PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Impavido® 10 mg capsules

Active substance: miltefosine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Impavido® is and what it is used for

Impavido® is a medicine that is active against a special type of protozoa (single-celled pathogens that cause infection) called Leishmania.

Impavido® is used for visceral leishmaniasis, a serious infection of the internal organs caused by Leishmania *donovani*, as well as cutaneous leishmaniasis, a skin infection caused by one of several subspecies of Leishmania *brasiliensis* or Leishmania *mexicana*.

2. What you need to know before you take Impavido®

Do not take Impavido®
- if you are hypersensitive (allergic) to miltefosine or any of the other ingredients of this medicine (listed in section 6),
- if you have severe liver or kidney damage (see also section below “Patients with impaired liver and kidney function”),
- if you suffer from Sjögren-Larsson syndrome (a very rare, congenital, metabolic disorder leading to cornification of the skin),
- if you are pregnant.

Women of childbearing age must not take Impavido® without practising reliable contraceptive protection. This must be ensured for a further 3 months after treatment has ended (see also section below on “Pregnancy”).

Warnings and precautions
Talk to your doctor or pharmacist before taking Impavido®. A damaging effect of Impavido® on the kidneys and liver cannot be ruled out. For this reason, your doctor will perform weekly urine and blood tests to monitor your kidney and liver function. If kidney function values differ considerably from normal values at the end of treatment, monitoring should be continued until values return to normal.

Vomiting and diarrhoea are possible side effects of therapy with Impavido® (see also section below on "Side effects"). If these side effects persist over a prolonged period, it is important that you drink sufficient liquid to compensate for fluid loss, so that the risk of impaired kidney function is avoided.

Eye problems, such as inflammation of the cornea (keratitis), can be symptoms of the Leishmania infection. However, in some cases, eye problems up to blindness, sometimes permanent, occurred after taking Impavido® for a few days or several weeks. Before starting the treatment, tell your healthcare professional if you have any eye problem or history of eye problem as an ophthalmological examination should be done first. If you experience any eye discomfort during the treatment, discontinue miltefosine immediately and contact your doctor as soon as possible (see also below under "Side effects").

Patients with impaired liver and kidney function
Patients with severe liver and kidney dysfunction have not been studied.

There are no sufficient data on patients with mild to moderate liver and kidney dysfunction. Patients with liver values (AST, ALT, alkaline phosphatases) 3 times over the normal range were excluded from the clinical study, as were patients with kidney values (serum creatinine, BUN) 1.5 times over the normal range.

Patients with a weakened immune system
In patients with a weakened immune system, Impavido® may be used only after standard therapy has failed, as there is only limited experience with the therapeutic use of Impavido® in such patients.

Impavido® was used in 39 HIV patients with an average body weight of 59 kg (range: 43 – 99 kg) at a dose of 100 mg per day for the treatment of leishmaniasis co-infection not responding to drug-based treatment or which returned after such treatment. After a mean treatment period of 55 days (median value: 30 days, range 4 – 732 days), 25 patients (65 %) responded to therapy; out of these, 16 patients (43 %) had a negative parasitology. 22 patients received at least one further course of treatment with a similar success rate and tolerability.

Male patients
In animal trials, impaired reproductive ability was observed in male rats. Data from male patients treated in clinical studies with Impavido® have so far shown no evidence of impaired fertility.

Other medicines and Impavido®
Tell your doctor or pharmacist if you are taking, have recently taken or might take, any other medicines, including medicines obtained without a prescription.

Pregnancy, breast-feeding and fertility
Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy
Make sure that you are not pregnant before starting treatment with Impavido®. Women of childbearing age must practise reliable contraceptive protection during and up to 3 months after treatment.

Vomiting and diarrhoea are very common side effects of therapy with Impavido® and may impair the effectiveness of the contraceptive pill. Tell your doctor immediately if you experience these side effects, so that another reliable form of contraception can be used.

If you suspect that you are pregnant during treatment with Impavido® or within 3 months of ending treatment (e.g. absence of menstrual bleeding), you must inform your doctor immediately, so that a pregnancy test can be carried out. If this test confirms that you are pregnant, discuss the risk for your child with your doctor.

Breast-feeding
Impavido® may not be administered during breast-feeding; otherwise, weaning is required.

Fertility
Studies in animals revealed an impairment of fertility which, however, was reversible. Whether this impairment does also occur in men is not known so far.

Driving and using machines
Even when used as directed, the known side effects of Impavido® impair the ability to drive and use machines. For this reason, you must not drive, use machines or perform other hazardous activities. This particularly applies in combination with alcohol.

Important information about some of the ingredients of Impavido®
This medicine contains lactose. Therefore, please only take Impavido® after consulting your doctor if you know that you have an intolerance to certain sugars.

3. How to take Impavido®

Always take Impavido® exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how many Impavido® capsules you should take, for how long and at what times.

Visceral leishmaniasis
Impavido® 10 mg capsules are intended particularly for the treatment of patients with a body weight of 9 – 39 kg. There is no therapeutic experience yet with children below 3 years of age or with children weighing less than 9 kg. Patients weighing 40 kg or more should preferably take Impavido® 50 mg capsules.

Unless otherwise prescribed by the doctor, the usual dose is 1.5 – 2.5 mg/kg body weight. The following table gives the number of capsules to be taken each day:

Body weight	Daily dose	Number of capsules
9 – 11 kg	20 mg	2 Impavido® 10 mg capsules
12 – 16 kg	30 mg	3 Impavido® 10 mg capsules
17 – 20 kg	40 mg	4 Impavido® 10 mg capsules
21 – 25 kg	50 mg	5 Impavido® 10 mg capsules
26 – 31 kg	60 mg	6 Impavido® 10 mg capsules
32 – 39 kg	80 mg	8 Impavido® 10 mg capsules

You must take Impavido® over a period of 28 days. In patients with a weakened immune system, treatment over a longer period may be required.

Cutaneous leishmaniasis
There is no therapeutic experience yet with children below 12 years of age or with children weighing less than 30 kg. However, a therapy using the dosages recommended for visceral leishmaniasis (see table) can be considered.

Unless otherwise prescribed by the doctor, the daily dose for children aged 12 years and older, adolescents and adults weighing less than 45 kg is 100 mg miltefosine (5 Impavido® 10 mg capsules twice a day). Patients weighing more than 45 kg are given 150 mg miltefosine daily (5 Impavido® 10 mg capsules, 3 times a day). However, treatment with Impavido® 50 mg capsules should generally be preferred for such patients.

Please swallow the capsules whole (without chewing) with sufficient liquid (preferably a glass of drinking water). The capsules should be taken with meals. Dosages of 2 – 15 capsules daily should be divided into 2 – 3 single doses, taken either in the morning and evening, or morning, noon and evening.

Please talk to your doctor or pharmacist if you have the impression that the effect of Impavido® is too strong or too weak.

If you take more Impavido® than you should
Nothing will probably happen if you take one capsule too many by mistake. Contact your doctor if you accidentally take several capsules too many. If possible, take your capsules or the box with you to show the doctor or pharmacist.

In general, an overdose may enhance the symptoms described in section "Undesirable effects".

If you forget to take Impavido®
If you forget a dose, take it as soon as you realise, unless it is almost time for the next dose. Do not double the next dose to make up for the forgotten dose.

If you stop taking Impavido®
Take the total number of capsules prescribed by your doctor, even if you are feeling better, before you have taken them all. If you stop taking the capsules too early, the infection may flare up again.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Impavido® can cause side effects, although not everybody gets them.

The following frequency data are used for evaluating side effects:

Very common:	may affect more than 1 in 10 people
Common:	may affect up to 1 in 10 people
Uncommon:	may affect up to 1 in 100 people
Rare:	may affect up to 1 in 1,000 people
Very rare:	may affect up to 1 in 10,000 people
Not known:	frequency cannot be estimated from the available data

Possible side effects:
Very common side effects that may occur during treatment with Impavido® are vomiting, diarrhoea, nausea and a rise in liver enzymes (which can be determined via a blood test).

Common side effects are loss of appetite and increased blood levels of creatinine and urea (metabolic products), which indicate impaired kidney function.

Lower abdominal pain is uncommon.

These side effects are usually mild to moderate and transient or wear off after treatment has ended, so that a discontinuation of treatment or a dose reduction is not required.

In individual cases, a reduction in the number of blood platelets (thrombocytopenia) has been reported. First signs may be increased gum bleeding, nosebleeds or bruising. Patients should consult their doctor if new bleeding occurs.

In one case, Stevens-Johnson syndrome has been reported (a severe, sometimes life-threatening reaction of the skin and mucous membranes, accompanied by blistering). For this reason, tell your doctor immediately if you experience lesions on the skin or mucous membranes (e.g. in the mouth). These may require discontinuation of Impavido® and immediate treatment by your doctor.

Cases of eye complaints such as redness of the eye and inflammation of different eye segments (keratitis, scleritis, uveitis) and visual impairment up to blindness have been reported after taking Impavido® (exact frequency of occurrence cannot be estimated). Discontinue the treatment immediately and contact your doctor/next clinic as soon as possible if you notice any eye complaints including foreign body sensation, redness, pain, sensitivity to light, blurred vision or corneal opacity.

Tell your doctor if any of the other listed side effects gets serious or causes you severe problems, or if any side effect does not improve during the course of treatment.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly to the German Federal Institute for Drugs and Medical Devices (BfArM), Pharmacovigilance Department, Kurt-Georg-Kiesinger-Allee 3, 53175 Bonn, Germany. Website: www.bfarm.de
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Impavido®

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister and outer carton. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture.

Never throw away any medicines via wastewater (e.g. not in the toilet or sink). Ask your pharmacy how to throw away medicines you no longer use. These measures will help protect the environment. You will find further information at: www.bfarm.de/arzneimittelentsorgung

6. Contents of the pack and other information

What Impavido® contains

- The active substance is miltefosine. Each capsule contains 10 mg of miltefosine.
- The other ingredients are
  - Capsule content: colloidal anhydrous silica, microcrystalline cellulose, lactose monohydrate, talc, magnesium stearate (Ph. Eur.)
  - Capsule shell: gelatin, titanium dioxide (E171), red iron oxide (E172) and purified water
  - Printing ink consisting of: shellac, ethanol, propylene glycol, titanium dioxide (E 171).

What Impavido® looks like and contents of the pack

Impavido® 10 mg capsules are red, opaque hard capsules of size 3 with a white imprint “PLB” on the body and “MILT 10” on the cap.

Seven Impavido® 10 mg capsules are sealed in an aluminium/aluminium blister strip.

Impavido® 10 mg capsules are available in the following pack sizes:

56 capsules

Marketing Authorisation Holder and Manufacturer

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