Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Miglustat Dipharma

Hard capsules

Name of and quantity of active ingredient:

Each capsule contains:

miglustat 100 mg.

For the list of inactive ingredients in this medicine, see section 6 'Additional Information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

- treatment of mild to moderate type 1 Gaucher disease, only in patients who are considered unsuitable for treatment with enzyme replacement therapy
- treatment of progressive neurological symptoms in adults and in children with Niemann-Pick type C disease.

Therapeutic group: enzyme inhibitor that affects the metabolism.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient (miglustat) or to any of the other ingredients in this medicine (see section 6).
- you are pregnant or breast-feeding.

Special warnings about using this medicine

- **Before using Miglustat Dipharma, tell your doctor if:**
  - you have a kidney disease
  - you have a liver disease.

- If you have diarrhoea, your doctor may advise you to change your diet to reduce your lactose and carbohydrate intake such as sucrose (cane sugar), or not to take Miglustat Dipharma together with food, or to reduce your dose temporarily.

In some cases, the doctor may consider prescribing an anti-diarrhoeal medicine such as loperamide. Cases of Crohn's disease (an inflammatory bowel disease) have been reported in patients with Niemann-Pick type C disease who were treated with Miglustat Dipharma. If your diarrhoea does not respond to these measures, or if you have any other digestive system complaint, consult your doctor. If this happens, your doctor may decide to investigate further to see if there are other reasons for your symptoms.
- Male patients must use reliable birth control methods during their treatment with Miglustat Dipharma, and for 3 months after finishing treatment.

Children and adolescents

This medicine is not intended for children and adolescents (below 18 years old) with type 1 Gaucher disease because it is unknown how well it works in this age group.

Tests and follow-up

Your doctor will refer you for the following tests before and during treatment with this medicine:

- an examination of nerves in your arms and legs
- measurement of vitamin B_{12} levels
- monitoring growth in children and adolescents with Niemann-Pick type C disease
- monitoring blood platelet counts

The reason for these tests is that some patients may get tingling or numbness in the hands and feet, or a decrease in body weight, while taking this medicine. The tests will help your doctor decide whether these effects are due to your disease or other existing conditions, or to side effects of Miglustat Dipharma (see section 4, 'Side effects').

Interactions with other medicines

If you are taking or have recently taken other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- medicines containing imiglucerase, which are sometimes given together with Miglustat Dipharma; they may lower the amount of Miglustat Dipharma in your body.

Using this medicine and food

This medicine can be taken with or without food.

Pregnancy and breast-feeding

Do not take Miglustat Dipharma if you are pregnant or thinking of becoming pregnant. Your doctor can give you more information. You must use effective birth control while taking Miglustat Dipharma.

Do not breast-feed while you are taking Miglustat Dipharma.

Male patients should use reliable birth control methods during their treatment with Miglustat Dipharma, and for three months after finishing treatment.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

Taking this medicine may make you feel dizzy. Do not drive or operate dangerous machines if you feel dizzy.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine. The recommended dosage is usually:

- For type 1 Gaucher disease
  The adult dosage is usually one capsule (100 mg) 3 times a day (morning, afternoon and evening). The maximum amount is 3 capsules (300 mg) per day.
- For Niemann-Pick type C disease
  Adults and adolescents (over 12 years old): the usual dosage is 2 capsules (200 mg) 3 times a day (morning, afternoon and evening). The maximum amount is 6 capsules (600 mg).
  Children less than 12 years old: the doctor will adjust the dosage.

If you have a problem with your kidneys, you may be prescribed a lower starting dose. If you have diarrhoea while taking Miglustat Dipharma, your doctor may consider reducing your dosage, for example, to one capsule (100 mg), once or twice a day (see section 2 'Special warnings about using this medicine'). Your doctor will tell you how long your treatment will last.

Do not exceed the recommended dose.

- This medicine can be taken with or without food.
- You should swallow the capsules whole with a glass of water.

If you have accidentally taken a higher dose

If you have accidentally taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

When miglustat was used in clinical trials at doses up to 3000 mg, decreases in white blood cells and other side effects similar to those described in section 4 of this leaflet were observed.

If you forget to take this medicine at the scheduled time, take the next dose at the usual time and consult your doctor. Do not take a double dose to make up for a forgotten dose. Adhere to the treatment as recommended by your doctor.

If you stop taking this medicine

Do not stop this treatment without talking to your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, using Miglustat Dipharma may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

See your doctor immediately if you experience any of the following side effects:

- <u>Most serious side effects</u>:
  Some patients have had tingling or numbness in the hands and feet (seen commonly). These effects could be signs of peripheral neuropathy, due to side effects of Miglustat Dipharma or they could be due to existing conditions. Your doctor will refer you for tests before and during treatment with Miglustat Dipharma to assess this (see section 2, 'Tests and follow-up').
- If you get a slight tremor, usually trembling hands, call your doctor as soon as possible. In most cases, the tremor will disappear without you needing to stop the treatment; however, sometimes your doctor will consider reducing your dosage or stopping Miglustat Dipharma treatment to stop the tremor.

Additional side effects

Very common side effects–affect more than one in 10 users:

diarrhoea, bloated abdomen (wind), abdominal pain, weight loss, decreased appetite.

If you do lose some weight when you start treatment with Miglustat Dipharma, don't worry. This effect usually wears off in patients as treatment continues.

Common side effects–affect up to one in 10 users:

headache, dizziness, numbness or tingling, impaired coordination, reduced sensation to touch, heartburn, nausea, constipation, vomiting, swelling or discomfort in the stomach, reduced levels of blood platelets (thrombocytopenia). The neurological symptoms and reduced level of platelets in your blood could be due to your disease itself.

Other side effects include muscle spasms or muscle weakness, fatigue, chills and malaise, depression, difficulty sleeping, forgetfulness, and reduced libido.

Most patients get one or more of the above side effects, usually at the start of treatment or at intervals during treatment. In most cases, these effects are mild and disappear quite quickly. If any of these side effects cause problems, consult your doctor. Your doctor will consider reducing your dose of Miglustat Dipharma or recommend other medicines to help control these side effects.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects ,or you can use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions**
  Store below 30°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Capsule core:

magnesium stearate.

Capsule shell:

gelatin, titanium dioxide (E171), printing ink (shellac, propylene glycol, potassium hydroxide, black iron oxide).

What the medicine looks like and contents of the pack:

opaque, white capsules with 'DPH02' printed in black on the cap and '100' printed in black on the body.

This medicine is packaged in boxes of 4 blister strips, each blister strip containing 21 capsules providing a total of 84 capsules, or in wallet packs of 84 capsules.

Not all pack sizes may be marketed.

Registration holder's name and address: MBI Pharma Ltd., P.O.B 5061, Kadima.

Manufacturer's name and address:

Doppel Farmaceutici S.R.L.,

Via Volturno 48, Quinto de' Stampi - Rozzano (MI) 20089, Italy.

Revised in June 2024.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 165-46-36284.