PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS - 1986

This medicine is dispensed with a physician's prescription only

Impavido 10 mg, 50 mg

Hard capsules

Composition:

Active ingredient:

Miltefosine 10 mg, 50 mg

For the full list of ingredients and a list of allergens, see: Section 6, "Additional Information" in the leaflet.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, consult your physician 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 illness is similar.

In addition to the leaflet, there is a patient safety information card for the **Impavido**. This card contains important safety information that you should know before starting treatment and during treatment with **Impavido**. Refer to the patient safety information card and the patient leaflet before you start using this medicine. Keep the card for further reference if necessary.

The medicine is not intended for children under the age of 12 years or patients weighing less than 30 kg.

Fetal toxicity

Impavido may cause harm to the fetus. Death of the fetus and developmental defects in the fetus have occurred in animals which had received miltefosine in lower doses than those recommended for humans. The medicine is contraindicated for pregnant women. Before starting treatment women who might be pregnant must take a pregnancy test. Women of childbearing age should use effective methods of contraception while being treated with Impavido and for a further five months after treatment, in order to ensure not getting pregnant during this period.

1. What is this medicine intended for?

Impavido contains active ingredient acting against single cell pathogenic protozoa called *Leishmania*.

Impavido is intended for the treatment of visceral Leishmaniasis caused by Leishmania donovani.

In addition, **Impavido** is intended for the treatment of cutaneous Leishmaniasis caused by Leishmania brasiliensis complex or Leishmania mexicana complex.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient Miltefosine or to any of the additional ingredients that the medicine contains (please see section 6 - "Additional information")
- You have severe liver or kidney impairment
- You suffer from ***Sjogren-Larsson*** syndrome (a rare congenital metabolic disorder causing cornification of the skin)
- You are breastfeeding
- You are pregnant
- Women who may be pregnant and have not had a pregnancy test. Women who may be pregnant must take a pregnancy test (blood or urine) before taking the medicine
- Women who may be pregnant and are not using effective methods of contraception during use of the medicine or for 5 months after ending treatment

Special warnings regarding use of the medicine

- Treatment with **Impavido** may cause damage to the kidneys and liver. Because kidney and liver damage resulting from treatment with **Impavido** cannot be ruled out, you must have weekly blood and urine tests performed in order to monitor kidney and liver function. If values for kidney and liver function at the end of treatment differ significantly from normal values, monitoring must be continued until values return to normal.
- **Impavido** is liable to cause side effects such as vomiting and diarrohea. If these side effects persist over a prolonged period, you must drink large quantities of water in order to compensate for fluid loss and avoid kidney failure.
- Eye problems, such as inflammation of the cornea (keratitis) can be symptoms of the Leishmania infection. In a few cases, eye problems occurred after taking **Impavido** for several weeks. Consult your physician immediately if you notice any eye problems.

Patients with kidney or liver failure

There is insufficient clinical data on patients with kidney or liver failure.

Children and adolescents

Impavido is not intended for children under the age of 12 years or for patients weighing less than 30 kg.

Patients with a weakened immune system

In patients with a weakened immune system, **Impavido** should be used only after standard treatment has failed, as there is insufficient clinical data on treatment with **Impavido** in these patients.

Drug interactions:

If you are taking or have recently taken any other medicines, including non-prescription medicines or nutritional supplements, tell your physician or pharmacist.

Use of the medicine and food

Take the capsules with meals.

Pregnancy, breastfeeding and fertility:

Pregnancy

Make sure that you are not pregnant before starting treatment with **Impavido**.

Women of childbearing age should use effective methods of contraception while being treated with **Impavido** and for a further five months after treatment in order to ensure not getting pregnant during this period.

Vomiting and diarrhoea are very common side effects during treatment with this medicine, and therefore the effectiveness of the contraceptive pills may be impaired. Inform your physician if you experience these side effects so that an additional contraceptive method can be recommended to you.

If you suspect that you are pregnant during the course of treatment with **Impavido** or within the five months after treatment, ask your physician for advice immediately so that a pregnancy test can be performed. If the test indicates that you are pregnant, discuss the risks to the fetus with your physician.

Breastfeeding

Do not use **Impavido** during breastfeeding and breastfeeding should be avoided for 5 months after **Impavido** treatment. If your infant is breastfeeding and you need to be treated with **Impavido**, consider weaning your infant from breastfeeding.

Fertility

Animal studies revealed an impairment of fertility, which, however, was reversible. It is not known whether **Impavido** causes impairment of fertility in humans.

Driving and using machines

Do not drive or operate dangerous machines during treatment with **Impavido** because the side effects of this medicine may impair these abilities.

Drinking alcohol will exacerbate these side effects.

Important information about some of the medicine's ingredients

Each 10 mg capsule contains 80.85 mg lactose.

Each 50 mg capsule contains 87.10 mg lactose.

Before starting treatment with **Impavido**, ask your physician for advice if you know that you are intolerant to certain types of sugars, as these capsules contain lactose.

3. How should you use the medicine?

Always use this medicine according to your physician's instructions. You should check with your physician or pharmacist if you are unsure about the dosage or treatment regimen with this medicine.

The dosage and treatment regimen will be determined by your physician only.

- **The usual dosage of Impavido** is determined by the physician in accordance with the patient's weight.
- The usual dosage for treatment of serious infection of the internal organs is generally:

Body weight	Daily dosage	Number of capsules
30-31 kg	60 mg	6 capsules of Impavido 10 mg
32-39 kg	80 mg	8 capsules of Impavido 10 mg
Over 40 kg	100 mg	2 capsules of Impavido 50 mg

- **The usual dosage** for treatment of serious skin infection is generally:
  The usual daily dosage for children aged 12 years and older weighing more than 30 kg and adolescents and adults weighing less than 45 kg is 100 mg a day (one capsule of **Impavido** 50 mg twice a day).
  The usual daily dosage for adults weighing more than 45 kg is 150 mg a day (one capsule of **Impavido** 50 mg three times a day).
  - Swallow the capsule whole with a glass of water during meals.
  - Do not chew.
  - If the required dosage is 2-8 capsules a day, divide the dosage over 2-3 times a day, i.e., morning and evening or morning, noon and evening.
  - **Do not exceed the recommended dose**
  - The usual treatment duration is 28 days. Patients with a weakened immune system may be required to continue treatment for a longer period.

If you accidentally took a higher dosage or if a child has accidentally swallowed the medicine, immediately consult a physician or proceed to a hospital emergency room and bring the package of the medicine with you. Taking an overdose may exacerbate the side effects. In the event of an acute overdose you may suffer from symptoms in the digestive tract (nausea, vomiting, lack of appetite). In the event of a significant overdose, adverse effects on the function of the liver, kidney and retina cannot be ruled out.

If you forget to take the medicine at the regular time, take the dose as soon as you remember, unless it is almost time for the next dose. Do not take a double dose to make up for the forgotten dose.

Adhere to the treatment regimen as recommended by your physician.

Do not stop taking the medicine too early. Even if your health has improved, complete the treatment as recommended by the physician. If you stop the treatment prior to completion, the infection may recur.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any further questions regarding use of the medicine, consult your physician or pharmacist.

4. Side effects

As with any medicine, the use of **Impavido** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

A single case of Stevens-Johnson syndrome has been reported (a severe reaction of the skin or mucosal tissues which can sometimes be life-threatening, accompanied by skin blisters)**. Consult your physician immediately** if you notice lesions on the skin or mucosal tissues (in the mouth, for example). Your physician may discontinue treatment with **Impavido** and decide on immediate treatment.

In a few cases a drop in the blood platelet count (thrombocytopenia) has been reported. The first symptoms of this may be bleeding gums, nosebleed, or bruising. **Contact your physician as soon as possible** if new bleeding occurs.

Eye problems such as corneal inflammation (keratitis), corneal disease (keratopathy) or inflammation of the white of the eye (scleritis) were reported after **Impavido** had been taken for several weeks (the frequency of occurrence of the phenomenon cannot be determined). Consult your physician immediately if you notice any eye problems such as a foreign body sensation, redness, pain, light sensitivity, blurred vision or corneal opacity.

Very common side effects (effects that occur in more than one user in ten):

- Vomiting, diarrhoea, nausea
- Increased levels of liver enzymes (observed after blood testing)

Common side effects (effects that occur in 1-10 users out of 100):

- Loss of appetite
- Increased blood levels of creatinine and urea, indicating kidney dysfunction.

Uncommon side effects (effects that occur in 1-10 users out of 1,000):

- Pain in the lower abdomen

These side effects are usually mild to moderate and wear off after the treatment has ended, therefore neither treatment discontinuation nor dosage adjustment is required.

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking the link "Report Side Effects of Drug Treatment" on the homepage of the Ministry of Health website (www.health.gov.il), which will direct 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 closed 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 your physician.
- 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 at a temperature below 30°C.
- Store in the original package in order to protect the product from moisture.
- Do not throw away medicines in wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

- In addition to the active ingredient Miltefosine, this medicine also contains:
  Capsule content:
  Lactose monohydrate, cellulose, microcrystalline, Talc, Silica, colloidal anhydrous, Magnesium stearate
  Capsule shell:
  Gelatin, Water, purified, Iron oxide red (E172), Titanium dioxide (E171)
  Inscription on the capsules:
  Shellac, Ethanol, Propylene Glycol, Titanium dioxide (E171)
- What the medicine looks like and what the package contains:
  Impavido 10 mg: Red, hard, size 3 capsules, with "PLB" imprinted in white on the body of the capsule and "MILT 10" imprinted in white on the cap of the capsule
  Packaged in blisters:
  56 capsules - 8 blisters of 7 capsules each.
  Impavido 50 mg: Red, hard, size 2 capsules, with "PLB" imprinted in white on the body of the capsule and "MILT 50" imprinted in white on the cap of the capsule
  Packaged in blisters in the following package sizes:
  56 capsules - 8 blisters of 7 capsules each.
  28 capsules - 4 blisters of 7 capsules each.
- Registration holder and address: MegaPharm Ltd., P.O.B. 519, Hod Hasharon 4510501
- Manufacturer and address: **PAESEL + LOREI GMBH & CO. KG**, Rheinberg, Germany
- Revised in June 2021 according to Ministry of Health guidelines
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  Impavido 10 mg: 154-05-34311
  Impavido 50 mg: 154-06-34313