

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **OPSYNVI**[®]

Macitentan and Tadalafil Film-Coated Tablets

Read this carefully before you start taking **OPSYNVI**[®] and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **OPSYNVI**[®].

What is OPSYNVI[®] used for?

OPSYNVI[®] is used in adults to treat certain types of a condition called pulmonary arterial hypertension (PAH), which is high blood pressure in the blood vessels leading to your lungs. **OPSYNVI**[®] can be taken on its own, or with other PAH medications as prescribed by your healthcare professional.

How does OPSYNVI[®] work?

OPSYNVI[®] is a tablet that contains 2 different medicines called macitentan and tadalafil. The two medicines work together to widen the blood vessels leading to your lungs, which makes it easier for your heart to pump blood through them. This lowers high blood pressure in-your lungs and lets your heart pump blood better.

OPSYNVI[®] may lower the chance of your disease getting worse.

What are the ingredients in OPSYNVI[®]?

Medicinal ingredients: macitentan and tadalafil.

Non-medicinal ingredients: hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, low-substituted hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, polysorbate 80, povidone K30, sodium lauryl sulfate, sodium starch glycolate Type A, talc, titanium dioxide, and triacetin

OPSYNVI[®] comes in the following dosage forms:

Tablets; 10 mg of macitentan and 40 mg of tadalafil. The film-coated tablets are oblong, white to almost white in color, and debossed with “MT” on one side and “1040” on the other side.

Do not use OPSYNVI[®] if:

- you are allergic to macitentan or tadalafil or to any of the other ingredients of **OPSYNVI**[®].
- you are pregnant, think you may be pregnant, plan to become pregnant, or could become pregnant because you are not using reliable birth control. **OPSYNVI**[®] can cause serious birth defects if taken during pregnancy.

- you are breastfeeding, or plan to breastfeed. It is not known if OPSYNVI® can pass through your breast milk and harm your baby.
- you are taking any medicines that contain nitrates in any form (oral, under the tongue, skin patch, or by inhalation); if you are unsure, ask your healthcare professional.
- you have ever had a type of eye disease called Non-Arteritic Anterior Ischaemic Optic Neuropathy (NAION), which causes a sudden decrease or loss of vision in one or both eyes.
- you are taking any medicines that are called “guanylate cyclase stimulators” such as riociguat; if you are unsure, ask your healthcare professional.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take OPSYNVI®. Talk about any health conditions or problems you may have, including if you:

- have pulmonary veno-occlusive disease (PVOD), a condition where your blood vessels are blocked.
- have heart disease or previously had a heart attack.
- have a condition called aortic stenosis (narrowing of the aortic heart valve).
- have had a stroke.
- have low blood pressure or uncontrolled high blood pressure.
- have liver problems.
- have kidney problems. OPSYNVI® may lead to a reduction in blood pressure and decrease in haemoglobin in patients with kidney problems.
- are on dialysis.
- have sickle cell anemia (an abnormality of red blood cells), multiple myeloma (cancer of the bone marrow), or leukemia (cancer of the blood cells).
- have a deformed penis or are at risk of developing a condition called “priapism”.
- are at risk of developing an eye disorder such as retinitis pigmentosa (a rare genetic eye disease).
- have one of the following rare hereditary diseases, because OPSYNVI® contains lactose:
 - galactose intolerance;
 - Lapp lactase deficiency;
 - glucose-galactose malabsorption.

Other warnings you should know about:

Chest Pain: If you feel chest pain after taking OPSYNVI®, do NOT take nitroglycerin or nitrates. Instead, get immediate medical help.

Sudden Loss of Hearing or Vision: Some patients using medicines like OPSYNVI® have experienced a sudden decrease or loss of hearing or a sudden loss of vision in one or both eyes. Get immediate medical help if either of these happen to you.

Pregnancy: OPSYNVI® may harm your unborn baby. You should not become pregnant while taking OPSYNVI® and for at least 1 month after stopping your treatment. Females who are able to get pregnant must take a pregnancy test before starting OPSYNVI®. Your healthcare professional may recommend that you take a pregnancy test every month during your treatment to allow the early detection of pregnancy.

Talk with your doctor or gynecologist (a doctor who specializes in female reproduction) to find out about how to prevent pregnancy. Do not have unprotected sex. Tell your healthcare professional right away if you have unprotected sex or if you think your birth control has failed.

If you become pregnant, tell your healthcare professional **right away**. Stop taking OPSYNVI®.

Fertility in Men: Decreases in sperm count have been observed with OPSYNVI® and related drugs. Speak with your healthcare professional if you plan on fathering a child.

Driving and Operating Machinery: Give yourself time after taking OPSYNVI® to see how you feel before driving or using machinery.

Tests during Treatment: Some patients taking macitentan were found to have abnormal liver function values (increase in liver enzymes) and some patients developed anemia (reduction in red blood cells). Because these findings may not cause symptoms you can feel or observe yourself, your healthcare professional will do regular blood tests to assess any changes in your liver function and hemoglobin level.

Liver Function:

This blood test will be done:

- prior to initiation of OPSYNVI®;
- every month during the first year of treatment or more frequently, if needed.

If you develop abnormal liver function, your healthcare professional may decide to stop treatment with OPSYNVI®.

When your blood test results for liver function return to normal, your healthcare professional may decide to restart treatment with OPSYNVI®.

Anemia:

This blood test will be done:

- prior to initiation of OPSYNVI®;
- at one month after treatment start and as decided by your healthcare professional thereafter.

If you develop anemia, your healthcare professional may decide to perform further tests to investigate the cause.

Your regular blood tests, both for liver function and anemia, are an important part of your treatment.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Do NOT take OPSYNVI® with:

- guanylate cyclase stimulators, medicines that are also used to treat high blood pressure in the lungs (e.g., riociguat).
- medicines that contain nitrates in any form (oral, under the tongue, skin patch, or by inhalation).

If you are unsure, ask your healthcare professional.

The following may interact with OPSYNVI®:

- rifampicin, clarithromycin, ciprofloxacin, erythromycin (antibiotics used to treat infection).
- phenytoin, carbamazepine, phenobarbital (medicines used to treat seizures).
- ritonavir, saquinavir (used to treat HIV infections).
- nefazodone (used to treat depression).
- ketoconazole, itraconazole, fluconazole, miconazole, voriconazole (medicines used against fungal infections).
- amiodarone (medicine used to control heartbeat).
- cyclosporine (used to prevent organ rejection after transplant).
- bosentan (another treatment for pulmonary arterial hypertension).
- theophylline (medicine used to treat lung disease).
- alpha blockers such as doxazosin (medicines used to treat high blood pressure).
- diltiazem, verapamil (used to treat high blood pressure of specific heart problems).
- tablets for erectile dysfunction such as tadalafil.
- grapefruit juice.
- alcohol.

How to take OPSYNVI®:

- Always take OPSYNVI® exactly as your healthcare professional has told you to. Check with your healthcare professional if you are not sure. Do not stop taking OPSYNVI® unless your healthcare professional tells you to.
- Swallow the tablets whole. Do NOT break, crush, or chew the tablets.
- OPSYNVI® can be taken with or without food.
- Try to take OPSYNVI® at the same time each day.

Usual dose:

The recommended dose of OPSYNVI® is 1 tablet, once a day.

Overdose:

If you think you, or a person you are caring for, have taken too much OPSYNVI®, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

If you miss a dose of OPSYNVI®, take your tablet as soon as you remember. Otherwise, skip the missed dose and take the next dose at your regular time. Do not take 2 doses on the same day to make up for a missed dose.

What are possible side effects from using OPSYNVI®?

These are not all the possible side effects you may have when taking OPSYNVI®. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Back pain;
- Blurred vision;
- Constipation;
- Diarrhea;
- Eye pain;
- Fainting;
- Fast heartbeat;
- Fatigue;
- Flu (influenza);
- Flushing of the face;
- Headache;
- Heartbeat feels fast or uneven (palpitations);
- Increased or abnormal menstrual bleeding;
- Indigestion;
- Infected nose, sinuses or throat (cold);
- Migraine;
- Muscle pain, spasms or stiffness;
- Nausea or vomiting;
- Nose bleeds;
- Pain in the arms or legs;
- Rash;
- Sore throat (pharyngitis);
- Stomach discomfort;
- Stomach pain;
- Stuffy or congested nose (nasopharyngitis);
- Upset stomach or heartburn.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Anemia (decreased number of red blood cells): fatigue, loss of energy, irregular heartbeats, pale complexion, shortness of breath, weakness	✓		
Bronchitis (irritation of the airways): coughing, mucus production, fatigue, shortness of breath, slight fever and chills, chest discomfort	✓		
Edema: unusual swelling of the arms, hands, legs, feet and ankles, face or airway passages	✓		
COMMON			
Angina (chest pain): discomfort in the shoulder, arm, back, throat, jaw or teeth, shortness of breath, pain or pressure in the chest			✓
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)	✓		
Urinary tract infection (infection in urinary system including kidneys, ureters, bladder and urethra): pain or burning sensation while urinating, frequent urination, blood in urine, pain in the pelvis, strong smelling urine, cloudy urine	✓		

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
RARE			
Liver problems: yellowing of your skin and eyes (jaundice), right upper stomach area pain or swelling, fever, nausea or vomiting, unusual dark urine, unusual tiredness		✓	
UNKNOWN FREQUENCY			
Allergic reaction: fever, skin rash, hives, itching, swelling, shortness of breath, wheezing, runny nose, itchy, watery eyes, difficulty swallowing or breathing			✓
Priapism (painful erection of the penis lasting longer than 4 hours in duration)			✓
Sudden decrease or loss of hearing			✓
Sudden decrease or loss of vision in one or both eyes			✓
Temporary memory loss (transient global amnesia)		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store OPSYNVI® tablets at room temperature between 15°C and 30°C in the original package.

Keep out of reach and sight of children.

If you want more information about OPSYNVI®:

- Talk to your healthcare professional.
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<https://www.janssen.com/canada/>), or by calling 1-800-567-3331 or 1-800-387-8781.

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