eye pain. Inflammation of the eyelid (blepharitis) is an uncommon side effect (may affect up to 1 in 100 people).

In AKU patients, eye irritation (keratopathy) and eye pain are very commonly reported side effects (may affect more than 1 in 10 people).

### **Other side effects reported in patients with hereditary tyrosinemia type 1 are listed below:**

#### Other common side effects

- Reduced number of platelets (thrombocytopenia) and white blood cells (leukopenia), shortage of certain white blood cells (granulocytopenia).

#### Other uncommon side effects

- increased number of white blood cells (leucocytosis),
- itching (pruritus), skin inflammation (exfoliative dermatitis), rash.

### **Other side effects reported in patients with AKU are listed below:**

#### Other common side effects

- bronchitis
- pneumonia
- itching (pruritus), rash

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Yellow Card Scheme

Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)  
or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Orfadin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the carton after “EXP”. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).

The medicine can be stored for a single period of 2 months (for 2 mg capsules) or 3 months (for 5 mg, 10 mg and 20 mg capsules) at a temperature not above 25°C, after which it must be discarded.

Do not forget to mark the date on the bottle, when removed from the refrigerator.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

## 6. Contents of the pack and other information

### What Orfadin contains

- The active substance is nitisinone.  
*Orfadin 2 mg*: Each capsule contains 2 mg nitisinone.  
*Orfadin 5 mg*: Each capsule contains 5 mg nitisinone.  
*Orfadin 10 mg*: Each capsule contains 10 mg nitisinone.  
*Orfadin 20 mg*: Each capsule contains 20 mg nitisinone.
  
- The other ingredients are  
Capsule content:  
starch, pregelatinised (maize)  
Capsule shell:  
gelatine  
titanium dioxide (E 171)  
Printing ink:  
iron oxide (E 172)  
shellac  
propylene glycol  
ammonium hydroxide

### What Orfadin looks like and contents of the pack

The hard capsules are white, opaque, imprinted with “NTBC” and the strength “2 mg”, “5 mg”, “10 mg” or “20 mg”, in black. The capsule contains a white to off-white powder.

The capsules are packaged in plastic bottles with tamper-proof closures. Each bottle contains 60 capsules.

### Marketing Authorisation Holder

Swedish Orphan Biovitrum International AB  
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Sweden

**Manufacturer**

Apotek Produktion & Laboratorier AB  
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