Package leaflet: Information for the user

Nitisinone Dipharma 5 mg hard capsules
Nitisinone Dipharma 10 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 only. 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 Nitisinone Dipharma is and what it is used for

Nitisinone Dipharma contains the active substance nitisinone. Nitisinone Dipharma 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. Nitisinone Dipharma 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 advice you to follow a special diet.

2. What you need to know before you take Nitisinone Dipharma

Do not take Nitisinone Dipharma
- 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 Nitisinone Dipharma.
- 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 Nitisinone Dipharma 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 Nitisinone Dipharma
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Nitisinone Dipharma may interfere with the effect of other medicines, such as:
- Medicines for epilepsy (such as phenytoin)
- Medicines against blood clotting (such as warfarin)

Nitisinone Dipharma 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 Nitisinone Dipharma".

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 Nitisinone Dipharma

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 Nitisinone Dipharma 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 Nitisinone Dipharma

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 Nitisinone Dipharma
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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nitisinone Dipharma

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, the blister and the carton after “EXP”. The expiry date refers to the last day of that month.

Store below 30°C.

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 protect the environment.

6. Contents of the pack and other information

What Nitisinone Dipharma contains

- The active substance is nitisinone

  Nitisinone Dipharma 5 mg. Each capsule contains 5 mg nitisinone
  Nitisinone Dipharma 10 mg. Each capsule contains 10 mg nitisinone

- The other ingredients are:
  Hard capsule content
  Starch, pregelatinised
  Stearic acid
  Capsule shell
  Gelatin
  Titanium dioxide (E 171)
  Printing ink
  Shellac
  Propylene glycol
  Indigotine aluminum lake (E 132)

What Nitisinone Dipharma looks like and contents of the pack
The hard capsules are white, opaque, imprinted with the strength "5" or "10" and the "company logo", in dark blue. The capsule contains a white to off-white powder.

Nitisinone Dipharma is available in plastic bottles with child-proof closures of 60 capsules, and OPA/Alu/PVC – Alu perforated unit dose blisters of 60 capsules.

Not all pack sizes may be marketed.
Marketing Authorisation Holder
Dipharma Arzneimittel GmbH
Offheimer Weg 33
65549 Limburg a.d. Lahn
Germany
Manufacturer
Doppel Farmaceutici S.r.l.
Via Volturno 48
20089 Quinto de' Stampi - Rozzano (MI), Italy

This medicinal product is authorised in the Member States of the European Economic Area under the following names:

Austria	Nitisinon Dipharma
Belgium	Nitisinone Dipharma
Denmark	Nitisinone Dipharma
France	Nitisinone Dipharma
Germany	Nitisinone Dipharma
Ireland	Nitisinone Dipharma
Italy	Nitisinone Dipharma
Netherlands	Nitisinone Dipharma
Norway	Nitisinone Dipharma
Portugal	Nitisinona Dipharma
Spain	Nitisinona Dipharma
Sweden	Nitisinone Dipharma
United Kingdom	Nitisinone Dipharma

This leaflet was last revised in

Detailed information on this medicine is available on the website of HPRA (https://www.hpra.ie/).