Janssen CarePath

Opsumit® macitentan tablets 10 mg

Janssen PAH Link for OPSUMIT®

Supports eligible, commercially insured patients until they receive coverage for their prescribed treatment

Janssen PAH Link enables eligible patients to receive OPSUMIT® (macitentan) **at no cost** until they receive coverage or until the end of the current program year if the following program requirements are met.

Janssen PAH Link Program Requirements

- Patient has been prescribed OPSUMIT® for an on-label, FDA-approved indication
- Patient has commercial insurance that has delayed (>5 business days) or denied their treatment
- Patient does not use any state or federal government-funded healthcare program to cover a portion of medication costs, such as Medicare, Medicaid, TRICARE, Department of Defense, or Veterans Administration
- Patient cannot submit the value of the free product as a claim for payment to any third-party payer
- Patient is not eligible if the prior authorization is denied due to missing information on coverage determination form, use for a non-FDA-approved indication, or invalid clinical rationale
- Patient must contact Janssen CarePath if the patient switches from commercial health insurance coverage to a government-funded healthcare program at any point during the program year

- Prescriber must complete and submit a Prescription and Statement of Medical Necessity form to Janssen CarePath to enroll patient in the Janssen PAH Link Program
  - Janssen CarePath cannot accept any information without a Patient Authorization on file. The patient authorization can be found on the Prescription and Statement of Medical Necessity
- Prescriber completes and submits a form of coverage determination (ie, prior authorization or prior authorization with exception) to the commercial insurance
- If coverage is denied, prescriber challenges the coverage denial with an exception, Letter of Medical Necessity, or appeal

How Janssen PAH Link Works

- Program covers the cost of therapy only
- No portion of the value of the free product will count towards the patient's applicable out-of-pocket cost-sharing obligations
- Program year runs January 1 – December 31
- Janssen CarePath reserves the right to cancel or modify Janssen PAH Link at any time

Getting started with Janssen PAH Link

Complete the Prescription and Statement of Medical Necessity form and fax to Janssen CarePath at 866-279-0669.

Participating prescribers authorize Janssen CarePath to:

- Conduct a benefits investigation and confirm prior authorization requirements
- Provide prior authorization form assistance and status monitoring, including the exceptions and appeals processes
- Coordinate shipment of OPSUMIT® from the program Specialty Pharmacy to eligible patients at no charge until they have coverage or until the end of the current program year
- Support the transition of patients to commercial product if a favorable coverage determination is made within 90 days of the PA submission
- Conduct verification of insurance coverage annually for patients enrolled in the program and anytime for patients who have coverage change throughout the program year to confirm eligibility criteria are met for continued participation.

Please see full Prescribing Information, including BOXED WARNING, and Medication Guide for OPSUMIT®. Provide the Medication Guide to your patients and encourage discussion.

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INDICATION

OPSUMIT® is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to reduce the risks of disease progression and hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

IMPORTANT SAFETY INFORMATION

BOXED WARNING: EMBRYO-FETAL TOXICITY

- **Do not administer OPSUMIT® to a pregnant female because it may cause fetal harm.**
- **Females of reproductive potential: Exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment. Prevent pregnancy during treatment and for one month after stopping treatment by using acceptable methods of contraception.**
- **For all female patients, OPSUMIT® is available only through a restricted program called the OPSUMIT® Risk Evaluation and Mitigation Strategy (REMS).**

CONTRAINDICATIONS

Pregnancy: OPSUMIT® may cause fetal harm when administered to a pregnant woman. OPSUMIT® is contraindicated in females who are pregnant. If OPSUMIT® is used during pregnancy, advise the patient of the potential risk to a fetus.

Hypersensitivity: OPSUMIT® is contraindicated in patients with a history of a hypersensitivity reaction to macitentan or any component of the product.

WARNINGS AND PRECAUTIONS

Embryo-fetal Toxicity and OPSUMIT® REMS Program

Due to the risk of embryo-fetal toxicity, OPSUMIT® is available for females only through a restricted program called the OPSUMIT® REMS Program. For females of reproductive potential, exclude pregnancy prior to initiation of therapy, ensure use of acceptable contraceptive methods, and obtain monthly pregnancy tests.

Notable requirements of the OPSUMIT® REMS Program include:

- Prescribers must be certified with the program by enrolling and completing training.
- All females, regardless of reproductive potential, must enroll in the OPSUMIT® REMS Program prior to initiating OPSUMIT®. Male patients are not enrolled in the REMS.
- Females of reproductive potential must comply with the pregnancy testing and contraception requirements.
- Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive OPSUMIT®.

Hepatotoxicity

- ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. The incidence of elevated aminotransferases in the SERAPHIN study >3 x ULN was 3.4% for OPSUMIT® vs 4.5% for placebo, and >8 x ULN was 2.1% vs 0.4%, respectively. Discontinuations for hepatic adverse events were 3.3% for OPSUMIT® vs 1.6% for placebo.
- Obtain liver enzyme tests prior to initiation of OPSUMIT® and repeat during treatment as clinically indicated.
- Advise patients to report symptoms suggesting hepatic injury (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching).
- If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or by clinical symptoms of hepatotoxicity, discontinue OPSUMIT®. Consider re-initiation of OPSUMIT® when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity.

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IMPORTANT SAFETY INFORMATION (continued)

Fluid Retention

- Peripheral edema and fluid retention are known consequences of PAH and ERAs. In the pivotal PAH study SERAPHIN, edema was reported in 21.9% of the OPSUMIT® group vs 20.5% for placebo.
- Patients with underlying left ventricular dysfunction may be at particular risk for developing significant fluid retention after initiation of ERA treatment. In a small study of pulmonary hypertension due to left ventricular dysfunction, more patients in the OPSUMIT® group developed significant fluid retention and had more hospitalizations due to worsening heart failure compared to placebo. Postmarketing cases of edema and fluid retention occurring within weeks of starting OPSUMIT®, some requiring intervention with a diuretic or hospitalization for decompensated heart failure, have been reported.
- Monitor for signs of fluid retention after OPSUMIT® initiation. If clinically significant fluid retention develops, evaluate the patient to determine the cause and the possible need to discontinue OPSUMIT®.

Hemoglobin Decrease

- Decreases in hemoglobin concentration and hematocrit have occurred following administration of other ERAs and in clinical studies with OPSUMIT®. These decreases occurred early and stabilized thereafter.
- In the SERAPHIN study, OPSUMIT® caused a mean decrease in hemoglobin (from baseline to 18 months) of about 1.0 g/dL vs no change in the placebo group. A decrease in hemoglobin to below 10.0 g/dL was reported in 8.7% of the OPSUMIT® group vs 3.4% for placebo. Decreases in hemoglobin seldom require transfusion.
- Initiation of OPSUMIT® is not recommended in patients with severe anemia. Measure hemoglobin prior to initiation of treatment and repeat during treatment as clinically indicated.

Pulmonary Edema with Pulmonary Veno-occlusive Disease (PVOD)

Should signs of pulmonary edema occur, consider the possibility of associated PVOD. If confirmed, discontinue OPSUMIT®.

Decreased Sperm Counts

OPSUMIT®, like other ERAs, may have an adverse effect on spermatogenesis. Counsel men about potential effects on fertility.

ADVERSE REACTIONS

Most common adverse reactions (more frequent than placebo by ≥3%) were anemia (13% vs 3%), nasopharyngitis/pharyngitis (20% vs 13%), bronchitis (12% vs 6%), headache (14% vs 9%), influenza (6% vs 2%), and urinary tract infection (9% vs 6%).

DRUG INTERACTIONS

- Strong inducers of CYP3A4 such as rifampin significantly reduce macitentan exposure. Concomitant use of OPSUMIT® with strong CYP3A4 inducers should be avoided.
- Strong inhibitors of CYP3A4 like ketoconazole approximately double macitentan exposure. Many HIV drugs like ritonavir are strong inhibitors of CYP3A4. Avoid concomitant use of OPSUMIT® with strong CYP3A4 inhibitors. Use other PAH treatment options when strong CYP3A4 inhibitors are needed as part of HIV treatment.
- Moderate dual inhibitors of CYP3A4 and CYP2C9 such as fluconazole and amiodarone are predicted to increase macitentan exposure. Avoid concomitant use of OPSUMIT® with moderate dual inhibitors of CYP3A4 and CYP2C9.
- Concomitant treatment of both a moderate CYP3A4 inhibitor and moderate CYP2C9 inhibitor with OPSUMIT® should also be avoided.

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