PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Zavesca®

Capsules

The active ingredient and its quantity

Each capsule contains:

Miglustat 100 mg

For a list of inactive and allergenic ingredients in the preparation, see section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

- Treatment of mild to moderate type 1 Gaucher disease only in patients who have been found unsuitable for enzyme replacement therapy.
- Treatment of progressive neurological symptoms in adults and children who suffer from Niemann-Pick type C disease.

Therapeutic group: An enzyme inhibitor that affects metabolism.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient (miglustat) or any of the additional ingredients of the medicine (see section 6 "Further Information").
- You are pregnant or breast-feeding.

Special warnings regarding use of the medicine

- **Before beginning treatment with Zavesca, tell the doctor if:**
  - You suffer from kidney disease.
  - You suffer from liver disease.
- If you have diarrhea, your doctor may ask you to change your diet to reduce your lactose and carbohydrate intake such as sucrose (cane sugar), or not to take Zavesca together with food, or to temporarily reduce your dose. In some cases the doctor may prescribe an anti-diarrheal medicine such as loperamide. Cases of Crohn's disease (an inflammatory disease affecting the gut) have been reported in patients with Niemann-Pick type C disease treated with Zavesca. If the diarrhea

does not respond to these measures, or if you have any other abdominal complaint, consult your doctor. In such case, your doctor may decide to conduct further investigation to determine if there is another cause of your symptoms.
- Male patients must use reliable birth control methods during the course of treatment with Zavesca and for 3 months after finishing treatment.

Tests and follow-up

Before and during treatment with this medicine, the doctor will refer you to perform the following tests:
- An examination of nerves in the arm and legs
- Measurement of vitamin B12 levels
- Monitoring growth in children and adolescents with Niemann-Pick type C disease
- Monitoring of blood platelet count

The reason for these tests is that some patients have had tingling or numbness in the hands and feet, or a decrease in body weight, while taking Zavesca. The tests will help the doctor decide whether these effects are due to your disease, due to other existing conditions, or due to side effects of Zavesca (see section 4 “Side Effects”).

Children and adolescents

Do not give this medicine to children and adolescents (below 18 years old) with type 1 Gaucher disease because it is not known if it works in this disease.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular if you are taking:
- Medicines containing imiglucerase, which are sometimes given together with Zavesca, may lower the amount of Zavesca in your body.

Use of the medicine and food

The medicine may be taken with or without food.

Pregnancy, breast-feeding and fertility

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

Do not breast-feed while you are taking Zavesca.

Male patients must use reliable birth control methods during the course of treatment with Zavesca and for 3 months after finishing the treatment.

If you are pregnant, breast-feeding, think you may be pregnant or planning to become pregnant, ask your doctor for advice before using this medicine.

Driving and operating machinery

Using Zavesca may cause dizziness. Do not drive or operate dangerous machinery if you feel dizzy.

Important information about some of the ingredients of the medicine

Zavesca contains sodium.
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially ‘sodium-free’.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the medicine according to the doctor’s instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.

The dosage and treatment regimen will be determined by the doctor only. The usual dose is generally:

- For type 1 Gaucher disease
  The dose in adults is generally one capsule (100 mg) three times a day (morning, afternoon and evening). This means a daily maximum of three capsules (300 mg).
- For Niemann-Pick type C disease
  Adults and adolescents (over 12 years of age): The usual dose is two capsules (200 mg) three times a day (morning, afternoon and evening). This means a daily maximum of six capsules (600 mg).
  Children less than 12 years of age: Your doctor will adjust the dose.

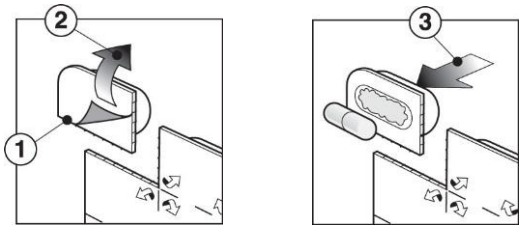
If you have a problem with your kidneys you may receive a lower starting dose. Your doctor may reduce your dose, e.g., to one capsule (100 mg) once or twice a day, if you suffer from diarrhea when taking Zavesca (see section 2 “Special warnings regarding use of the medicine”). Your doctor will explain to you how long your treatment will last.

Do not exceed the recommended dosage.

- The medicine may be taken with or without food.
- Swallow the capsules whole with a glass of water.

Opening instructions:

To remove the capsule:



1. Separate along the perforated line
2. Peel back the paper as indicated by the arrows
3. Push the capsule through the foil

If you accidentally take a higher dosage
If you accidentally took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.
During the use of Zavesca in clinical trials at doses up to 3000 mg, a decrease in white blood cells was observed, as well as other side effects similar to those described in section 4 of this leaflet.

If you forgot to take this medicine
If you forgot to take this medicine at the required time, take the next dose at the regular time and consult the doctor. Do not take a double dose to make up for a forgotten dose. Adhere to the treatment regimen as recommended by the doctor.

If you stop taking the medicine
Do not stop the treatment without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Zavesca may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer to the doctor immediately if any of the following side effects occur:

- The most serious side effects:
  Some patients have had tingling or numbness in the hands and feet (seen commonly). These effects may be signs of peripheral nerve disease (neuropathy), due to side effects of Zavesca or due to existing conditions. Your doctor will refer you to perform some tests before and during treatment with Zavesca to assess this (see section 2 “Tests and follow-up”).
- **If you feel a slight tremor**, usually **trembling hands, refer to your doctor** as soon as possible. The tremor often disappears without needing to stop the treatment. Sometimes your doctor will consider to reduce the dose or stop Zavesca treatment to stop the tremor.

Very common side effects: (may affect more than 1 in 10 people)
Diarrhea, flatulence (wind), abdominal pain, weight loss, decreased appetite.
If you do lose some weight when you start treatment with Zavesca do not worry. People usually stop losing weight as treatment goes on.

Common side effects: (may affect up to 1 in 10 people)
Headaches, dizziness, paraesthesia (tingling or numbness), abnormal coordination, hypoaesthesia (reduced sensation to touch), dyspepsia (heartburn), nausea (feeling sick), constipation, vomiting, swelling or discomfort in the abdomen (stomach), thrombocytopenia (reduced level of blood platelets). The neurological symptoms and thrombocytopenia could be due to underlying disease.

Other side effects include muscle spasms or weakness, fatigue, chills and malaise, depression, difficulty sleeping, forgetfulness, and less libido.
Most patients get one or more of these side effects, usually at the start of treatment or at intervals during treatment. Most cases are mild and disappear quite quickly. If any of these side effects cause problems, consult your doctor. Your doctor may reduce the dose of Zavesca or recommend other medicines to help control side effects.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. Date) that appears on the package. The expiry date refers to the last day of that month.
- Store at a temperature below 30°C.
- Do not throw away medicines via wastewater or in the rubbish. Ask the pharmacist how to discard medicines that are not in use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sodium starch glycollate, povidone (K30), magnesium stearate, ethanol 99/100%.

The capsule shell contains:
Gelatin, titanium dioxide.

Printing colors contain:
Opacode Black S-1-27794: shellac, I.M.S 74 OP², n-butyl alcohol, isopropyl alcohol, purified water, propylene glycol, black iron oxide.

or
Tekprint sw-9008 black ink: shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, purified water, strong amonia solution, potassium hydroxide, black iron oxide.
or
10A1 black: shellac glaze 45% (20% esterified) in ethanol, black iron oxide, propylene glycol, ammonium hydroxide 28%.
or
10A2 black: shellac, propylene glycol, strong amonia solution, potassium hydroxide, black iron oxide.

What the medicine looks like and contents of the package:
White capsules with “OGT 918” marked in black on the capsule cap and “100” marked in black on the capsule body.
The medicine is packaged in boxes of 4 trays (blisters); each tray contains 21 capsules – a total of 84 capsules.

Manufacturer: Actelion Pharmaceuticals Ltd., Gewerbestrasse 12/14/16, 4123 Allschwil, Switzerland.

Registration Holder: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
128 34 30714 00

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Based on the EU SmPC from November 2023.

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