

MEDICATION GUIDE
OPSYNVI® (op-SIN-vee)
(macitentan and tadalafil)
tablets

Read this Medication Guide for OPSYNVI before you start taking OPSYNVI and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about OPSYNVI?

- **Serious birth defects.**

OPSYNVI can cause serious birth defects if taken during pregnancy.

- **Females must not be pregnant when they start taking OPSYNVI or become pregnant during treatment with OPSYNVI or for 1 month after stopping treatment with OPSYNVI.**

- Females who are able to get pregnant must have a negative pregnancy test before beginning treatment with OPSYNVI, each month during treatment with OPSYNVI and 1 month after stopping OPSYNVI.

Talk to your healthcare provider about your menstrual cycle. Your healthcare provider will decide when to do the pregnancy test and will order a pregnancy test for you depending on your menstrual cycle.

- Females who are able to get pregnant are females who:

- have entered puberty, even if they have not started their menstrual period, **and**
- have a uterus, **and**
- have not gone through menopause. Menopause means that you have not had a menstrual period for at least 12 months for natural reasons, or that you have had your ovaries removed.

- Females who are not able to get pregnant are females who:

- have not yet entered puberty, **or**
- do not have a uterus, **or**
- have gone through menopause. Menopause means that you have not had a menstrual period for at least 12 months for natural reasons, or that you have had your ovaries removed, **or**
- are infertile for other medical reasons and this infertility is permanent and cannot be reversed.

Females who are able to get pregnant must use 2 acceptable forms of birth control during treatment with OPSYNVI, and for 1 month after stopping OPSYNVI because the medicine may still be in the body.

- If you have had a tubal sterilization, have a progesterone implant, or have an IUD (intrauterine device), these methods can be used without another form of birth control.
- Talk with your healthcare provider or gynecologist (a doctor who specializes in female reproduction) to find out about options for acceptable birth control that you may use to prevent pregnancy during treatment with OPSYNVI.
- If you decide that you want to change the form of birth control that you use, talk with your healthcare provider or gynecologist to be sure that you choose another acceptable form of birth control.

See the chart below for Acceptable Birth Control Options during treatment with OPSYNVI.

Acceptable birth control options

Option 1 One method from this list:	OR	Option 2 One method from this list:	OR	Option 3 One method from this list:	OR	Option 4 One method from this list:
Standard intrauterine device (Copper T 380A IUD) Intrauterine system (LNg 20 IUS: progesterone IUS) Progesterone implant Tubal sterilization		Estrogen and progesterone oral contraceptives ("the pill") Estrogen and progesterone transdermal patch Vaginal ring Progesterone injection		Diaphragm with spermicide Cervical cap with spermicide PLUS One method from this list: Male condom		Partner's vasectomy PLUS One method from this list: Male condom Diaphragm with spermicide Cervical cap with spermicide Estrogen and progesterone oral contraceptives ("the pill") Estrogen and progesterone transdermal patch Vaginal ring Progesterone injection
		PLUS One method from this list: Male condom Diaphragm with spermicide Cervical cap with spermicide				

- **Do not have unprotected sex.** Talk to your healthcare provider or pharmacist right away if you have unprotected sex or if you think your birth control has failed. Your healthcare provider may talk with you about using emergency birth control.
- **Tell your healthcare provider right away if you miss a menstrual period or think you may be pregnant.**

Females can only receive OPSYNVI through a restricted program called the Macitentan-Containing Products Risk Evaluation and Mitigation Strategy (REMS). If you are a female who can get pregnant, you must talk to your healthcare provider, understand the benefits and risks of OPSYNVI, and agree to all of the instructions in the Macitentan-Containing Products REMS.

Males can receive OPSYNVI without taking part in the Macitentan-Containing Products REMS.

See **"What are the possible side effects of OPSYNVI?"** for more information about side effects.

What is OPSYNVI?

- OPSYNVI is a prescription medicine that contains 2 medicines called macitentan and tadalafil. OPSYNVI is used for long-term treatment of adults with pulmonary arterial hypertension (PAH), which is high blood pressure in the arteries of your lungs.
- It is not known if OPSYNVI is safe and effective in children.

Who should not take OPSYNVI?

Do not take OPSYNVI if you:

- are pregnant, plan to become pregnant, or become pregnant during treatment with OPSYNVI. OPSYNVI can cause serious birth defects (see “What is the most important information I should know about OPSYNVI?”)
- are allergic to macitentan, tadalafil, or any of the ingredients in OPSYNVI. See the end of this Medication Guide for a complete list of ingredients in OPSYNVI.
- take any medicines called nitrates
- take any medicines called guanylate cyclase (GC) stimulators

Before taking OPSYNVI, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- have low blood pressure
- have anemia
- have heart problems including heart attack or heart failure
- have pulmonary veno-occlusive disease (PVOD)
- have any eye problems, including NAION or an inherited eye disorder called retinitis pigmentosa
- have hearing problems such as ringing in the ears, dizziness, or loss of hearing
- have a deformed penis shape or Peyronie’s disease or have blood cell problems such as sickle cell anemia, multiple myeloma, or leukemia. These conditions increase your risk of getting a prolonged erection.
- have kidney problems or get dialysis
- are pregnant or plan to become pregnant during OPSYNVI treatment. OPSYNVI can cause serious birth defects. See “What is the most important information I should know about OPSYNVI?”
- are breastfeeding or plan to breast feed. It is not known if OPSYNVI passes into your breastmilk. **Do not** breastfeed during treatment with OPSYNVI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking OPSYNVI with other medicines may affect the way OPSYNVI and the other medicines work, and may increase your risk of side effects. **Do not** start any new medicine until you check with your healthcare provider.

Especially tell your healthcare provider if you take:

- nitrate medicines
- HIV medicines
- antifungal medicines
- antiseizure medicines
- medicines used to treat infection
- erectile dysfunction medicines
- blood pressure medicines
- medicines used to treat PAH or heart problems

Ask your healthcare provider or pharmacist if you are not sure if your medicine is one that is listed above. Know the medicines you take. Keep a list and show it to your healthcare provider or pharmacist when you get a new medicine.

How should I take OPSYNVI?

OPSYNVI will be mailed to you by a specialty pharmacy. Your healthcare provider will give you complete details.

- Take OPSYNVI exactly as your healthcare provider tells you to take it. **Do not** stop taking OPSYNVI unless your healthcare provider tells you.
- Take OPSYNVI with or without food.
- **Do not** cut, crush, or chew OPSYNVI tablets.
- If you take too much OPSYNVI, call your healthcare provider or go to the nearest hospital emergency room right away.
- If you miss a dose of OPSYNVI, take it as soon as you remember that day. Take the next dose at your regular time. **Do not** take 2 doses at the same time to make up for a missed dose.

What should I avoid while taking OPSYNVI?

- **Do not** have more than 4 alcohol-containing drinks in a short period of time during treatment with OPSYNVI. Drinking too much alcohol can increase your chances of getting low blood pressure, increased heart rate, dizziness, and headache.

What are the possible side effects of OPSYNVI?

OPSYNVI can cause serious side effects, including:

- **Serious birth defects.** See “What is the most important information I should know about OPSYNVI?”
- **Liver problems.** OPSYNVI can cause liver problems. Your healthcare provider should do blood tests to check your liver before you start taking OPSYNVI. Tell your healthcare provider if you have any of the following symptoms of liver problems during treatment with OPSYNVI.
 - nausea or vomiting
 - pain in the upper right stomach
 - tiredness
 - loss of appetite
 - yellowing of your skin or whites of your eyes
 - dark urine
 - fever
 - itching
- **Decreased blood pressure (hypotension).** OPSYNVI can cause low blood pressure that lasts for a short time.
- **Low red blood cell levels (anemia) can occur with OPSYNVI treatment, usually during the first weeks after starting therapy.** Your healthcare provider will do blood tests to check your red blood cells before starting and as needed during treatment with OPSYNVI.
- **Vision loss.** OPSYNVI can cause decreased eyesight or permanent loss of vision in 1 or both eyes, which could be a sign of NAION. There is an increased risk of NAION in people who have already had NAION in 1 eye. If you notice a sudden decrease or loss of vision in 1 or both eyes, contact your healthcare provider right away.
- **Hearing problems.** Sudden decrease or loss of hearing, sometimes with ringing in the ears and dizziness, can happen during treatment with OPSYNVI. If you notice a sudden decrease or loss of hearing, contact your healthcare provider right away.
- **Fluid retention.** Fluid retention can happen within weeks after starting OPSYNVI and could lead to hospitalization. Tell your healthcare provider right away if you have any unusual weight gain, trouble breathing, or swelling of your ankles or legs. Your healthcare provider will look for the cause of any fluid retention and may stop treatment with OPSYNVI.
- **Decreased sperm count.** OPSYNVI can cause decreased sperm counts in males and may affect the ability to father a child. Tell your healthcare provider if being able to have children is important to you.
- **Prolonged erection.** Erections that last more than 4 hours, with or without pain, can happen during treatment with OPSYNVI. Painful erections (priapism) can cause permanent damage to the penis if not treated right away. Tell your healthcare provider right away if you have an erection that lasts longer than 4 hours, with or without pain.

The most common side effects of OPSYNVI include:

- too much fluid in your body (fluid retention) and swelling caused by too much fluid (edema)
- anemia
- headache, including migraine headache

These are not all the possible side effects of OPSYNVI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store OPSYNVI?

- Store OPSYNVI tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- Store OPSYNVI in the package that it comes in to protect from moisture.
- OPSYNVI contains a desiccant to help keep the tablets dry. **Do not** discard or eat the desiccant.
- OPSYNVI bottles have a child-resistant cap.
- **Keep OPSYNVI and all medicines out of the reach of children.**

General information about the safe and effective use of OPSYNVI.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use OPSYNVI for a condition for which it was not prescribed. Do not give OPSYNVI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about OPSYNVI that is written for health professionals.

What are the ingredients in OPSYNVI?

Active ingredients: macitentan and tadalafil

Inactive ingredients: tablet core: hydroxypropyl cellulose, hydroxypropyl cellulose (low substituted), lactose monohydrate, magnesium stearate, microcrystalline cellulose, polysorbate 80, povidone, sodium starch glycolate, sodium lauryl sulfate.

10 mg/20 mg film-coating: hydroxypropyl methylcellulose, iron oxide red, iron oxide yellow, lactose monohydrate, talc, titanium dioxide, triacetin. **10 mg/40 mg film-coating:** hydroxypropyl methylcellulose, lactose monohydrate, talc, titanium dioxide, triacetin.

Manufactured for:

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For patent information: www.janssenpatents.com

For more information, call 1-800-526-7736 (1-800-JANSSEN), or visit www.OPSYNVI.com.

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