Riociguat (Adempas)
Updated June 2023

Riociguat is an oral medication that treats pulmonary arterial hypertension (PAH), also known as Group 1 pulmonary hypertension. The therapy is intended to improve exercise ability.

Riociguat also is approved to treat inoperable or recurrent/persistent (after pulmonary thromboendarterectomy) chronic thromboembolic pulmonary hypertension (CTEPH). This therapy aims to improve exercise ability and functional class.

The Food and Drug Administration approved Adempas in 2013 to treat PAH and CTEPH.

How riociguat works
Riociguat is a drug known as a cyclic guanosine monophosphate (cyclic GMP) stimulator. Cyclic CMP, produced in the lungs and other parts of the body in response to nitric oxide, causes arteries to relax and widen. Riociguat leads to further relaxation or widening of blood vessels in the lungs.

When arteries in the lungs relax and widen, the pulmonary blood pressure decreases, which reduces stress on the right heart and helps improve heart function. Low lung pressures and improved right heart function help patients with PAH and CTEPH be more active, based on data from clinical studies.

Dosage
Riociguat is taken orally three times a day, about six to eight hours apart (morning, midday and evening.) It can be taken with or without food.

Patients can crush tablets and mixed the with water or soft food (such as applesauce) immediately before ingesting.

Tablets are round and available in the following strengths:

- 5 mg (white).
- 1 mg (yellow-orange).
- 5mg (peach).
- 2 mg (orange).
- 5 mg (red).

Medication typically starts at 0.5 mg or 1 mg three times daily and is increased by 0.5 mg every two to four weeks if there are no signs of low blood pressure. The maximum dose is 2.5 mg taken three times a day. Your physician may lower the dose if your blood pressure decreases significantly.
Obtaining riociguat

Riociguat is available to women only through a restricted distribution program because of serious birth defect risks. The distribution program, called Risk Evaluation and Mitigation Strategy (REMS) for Adempas, is required by the FDA. All women, regardless of reproductive potential, must enroll in the Adempas REMS before starting therapy. Women of reproductive potential must comply with monthly pregnancy testing and contraception requirements.

Men don’t have to participate in the REMS program to receive riociguat.

Health care providers must enroll in the REMS program to prescribe this therapy. Riociguat isn’t sold at local pharmacies. The drug is dispensed monthly by mail-order specialty pharmacies determined by patients’ insurance companies. The specialty pharmacies are Accredo, CVS Specialty and Kaiser Permanente Specialty Pharmacy.

Insurance coverage

Patients must obtain insurance approval before starting therapy. Most health insurance plans will pay part of the cost of this medication. However, some patients will still have high out-of-pocket costs. Ask your insurance company about specific copay or out-of-pocket costs. Depending on your insurance plan, you might be eligible for assistance from the drug manufacturing company or copay assistance from a non-profit charitable organization. See the list or call 301-565-3004.

Common side effects

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

- Headache.
- Upset stomach.
- Dizziness.
- Nausea.
- Diarrhea.
- Low blood pressure.
- Vomiting.
- Anemia.
- Gastroesophageal reflux (heartburn).
- Constipation.

Other potential side effects include:

- Palpitations.
- Nasal congestion.
- Nosebleeds.
- Difficulty swallowing.
- Abdominal swelling.
- Swelling in feet.
- Low blood pressure throughout the body (riociguat relaxes blood vessels throughout the body).

Patients who take blood pressure medicine should use caution, as well as those whose medications might interact with riociguat, and those with low blood. Patients with dehydration, left heart disease and abnormalities of the nervous system also should take caution.

As with all medicines, notify your doctor immediately if you experience serious side effects or symptoms that might be caused by riociguat.

No differences in side effects have been reported between men and women.

If you experience any symptoms mentioned above, promptly notify your physician.

**Monitoring side effects**

Regular blood work for side effects isn’t required.

Blood pressure monitoring when you start riociguat is necessary. It should be checked about every two weeks to help your doctor decide the best dose of riociguat for you.

**Who shouldn’t take riociguat**

**Pregnant women/nursing mothers:** Riociguat can cause serious birth defects if taken during pregnancy. Women must not be pregnant when starting riociguat or become pregnant during treatment. Two forms of contraception are recommended to prevent pregnancy when taking riociguat. One option is surgical treatment to prevent pregnancy, such as tubal ligation. Another is a copper T380A or LNG 20 intrauterine device.

Women who can become pregnant must have regular testing to ensure they aren’t pregnant or become pregnant during therapy or within a month of stopping riociguat. It’s not known whether riociguat passes into breast milk. Nursing mothers shouldn’t use this drug.

**People with severe liver disease.**

**People with severe kidney dysfunction and those on dialysis.**

**Children:** The safety and effectiveness of riociguat for pediatric patients hasn’t been established.

**Warning:** Riociguat can cause fluid to build up in the lungs of people with pulmonary veno-occlusive disease. If that occurs, patients might need to stop taking riociguat.

**Drug interactions**

Riociguat shouldn’t be used in combination with nitrates or nitric oxide donors; phosphodiesterase inhibitors such
as sildenafil, tadalafil or vardenafil; or non-specific phosphodiesterase inhibitors such as dipyrimadole or theophylline. Simultaneous use can result in dangerous blood pressure drops.

Riociguat interacts with certain liver enzymes. Some medicines like ketoconazole, itraconazole or protease inhibitors (prescribed for human immunodeficiency virus, HIV or AIDS) can interact with those enzymes and increase riociguat levels. People taking these medicines can have more side effects, especially low blood pressure, and might need different doses of riociguat and/or more careful blood pressure monitoring.

Riociguat doesn’t affect warfarin levels.

Although a slight drug interaction has been demonstrated with riociguat and bosentan, dose adjustments aren’t recommended for either drug.

Antacids containing magnesium or aluminum hydroxide (such as Maalox or Mylanta) can prevent riociguat from being absorbed. Antacids shouldn’t be taken within an hour of taking riociguat.

Patients should discuss with their physician the medications they take, including over-the-counter and herbal preparations, to avoid potential or known drug interactions.

Allergies are possible, but not likely. Talk to your physician if you think you’re having an allergic reaction to treatment.

**Other considerations**

**Smoking:** Smoking can decrease the amount of riociguat in the body. Your doctor might need to adjust your dose. Smoking isn’t recommended for people with PAH.

**Dose interruption:** If you stop taking riociguat for three days or more, your doctor likely will decrease your medicine to the original starting dose, then slowly increase to the maximum dose as tolerated.