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

The medicine is dispensed with a doctor's prescription only

Opsumit® 10 mg

Film-coated Tablets

Active ingredient and its quantity
Each film-coated tablet contains:
Macitentan 10 mg

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

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to your doctor or pharmacist.
This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if you think that their illness is similar.

Patient Safety Information Card
In addition to the leaflet, Opsumit also has a patient safety information card. This card contains important safety information that you should know, before beginning and during treatment with Opsumit and act accordingly. Refer to the patient safety information card and patient leaflet before using the preparation. Keep the card and the leaflet for further reference if required.

Do not use Opsumit if you are pregnant, since use of this medicine may cause harm to the fetus (see section 2 "Before you take the medicine" subsections "Do not use the medicine if" and "Pregnancy, breastfeeding and fertility").
If you are a woman of child-bearing age who could become pregnant, you should take a pregnancy test before you start taking Opsumit and regularly every month while you are taking the medicine and a month after termination of treatment. A negative result in each pregnancy test must be assured. You must use a reliable contraceptive method while taking Opsumit and one additional month after termination of treatment (see section 2 subsection "Pregnancy, breastfeeding and fertility").

1. WHAT IS THE MEDICINE INTENDED FOR?

- The medicine is intended for treatment of pulmonary arterial hypertension (PAH) in adults, and is used to slow down disease progression.
- Pulmonary arterial hypertension is high blood pressure in the blood vessels that carry blood from the heart to the lungs (the pulmonary arteries).
- Opsumit widens the pulmonary arteries, making it easier for the heart to pump blood through them. This lowers the blood pressure, relieves the symptoms and improves the course of the disease.

- The medicine can improve your ability to perform physical activity, relieve the symptoms and postpone the need for additional treatment. Additionally, the medicine can reduce your chances of hospitalization as a result of the disease.

Therapeutic group: Endothelin receptor antagonists.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient (macitentan), soya or to any of the additional ingredients contained in the medicine. For the list of additional ingredients, see section 6 "Further information".
- You are pregnant, planning pregnancy, or if you may get pregnant because you are not using reliable contraceptives. See also section "Pregnancy, breastfeeding and fertility".
- You are breastfeeding. See also section "Pregnancy, breastfeeding and fertility".
- You suffer from liver disease or if you have very high levels of liver enzymes in your blood. Consult the doctor, who will decide whether this medicine is suitable for you.

Tell your doctor if any of these apply to you.

Special warnings regarding the use of this medicine
Before taking Opsumit, tell your doctor if:

- You suffer from kidney problems. The medicine may cause further reduction of blood pressure and decrease in hemoglobin levels in patients with kidney problems.
- You are sensitive to any type of food or medicine, inform your doctor before you start taking the medicine.

In patients with pulmonary veno-occlusive disease (obstruction of the lung veins), the use of medicines for treatment of PAH, including Opsumit, may lead to pulmonary edema. If you have signs of pulmonary edema when using Opsumit, such as a sudden, significant increase in breathlessness and low oxygen, **tell your doctor immediately**. Your doctor may perform additional tests, and will determine what treatment regimen is most suitable for you.

Children and adolescents
Opsumit is not intended for the treatment of children and adolescents under 18 years of age.

Use in the elderly
There is limited experience with Opsumit in patients older than 75 years. Opsumit should be used with caution in this age group

Tests and follow-up
Before starting use of this medicine and during treatment the doctor will refer you to perform blood tests to check:

- whether you have anemia (low number of red blood cells)
- whether your liver functions are normal

If you have anemia (a reduced number of red blood cells), you may have the following signs:

- dizziness

- fatigue/malaise/weakness
- fast heart rate, palpitations
- pallor

If you notice any of these signs, **tell your doctor**.

Signs indicating liver dysfunction include:

- Nausea (urge to vomit)
- Vomiting
- High fever
- Abdominal pain
- Yellowing of the skin or the whites of your eyes (jaundice)
- Dark-colored urine
- Itching of your skin
- Unusual tiredness or exhaustion
- Flu-like syndrome (joint and muscle pain accompanied by fever)

If you feel any of these signs, **tell your doctor immediately**.

Drug interactions

If you take Opsumit together with other medicines including those listed below, the effect of Opsumit or other medicines might be altered.

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist. Especially if you are taking:

- Rifampicin, clarithromycin, telithromycin, ciprofloxacin, erythromycin (antibiotics used to treat infections)
- Phenytoin (a medicine used to treat seizures)
- Carbamazepine (used to treat depression and epilepsy)
- St. John's Wort (*Hypericum*, an herbal preparation used to treat depression)
- Ritonavir, saquinavir (used to treat HIV infections)
- Nefazodone (used to treat depression)
- Ketoconazole (except shampoo), fluconazole, itraconazole, miconazole, voriconazole (used to treat fungal infections)
- Amiodarone (to control the heartbeat)
- Cyclosporine (used to prevent organ rejection after transplant)
- Diltiazem, verapamil (to treat high blood pressure or specific heart problems)

Use of this medicine and food

Can be taken with or without food.

If you are taking piperine as a dietary supplement, this may alter how the body responds to some medicinal products, including Opsumit. Please talk to your doctor or pharmacist should this be the case.

Pregnancy, breastfeeding and fertility

Opsumit may harm unborn babies conceived before starting treatment or during treatment. If you are a woman of child-bearing age who could become pregnant, your doctor will ask you to take a pregnancy test before you start taking Opsumit and regularly every month while you are taking the medicine and a month after termination of treatment. A negative result in each pregnancy test must be assured.

Do not take the medicine if you are pregnant or planning to become pregnant.

You must use a reliable contraceptive method while taking Opsumit and for an additional month after termination of treatment.

Your doctor or gynecologist will instruct you about reliable contraceptive methods while taking Opsumit.
Your doctor will recommend a highly effective method of contraception to you such as an intra-uterine device or tubal sterilization or using a combination of methods (such as a hormonal method and barrier method [such as a diaphragm, contraceptive sponge, or your partner must also use a condom] or two barrier methods of contraception). Consult your doctor regarding the use of two methods of contraception. If the chosen method of contraception is the partner's vasectomy, hormonal or barrier contraception must be used concomitantly.

Tell your doctor immediately if you become pregnant while you are taking Opsumit, think you might be pregnant or plan to become pregnant in the near future.

It is unknown whether the medicine passes to breast milk. Do not breastfeed while using the medicine, talk to your doctor about this.

Fertility
If you are a man taking Opsumit, it is possible that this medicine may lower your sperm count. Talk to your doctor if you have any questions or concerns about this.

Driving and use of machinery
This medicine may cause side effects, such as headaches and hypotension (listed in section 4 "Side effects"), the symptoms of your disease may also make you less fit to drive or use machines.

Important information about some of the ingredients of this medicine
Opsumit contains lactose, lecithin from soya and sodium.
Opsumit tablets contain a sugar called lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking the medicine.
Additionally, Opsumit tablets contain lecithin derived from soya. If you are allergic to soya, do not take this medicine (see section 2 "Do not use the medicine if").
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. HOW SHOULD THE MEDICINE BE USED?

This medicine should only be prescribed to you by a doctor experienced in the treatment of pulmonary arterial hypertension.
Always use the preparation according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of the medicine.

The dosage and treatment regimen will be determined by the doctor only.
The usual recommended dosage is:
One 10 mg tablet, once a day. It is best to take the tablet at the same time each day.
Do not exceed the recommended dose.

- Swallow the tablet whole with a glass of water.
- Do not chew, halve or crush the tablet.
- You can take Opsumit with or without food.

If you have accidentally taken a higher dosage
If you have taken more tablets than you have been told to take, you may experience headache, nausea, or vomiting. If you have taken an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forget to take this medicine at the required time, take the next dose as soon as you remember, then continue at the usual times. Do not take a double dose to make up for a forgotten one.

If you stop taking this medicine
Adhere to the treatment regimen as recommended by the doctor, in order to control your disease. Even if there is an improvement in your health, do not stop treatment with this medicine without consulting your doctor.

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 the use of this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

Like all medicines, the use of Opsumit may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Refer to a doctor immediately if:
- You suffer from signs that may indicate liver dysfunction, such as: nausea, vomiting, fever, abdominal pain, yellowing of the skin and eyes (jaundice), dark-colored urine, itchy skin, unusual tiredness or exhaustion (fatigue or lethargy), flu-like syndrome (joint and muscle pain accompanied by fever).

Uncommon serious side effects (may affect up to 1 in 100 users):
- Allergic reactions (swelling around the eyes, face, lips, tongue or throat, itching and/or rash)

If you notice any of these signs**, tell your doctor immediately.**

Very common side effects (may affect more than 1 in 10 users):
- Anemia (low number of red blood cells) or reduced hemoglobin
- Headache
- Bronchitis (inflammation of the airways)
- Inflammation of the nose and throat
- Edema (swelling) especially of the ankles and feet

Common side effects (may affect up to 1 in 10 users):
- Inflammation of the throat
- Flu
- Urinary tract inflammation (bladder infection)
- Hypotension (low blood pressure)
- Nasal congestion (blocked nose)
- Elevated liver tests

- Leukopenia (decreased white blood cell counts)
- Thrombocytopenia (decreased blood platelet counts)
- Flushing (skin redness)
- Increased uterine bleeding

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 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 via the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Avoid poisoning! This medicine, and all other medicines must be stored 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 doctor.
Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
Do not store at temperature above 30˚C.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer used. These measures will help to protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
Lactose monohydrate, microcrystalline cellulose, sodium starch glycolate type A, povidone, magnesium stearate, polysorbate 80, purified water.
Tablet coating:
Polyvinyl alcohol partially hydrolyzed, titanium dioxide, talc, lecithin (soya), xanthan gum.

Each tablet contains about 37 mg lactose.

What the medicine looks like and contents of the pack:
Film-coated white to off-white, biconvex, round tablets with the inscription "10" on both sides
Each Opsumit pack contains 15 or 30 tablets in a blister.
Not all pack sizes may be marketed.

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

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

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
152-72-34061-00
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