

**PATIENT PACKAGE INSERT IN ACCORDANCE
WITH THE PHARMACISTS REGULATIONS (PREPARATIONS 1986)**
This medicine will be dispensed with a physician's prescription only

Orfadin™ 2 mg

Orfadin™ 5 mg

Orfadin™ 10 mg

Hard Capsules

COMPOSITION:

Active Ingredient:

Each capsule of Orfadin 2 mg contains Nitisinone 2 mg

Each capsule of Orfadin 5 mg contains Nitisinone 5 mg

Each capsule of Orfadin 10 mg contains Nitisinone 10 mg

Inactive ingredients: please refer to "Further information"

Read this package insert in its entirety before using this medicine. This insert includes concise information regarding this medicine. If you have any additional questions please refer to your doctor or pharmacist.

This medicine was prescribed for the treatment of your ailment. Do not give it to others. It may cause them harm even if they seem to have a similar disease.

WHAT IS ORFADIN AND WHAT IS IT USED FOR?

Orfadin is intended for the treatment of a hereditary disease called tyrosinemia type 1. In this disease your body is unable to completely break down the amino acid tyrosine (amino acids are the building blocks responsible for building the proteins in our body), as a result a harmful substance accumulates in your body. **Orfadin** blocks the breakdown of the amino acid tyrosine and prevents the harmful substance from accumulating in your body. Since tyrosine remains in the body, a special dietary regime based on foods with low quantities of tyrosine and phenylalanine should be maintained during treatment with **Orfadin**.

BEFORE YOU USE THIS DRUG:

Do not use this product if:

- You are sensitive (allergic) to the active ingredient Nitisinone or any of the additional ingredients that this drug contains (refer to "Further information")
- You are breast feeding

Special warnings related to the use of this drug:

- Refer to your doctor immediately for eye examination, if redness or any other sign appears in your eyes. Eye problems may indicate low nutritional control

Inform your doctor or pharmacist **if you are taking or have recently taken any other medicines**, including medicines obtained without a prescription and food supplements.

Taking Orfadin with food:

If you have started treatment with **Orfadin** together with food, it is recommended to continue taking this drug with food throughout the treatment.

Pregnancy and lactation:

Orfadin has not been tested on pregnant and lactating women. Your attending physician must be informed if you are planning to become pregnant. Your doctor must be informed immediately if you are pregnant. Do not use this drug during breast feeding.

Driving and operating machinery:

The effect on driving and operating machinery has not been tested. If you notice any side effects affecting your vision, you must consider your ability to drive and/ or operating machinery.

HOW TO USE ORFADIN?

Always use according to physician's instructions. You must check with your doctor or pharmacist if you are unsure.

Starting treatment with **Orfadin** will be under the instruction of a physician experienced in the treatment of patients with hereditary tyrosinemia type 1.

- **The accepted dose** is: 1 mg for each kilogram of your body weight per day. This dose will be divided to twice a day. Your physician will adjust your dose personally
- If you have problems swallowing, you may open the capsule and mix the powder with a small quantity of water or nutritional formula, just before taking the drug

Examinations and follow ups:

It is recommended that your physician will perform an eye examination before starting treatment. During the treatment period you will be referred to perform blood tests to check if the treatment is effective and make sure that no side effects appear that cause blood disorders. Your liver will also be checked once in a while at regular time intervals, as the disease tyrosinemia type 1 affects the liver. You must see your doctor for follow up every six months. You must see your doctor at shorter time intervals if side effects appear.

If you have accidentally taken a higher dose then you should or if a child had accidentally swallowed from this medicine, refer immediately to a doctor or a hospital's emergency room and bring the package of this medicine with you.

If you forgot to take this drug at the required time, do not take a double dose consult your doctor or pharmacist. Continue treatment as your doctor recommended. Do not stop taking the drug or change the dose without consulting your physician, even if you feel that the drug does not work properly. If you have any additional questions regarding the use of this drug, consult your physician or pharmacist.

SIDE EFFECTS:

Like all medicines, **Orfadin** may cause side effects in some patients. Do not be alarmed by the list of side effects, you may not experience any of them.

Refer to your doctor immediately:

- If you notice side effects related to your eyes

Additional side effects:

Common side effects:

- Symptoms related to your eyes, such as: conjunctivitis (inflammation in the eye), opacity or inflammation of the cornea, sensitivity to light or eye pain
- Decrease in blood platelets and white blood cells level, deficiency in a certain type of white blood cells (granulocytopenia)

Uncommon side effects:

- Inflammation of the eyelids
- Increase in the level of white blood cells
- Itching, skin inflammation (exfoliative dermatitis) and rash

Consult your doctor if one of these side effects becomes worse or if you experience a side effect that has not been mentioned in this leaflet.

HOW TO STORE ORFADIN?

- Avoid poisoning! This medicine and all other medicines must be stored in a safe place out of the reach of children and/ or infants. This will help avoid poisoning. Do not induce vomiting without being explicitly instructed to do so by your physician
- Do not take medicines in the dark! Check the label each time you take a medicine. Wear eye glasses if you need them
- Do not use this medicine after the expiry date (exp. date) which appears on the outer package. The expiry date refers to the last day of that month
- Store in the refrigerator (2-8°C): this is the temperature range in most household refrigerators
- You may store the capsules outside the refrigerator at a temperature that does not exceed 25°C for a period of up to two months. After this period the package need to be destroyed. Do not forget to mark on the package the date when the capsules were taken out of the refrigerator
- Use within two months after first opening

FURTHER INFORMATION:

In addition to the active ingredient Nitisinone, this medicine also contains:
Starch pregelatinised; Gelatine; Titanium dioxide; Black iron oxide (E172).

- What does **Orfadin** look like and what is the content of the package: hard, white cloudy colored capsules, imprinted "NTBC" in black on one side and the dosage of the drug on the other side: 2 mg/ 5 mg/ 10 mg. The capsule contains a white or off-white colored powder. **Orfadin** is marketed in a package of 60 capsules in plastic bottles covered with a child resistant closure
- Registration Holder and Address: MegaPharm Ltd., P.O. Box 519, Hod Ha'Sharon 45105
- Name of Manufacturer and Address: Apotek Produktion & Laboratorier AB, Kungens Kurva, Sweden **for** Swedish Orphan Biovitrum International AB (SOBI), Stockholm, Sweden
- This leaflet was checked and approved by the Ministry of Health in January 2012
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