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

This medicine is to be supplied by physician's prescription only

Impavido® 10 mg, 50 mg

Hard capsules

Composition:
Active ingredient:
Miltefosine 10 mg, 50 mg.

For the full ingredients list see: "Additional information".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the physician or to the 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 this leaflet, a patient safety information card for **Impavido** is attached. This card contains an essential data that you should know, before and during the treatment with **Impavido**. Refer to patient safety information card and to patient information leaflet before you start using this medicine. Please keep this card for further review if necessary.

This medicine is not intended for use in children below the age of 12 years or in patients whose body weight is below 30 Kg.

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.

Before using this medicine

Women of childbearing potential must use effective contraceptive methods during the treatment with **Impavido** and for five additional months following treatment completion to ensure that they do not get pregnant during this period.

Do not use this medicine if:
- You are sensitive (allergic) to the active ingredient Miltefosine or to any of the other ingredients that this medicine contains (please see "Additional information")
- You suffer from severe damage of liver or kidney
- You suffer from Sjogren - Larsson Syndrome (a rare genetic disorder of the metabolic system causing hardening and thickening of the skin)
- You are breastfeeding
- You are pregnant
- Women who may become pregnant and have not had a pregnancy test. Women who may get pregnant must have a pregnancy test (urine or blood) before taking the medicine
- Women of childbearing potential who do not use a reliable contraception during and up to 5 months after the end of treatment

Special warnings regarding the use of this medicine
- Treatment with **Impavido** may cause damage to the kidneys and liver. Since damage to the kidneys and liver as a result of treatment with **Impavido** cannot be excluded, you should perform urine and blood tests once a week to examine your kidney and liver functions. If the values of kidney and liver functions at the end of treatment are different from normal values, monitoring should be continued until the values return to normal.
- **Impavido** may cause side effects such as vomiting and diarrhea. If these side effects persist over a prolonged period, drink large quantities of water to compensate for the fluid loss and prevent renal insufficiency.

Patients with renal or hepatic insufficiency
There is no sufficient clinical data on patients with renal or hepatic insufficiency.

Patients with a weakened immune system
In patients with a weakened immune system, **Impavido** should be administered only after another appropriate treatment is provided, since there no sufficient clinical data on the treatment of these patients with **Impavido**.

If you are taking or have recently taken other medicines, including non-prescription medicines and food supplements, inform your physician or pharmacist.

Using the medicine and food
The capsules should be taken with meals.

Pregnancy and breastfeeding
Make sure that you are not pregnant prior to beginning treatment with **Impavido**.

Women of childbearing potential must use effective contraceptive methods during the treatment with **Impavido** and for five additional months following treatment completion to ensure that they do not get pregnant during this period.

Vomiting and diarrhea are very common side effects of treatment with this medicine, therefore the efficacy of oral contraceptives may be compromised. Tell the physician if you experience these side effects so that he can recommend an additional method of contraception to you.

If you suspect that you are pregnant during the treatment with **Impavido** or during five months following the treatment, immediately consult the physician in order to check whether you are pregnant. If the test reveals that you are pregnant, you should discuss the risks for the fetus with the physician.

Do not use **Impavido** during breastfeeding period. If you are breastfeeding your baby and you have to receive treatment with **Impavido**, consider weaning the baby from breastfeeding.

Animal studies have demonstrated impairment of fertility, which was reversible. It is unknown whether **Impavido** also causes impairment of fertility in humans.

Driving and using machines
Do not drive or operate dangerous machines while receiving treatment with **Impavido** since the side effects of this medicine may impair these abilities. Drinking alcohol will exacerbate these sensations.

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.

If you have been told that you are intolerant to certain types of sugar, consult the physician prior to taking **Impavido** since these tablets contain Lactose.

Tests and follow-up
Since damage to the kidneys and liver as a result of treatment with **Impavido** cannot be excluded, the physician will perform urine and blood tests once a week to examine your kidney and liver functions.

If the values of kidney and liver functions at the end of treatment are different from normal values, follow-up should be continued until the values return to normal.

How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician if you are unsure. The dosage and manner of treatment will be determined only by the physician.
- Swallow the capsule whole with a glass of water.
- Do not chew.
- If the required dose requires taking 2-15 capsules per day, divide the dose to 2-3 times per day, morning and evening or morning, noon and evening.

If you have accidentally taken a higher dose, or if a child has accidentally swallowed the medicine, go immediately to a hospital emergency room and bring the medicine package with you.
Taking a high dose may increase the risk of side effects.

If you forget to take the medicine at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult your physician. Persist with the treatment as recommended by the physician.

Do not stop taking the medicine, complete the treatment as prescribed to you by the physician. If you discontinue the treatment prior to its completion, the infection may return.

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

Side effects

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

Very common side effects:
- Vomiting, diarrhea, nausea
- A rise in liver enzymes

Common side effects:
- Loss of appetite
- Increased blood levels of creatinine and urea indicating impaired kidney function

Uncommon side effects:
- Lower abdomen pain

These side effects usually resolve following the end of treatment, therefore neither treatment discontinuation nor dose adjustment is required.

In individual cases, a reduction in the number of blood platelets (thrombocytopenia) has been reported. Its first symptoms may be gum bleeding, nosebleed or signs of bruising.

A single case of Stevens-Johnson syndrome has been reported (a severe and sometimes life threatening reaction of the skin and mucous membranes accompanied by skin blisters). If you notice lesions on the skin or on the mucous membranes, contact a physician immediately. The physician may discontinue the treatment with **Impavido** and will decide on immediate treatment.

If any side effect appears, if any side effects worsen, or if you suffer from a side effect not mentioned in this leaflet, consult with the physician.

Reporting of side effects

Side effects can be reported to the Ministry of Health by using an online form in the Ministry of Health web site home page www.health.gov.il, or in the following link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.
- Do not use the medicine after the expiry date (exp. date) appearing on the outer package. The expiry date refers to the last day of that month.
- Store at a temperature below 30ºC.
- Store in the original package in order to protect from moisture.

Additional information

- In addition to the active ingredient Miltefosine the medicine also contains:
  Silica, colloidal anhydrous, Cellulose, microcrystalline, Lactose monohydrate, Talc, Magnesium stearate, Gelatin, Titanium dioxide (E171), Iron oxide red (E172), Capsugel 00A1 White ink.
- What does the medicine look like and what are the contents of the package:
  Impavido 10 mg: red hard capsule of size 3, with a white imprint "PLB" on the body and white imprint "MILT 10" on the cap.
  Packed in blisters:
  56 capsules – 8 blisters of 7 capsules each.
  Impavido 50 mg: red hard capsule of size 2 with a white imprint "PLB" on the body and white imprint "MILT 50" on the cap.
  Packed in blisters with the following sizes:
  56 capsules – 8 blisters of 7 capsules each.
  28 capsules – 4 blisters of 7 capsules each.
- Marketing Authorization Holder and his address: MegaPharm Ltd., P.O.B. 519, Hod Hasharon 4510501.
- Manufacturer and his address: Paesel + Lorei GmbH & Co. KG, Rheinberg, Germany.
- This leaflet was checked and approved by the Ministry of Health in October 2015.
- 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