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 and quantity of active ingredient:

Each capsule contains:

miglustat 100 mg

For list of inactive ingredients in this medicine see section 6 "Additional Information". **Read this entire leaflet carefully before 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, in patients who are considered unsuitable for treatment with enzyme replacement therapy.
- Treatment of progressive neurological symptoms in adults and children who have Niemann-Pick type C disease.

Therapeutic group: enzyme inhibitor, 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.
- You are pregnant or breastfeeding.

Special warnings about using this medicine

- **Before treatment with Miglustat Dipharma tell your doctor if:**
  - You suffer from kidney disease.
  - You suffer from liver disease.

- If you have diarrhea, your doctor may recommend a change in your diet in order to reduce the amount of lactose and carbohydrates intake (such as sucrose), or that you not take Miglustat Dipharma together with food, or temporarily reduce your dosage.

In certain cases, your doctor may consider prescribing an anti-diarrheal medicine such as loperamide. If your diarrhea is not relieved by these measures or if you have some other gastrointestinal problem, consult your doctor. If this happens, your doctor may decide to conduct a further inquiry.
- Male patients must use reliable contraceptives during the treatment with Miglustat Dipharma and for three months after finishing treatment.

Children and adolescents

This medicine is not intended for children and adolescents under 18 years old who have type 1 Gaucher disease.

Tests and follow-up

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

- an examination to check the nerves in your hands and legs
- measurement of vitamin B_{12} levels
- monitoring growth in children and adolescents who have Niemann-Pick type C disease
- monitoring of blood platelet counts

The reason for these tests is that some patients may experience numbness or tingling in their hands and feet, or weight loss during treatment with the medicine. The tests will help your doctor decide whether these effects are due to your disease or other existing conditions, or due to side effects of Miglustat Dipharma (see section 4 "Side effects").

Other medicines and Miglustat Dipharma

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

- Medicines that contain imiglucerase, sometimes given together with Miglustat Dipharma, may reduce the amount of Miglustat Dipharma in your body.

Using this medicine and food

You can take this medicine with or without food.

Pregnancy, breastfeeding, and fertility

Do not use Miglustat Dipharma if you are pregnant or planning to become pregnant. You must use effective contraceptives during treatment with Miglustat Dipharma.

Do not breastfeed during treatment with Miglustat Dipharma.

Male patients must use reliable contraceptives during the treatment with Miglustat Dipharma and for three months after finishing treatment.

If you are pregnant or breastfeeding, think you might be pregnant, or are planning to become pregnant, consult your doctor before using this medicine. Your doctor will be able to give you more information.

Driving and using machines

Using this medicine may cause dizziness so 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
  Adults: The 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 dosage is usually 2 capsules (200 mg) 3 times a day (morning, afternoon and evening). The maximum amount is 6 capsules (600 mg).
  Children under 12 years old: Your doctor will adjust the dosage.

If you have a problem with your kidneys, you may be prescribed a lower starting dose. If you suffer from diarrhea 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 explain how long your treatment will last.

Do not exceed the recommended dose.

- You can take this medicine with or without food.
- Swallow the capsules whole with a glass of water.

If you have accidentally taken a higher dose 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 Dipharma was used in clinical trials at doses 10 times higher than the recommended dose, a decrease in white blood cells was observed, as well as other side effects similar to those described in section 4 in this leaflet.

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 taking the medicine without consulting your doctor. Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time 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

Like with all medicines, 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.

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

- The most serious side effects:
  Some patients may feel tingling or numbness in the hands and feet (seen commonly). These effects may be signs of a peripheral nerve disease (neuropathy) due to side effects of Miglustat Dipharma or due to existing conditions. Your doctor will perform some tests before and during treatment with Miglustat Dipharma to clarify this (see section 2 "Tests and follow-up").
- If you get a slight tremor, usually in the hands, seek medical advice from 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 (may affect more than 1 in 10 patients):

diarrhea, bloated abdomen (flatulence), abdominal (stomach) pain, weight loss, decreased appetite.

Do not worry if you lose some weight when you start treatment with Miglustat Dipharma. This effect usually stops in patients as treatment continues.

Common side effects (may affect up to 1 in 10 patients):

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

Other side effects including muscle spasms, muscle weakness, fatigue, chills and malaise, depression, insomnia (difficulty sleeping), memory loss, reduced sex drive.

Most patients experience one or more of these effects, usually at the beginning of treatment or on and off during treatment. In most cases these side effects are mild and disappear relatively quickly. If these effects cause problems, consult your doctor. Your doctor will either consider reducing the dosage of Miglustat Dipharma or recommend other medicines to treat 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. You can also 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 a 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 25°C.

Do not dispose of medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer in 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 capsule body.

This medicine is packaged in boxes of 4 blister cards, each blister card contains 21 capsules- a total of 84 capsules.

Registration holder's name and address: MBI Pharma Ltd., POB 5061, Kadima.

Manufacturer's name and address:

Doppel Farmaceutici S.R.L.,

VIA Volturno 48, Quito De Stampi - Rozzano (MI) 20089, Italy.

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