

MACITENTAN (Opsumit®)

Issued by PHA's Scientific Leadership Council

Information is based on the United States Food and Drug Administration drug labeling

Last Updated June 2014

WHAT IS MACITENTAN?

Macitentan is an oral medication classified as an endothelin receptor antagonist (ERA) which is approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 patients. The goal of this therapy is to slow progression of the disease. Progression of disease in the primary research study was defined as worsening symptoms with decreasing exercise capacity and need for additional medical therapy for PAH. The need for infused PAH therapy, hospitalization for PAH, lung transplantation and death were all indicators of disease progression. The research study showing the effectiveness of the medication included mostly patients with symptoms that were rated as WHO Functional Class II-III. Macitentan also reduced hospitalization for PAH. Macitentan was approved for PAH by the United States Food and Drug Administration (FDA) in 2013.

HOW DOES MACITENTAN WORK?

Macitentan works by blocking endothelin, a substance made by the body. Endothelin causes blood vessels to narrow (constrict). It also causes abnormal growth of the muscle in the walls of the blood vessels in the lungs. This narrowing increases the pressure required to push the blood through the lungs to get oxygen. By blocking the action of endothelin, macitentan decreases the pulmonary blood pressure. This delays disease progression.

HOW IS MACITENTAN GIVEN?

Macitentan is taken orally, with or without food. There is one FDA-approved dose which is a 10 mg tablet (white and round pill with a "10" on one side) once daily. The tablets should not be split, crushed or chewed.

HOW DO PATIENTS OBTAIN MACITENTAN?

Macitentan is a limited distribution medication, which means it cannot be purchased at a local pharmacy. For women, macitentan must be prescribed by a physician through the OPSUMIT Risk Evaluation and Mitigation Strategy (REMS) Program because of the risk to embryo or fetus if the woman becomes pregnant (NOT ADVISED—See below). Men can receive macitentan without taking part in the OPSUMIT REMS Program, however, if they are not enrolled, they will not receive the first month of drug free of charge. Insurance approval must be obtained prior to starting therapy. OPSUMIT REMS will forward the request to an authorized specialty pharmacy. Macitentan is then sent to patients monthly by any of the following specialty pharmacies: Accredo Health Group Inc., CVS Specialty Pharmacy, Axiom (Puerto Rico only) and WellCare (Exactus). It is anticipated that additional specialty pharmacies will be approved to provide macitentan in 2014.

MACITENTAN (Opsumit®)

Continued

WILL INSURANCE PAY FOR MACITENTAN?

It is expected that most insurance plans will pay for macitentan prescriptions; however, plans with a set percentage co-payment may result in large cost to the patient. In those cases, the patient may be offered copay assistance through Caring Voice Coalition or through the Actelion Patient Assistance Program.

If a patient is enrolled in the OPSUMIT REMS program, the first month of medication will be provided free of charge. The program will enable the patient to be on the medication while the insurance issues are being addressed.

Actelion PAH Pathways® (866-288-3546) may assist with either partial or full drug coverage for any patient with qualifying financial circumstances. Caring Voice Coalition (888-267-1440), an organization that provides grants to assist with drug cost for patients with chronic illnesses, may also provide coverage if the patient qualifies for such assistance.

WHAT ARE THE FREQUENT SIDE EFFECTS OF MACITENTAN?

Macitentan is generally well tolerated. The most frequent side effects are:

- Nasal inflammation (stuffy nose)
- Headache
- Anemia
- Bronchitis (irritation of the airways)
- Urinary tract infection
- Flu-like illness

Macitentan can cause serious birth defects if taken during pregnancy.

Liver problems can occur with ERAs like macitentan.

Low red blood cell levels can occur during the first weeks after starting therapy. In some cases, a blood transfusion may be needed, but this is not common.

Changes in sperm production may result in men taking macitentan, based on the effects of the medication that was observed in animals. Men taking macitentan should discuss this further with their health care provider.

Fluid retention is a known side effect of ERAs. It is important to notify your physician if you experience swelling or any other side effects. Treatment may be required including reducing salt and fluid in your diet, as well as a water pill (diuretic) to promote increased fluid removal through the kidneys.

MACITENTAN (Opsumit®)

Continued

HOW ARE SIDE EFFECTS OF MACITENTAN MONITORED?

Because of the potential harm to the fetus, women of childbearing potential must have a pregnancy test before initiating therapy and subsequently on a monthly basis as long as a patient is receiving macitentan.

Liver problems can occur with ERAs like macitentan. Although monthly liver function tests (LFT) monitoring is not required while receiving macitentan treatment, it is important to test liver function at the outset of all treatments for PAH and, at your doctor's discretion, at periodic intervals thereafter. Macitentan should be stopped if the blood tests for liver enzymes (LFTs) are accompanied by signs and symptoms of abnormal liver function or injury or by an increased total bilirubin (another blood test for liver function) to more than 2 times normal. A physician will guide a patient in managing their liver enzymes if they become elevated. This may require that a patient stop the medication.

Red blood cell counts should be checked before initiation of macitentan therapy and periodically thereafter.

WHAT ARE CONSIDERATIONS FOR USE OF MACITENTAN IN SPECIAL POPULATIONS?

Macitentan should not be used in pregnancy. Macitentan has been shown to be harmful to the fetus in research studies of rats and rabbits.

Patients should not become pregnant while taking macitentan. Women must use acceptable methods of contraception when taking macitentan to prevent pregnancy. Patients may choose between one highly effective form of contraception such as intrauterine device (IUD), contraceptive implants, or tubal ligation or a combination of methods such as hormonal therapy with a barrier method or two barrier methods. If a partner's vasectomy is the chosen contraceptive method, then the patient must also use an additional method such as hormonal or barrier. In addition, a negative pregnancy test prior to the initiation of macitentan and monthly thereafter is required. If a patient becomes pregnant while taking macitentan, she should stop taking macitentan and immediately notify her doctor. It is not known whether macitentan passes into breast milk; therefore, nursing mothers should not take macitentan. Please refer to the package insert for additional information.

There has not been research to determine whether macitentan is safe or effective for children.

Macitentan is not recommended in patients with significant liver disease.

For patients with significant kidney disease, the dose of macitentan does not need to be changed.

MACITENTAN (Opsumit®)

Continued

COULD A PATIENT BE ALLERGIC TO MACITENTAN?

This is possible but not likely.

WHAT ARE IMPORTANT DRUG INTERACTIONS WITH MACITENTAN? (PLEASE SEE PACKAGE INSERT FOR FULL DETAILS)

Macitentan blood levels may be increased if used with ketoconazole. The dosing should be adjusted by the doctor.

Ritonavir or ritonavir-containing combination drugs have not been studied but are likely to increase blood levels of macitentan similar to ketoconazole. The dosing should be adjusted by the doctor.

While there are changes in drug levels in the blood with combined use of sildenafil and macitentan, the differences do not appear to be clinically important.

Macitentan does not appear to alter the effect of warfarin (Coumadin).

Patients should discuss with their physician what medications (including over the counter and herbal preparations) they are currently taking so that any potential or known drug-drug interactions can be avoided.