PHARMA
Promise & Commitment

Macimit (Macitentan) 10mg.

FREQUENTLY ASKED QUESTIONS BROCHURE FOR HEALTHCARE PROFESSIONALS.

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

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What is the purpose of this brochure?

This Brochure is provided for healthcare professionals and doctors who are involved in the treatment of patients with Macitmit (Macitentan) for their information and safe use of Macitentan.

This Brochure will enable you to:

- To understand what is Macimit and how it should be used
- Learn about identified risks associated with Macimit and how they should be prevented and managed
- Understand potential side effects of Macimit and how they should be prevented
- Provide important safety information to patients

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What is Macimit ?

Macimit (Macitentan) is a drug belonging to the class of endothelin receptor antagonist.

Therapeutic indication:
As monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

Dosage and administration

Treatment should only be initiated and monitored by a physician experienced in the treatment of PAH. The recommended dose of Macimit 10 mg taken once daily with water, with or without food. Therapy should be continued long term Tablets are not breakable and should be taken whole, with water.

Should the dose of Macimit be adjusted for patients with hepatic or renal impairment or the elderly?

Based on pharmacokinetic (PK) data, no dose adjustment is required in patients with mild, moderate or severe hepatic impairment. There is no clinical experience with the use of Macimit in PAH patients with moderate or severe hepatic impairment. Macimit must not be initiated in patients with severe hepatic impairment or clinically significant elevated hepatic aminotransferases (greater than 3 times the Upper Limit of Normal (>3 x ULN); see sections 4.3 and 4.4 of the SmPC).

Based on PK data, no dose adjustment is required in patients with renal impairment. There is no clinical experience with the use of Macimit in PAH patients with severe renal impairment. Caution is recommended in this population. The use of Macimit is not recommended in patients undergoing dialysis.

No dose adjustment is required in patients aged over 65 years. There is limited clinical experience in patients aged over 75 years. Therefore Macimit should be used with caution in this population.

Contraindications

- Hypersensitivity to the active substance, soya or to any of the excipients listed in package leaflet.
- Pregnancy.
- Women of childbearing potential who are not using reliable contraception.
- Breastfeeding.
- Patients with severe hepatic impairment (with or without cirrhosis).
- Baseline values of hepatic aminotransferases (aspartate aminotransferases (AST) and/or alanine aminotransferase (ALT) > 3 × ULN).

WHAT ARE THE MAIN RISKS ASSOCIATED WITH MACIMIT USE?

As with other ERAs, treatment with Macimit is associated with a risk of anemia, teratogenicity and hepatotoxicity.

WHAT IS ANEMIA AND HOW IT CAN BE PREVENTED OR MANAGED?

A decrease in hemoglobin concentrations has been associated with endothelin receptor antagonists (ERAs) including Macimit (see section 4.8). In placebo-controlled studies, Macimit-related decreases in hemoglobin concentration were not progressive and stabilized after the first 4–12 weeks of treatment and remained stable during chronic treatment. Cases of anemia requiring blood cell transfusion has been reported with Macitentan and other ERAs.

Initiation of Macimit is not recommended in patients with severe anemia. It is recommended that hemoglobin concentrations be measured prior to initiation of treatment and tests repeated during treatment as clinically indicated.

If tests show a clinically significant decrease in hemoglobin or hematocrit, other causes should be excluded.

WHAT IS TERATOGENICITY AND HOW IT CAN BE PREVENTED?

There is no specific data or relevant clinical experience with respect to the teratogenic potential of Macitentan in the human foetus. However, developmental and reproductive toxicity studies in rabbits and rats showed that Macitentan is teratogenic at all doses tested in these animal species. In both species, there were cardiovascular and mandibular arch fusion abnormalities.

The risk for humans remains unknown but appropriate precautions must be taken for women of childbearing potential. Macitentan is contraindicated during pregnancy and in women of childbearing potential who are not using reliable contraception.Macitentan treatment should only be initiated in women of childbearing potential when the absence of pregnancy has been verified.

Monthly pregnancy tests in women of childbearing potential being treated with Macitentan are recommended allowing early detection of pregnancy.

Women should not become pregnant for 1 month after discontinuation of Macitentan.

WHAT ARE THE RISKS ASSOCIATED WITH PREGNANCY AND BREASTFEEDING?

Macimit is contraindicated during pregnancy and in women of childbearing potential who are not using reliable contraception. Ask your patient to have a pregnancy test before the initiation of Macimit and every month during the treatment.

RISKS ASSOCIATED WITH PREGNANCY AND BREASTFEEDING

- If a patient is already pregnant you should not prescribe a Macimit drug.
- Macimit may harm unborn babies. Pregnancy to be avoided soon after stopping the treatment with Macimit.
- Pregnancy can also lead to severe deterioration in pulmonary arterial hypertension symptoms.
- Ask your patient to see a doctor immediately if the women patient becomes pregnant or experiences any side effects during treatment with Macimit.
- If a pregnancy occurs during treatment, the risks to the foetus should be discussed with the patient and a decision taken whether to discontinue treatment, taking into account also the risk to the mother due to PAH
- Macimit is contraindicated in the Breastfeeding women patient.

WHAT ARE THE RISKS ASSOCIATED WITH HEPATOTOXICITY AND HOW THEY CAN BE MANAGED?

Elevations of liver aminotransferases (ALT, AST) have been associated with PAH and with endothelin receptor antagonists (ERAs).

Macimit is not to be initiated in patients with severe hepatic impairment or elevated aminotransferases (>3 x ULN) and is not recommended in patients with moderate hepatic impairment.

Liver enzyme tests should be obtained prior to initiation of Macimit.

Patients should be monitored for signs of hepatic injury and monthly monitoring of ALT and AST is recommended. If sustained, unexplained, clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or by clinical symptoms of liver injury (e.g., jaundice), Macimit treatment should be discontinued.

Re-initiation of Macimit may be considered following the return of hepatic enzyme levels to within the normal range in patients who have not experienced clinical symptoms of liver injury. The advice of a hepatologist is recommended.

What should I discuss with my patients, before initiating treatment with Macimit?

As HCP responsibility, you need to inform women patients of the childbearing potential of risks to the foetus in case of pregnancy due to PAH and due to Macimit use and of the need to:

- Use a reliable method of contraception
- Have monthly pregnancy tests
- Report pregnancy immediately if it occurs

A pregnancy test, liver function tests and measurement of hemoglobin concentrations should be performed before initiation of treatment with Macimit.

You will need to inform patients about the important side effects associated with Macimit

What is the role of the prescribing checklist?

A prescribing checklist is an educational tool to help you (all Health Care professionals) identify key risk information that should be evaluated and discussed with the patient before prescribing Macimit.
The completed checklist can be stored with the patient chart as helpful evidence that the patient has been informed of the risks associated with treatment with Macimit.

What is the patient card?

The patient card is a small, folding, credit-card-sized card, which should be carried by the patients at all times and will contain key information about their current treatment and concomitant medications. Also, it should mention all important safety details about the Macimit.

Reporting of Adverse Drug Reactions / Adverse Events

Please report all AE's and cases of pregnancy to the PPI @ **Abdulrahman@pharma.com.sa**

Also, report suspected adverse drug reactions (ADRs) to SFDA @ following details:

Saudi Food and Drug Authority (SFDA)

SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/

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