

Riociguat (Adempas®)

Issued by PHA's Scientific Leadership Council

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

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WHAT IS RIOCIQUAT?

Riociguat is an oral medication called a soluble guanylate cyclase stimulator approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 patients. The goal of this therapy for PAH is to improve exercise ability, WHO functional class and delay clinical worsening. Riociguat is also approved for patients with WHO Group 4 patients having chronic thromboembolic pulmonary hypertension (CTEPH) that is recurrent/persistent after surgical treatment or inoperable. The goal of this therapy for CTEPH is to improve exercise ability and WHO functional class. Research studies showing the effectiveness of the medication included mostly patients with symptoms that were rated as WHO Functional Class II-III.

Riociguat is marketed as Adempas® for PAH and CTEPH and was approved by the United States Food and Drug Administration (FDA) in October 2013.

HOW DOES RIOCIQUAT WORK?

Cyclic guanosine monophosphate (cyclic GMP) is a substance produced in the lungs and other parts of the body by an enzyme called guanylate cyclase in response to nitric oxide. Cyclic GMP causes the blood vessels (arteries) to relax and widen. Riociguat increases the activity of guanylate cyclase in 2 ways, so that more cyclic GMP is available for the blood vessels inside the lungs. This leads to relaxation, or widening, of those vessels. Relaxing and widening of the blood vessels in the lungs decreases the pulmonary blood pressure to the heart and improves its function. This reduces blood pressure in the lungs, which generally results in the ability to be more active. Research studies have verified this improvement.

HOW IS RIOCIQUAT SUPPLIED?

Adempas® is available as a round tablet in the following doses: white 0.5 mg pill, yellow 1 mg pill, yellow-orange 1.5 mg pill, a peach colored 2 mg pill and a red-orange 2.5 mg pill. The maximum dose is 2.5 mg taken three times daily. Medication would typically start at 1 mg three times daily and increased by 0.5 mg every 2-4 weeks as long as there are no signs of low blood pressure. Your physician may lower the dose if your blood pressure goes down significantly.

HOW CAN A PATIENT OBTAIN RIOCIQUAT?

Riociguat must be prescribed by a physician, and insurance approval must be obtained prior to starting therapy. It is carried by specialty pharmacies, including Accredo Health Inc., CVS Caremark and Walgreen Specialty. Female patients prescribed riociguat must also be enrolled by your doctor in a program to carefully monitor for possible pregnancy. (See special populations section below).

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WILL INSURANCE PAY FOR RIOCIQUAT?

It is expected that most health insurance plans will pay part of the cost of this medication. However, some plans still leave patients with a high out-of-pocket responsibility.

Depending on your insurance type, you may be eligible for assistance from the company that manufactures your therapy or from a non-profit charitable assistance organization. For more information visit www.PHAssociation.org/Help or call 301-565-3004.

WHAT ARE THE FREQUENT SIDE EFFECTS OF RIOCIQUAT?

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

- Headache
- Upset stomach
- Dizziness
- Nausea
- Diarrhea
- Low blood pressure
- Vomiting
- Anemia
- Gastroesophageal reflux (Known as GERD or heartburn)
- Constipation

Other side effects include:

- Palpitations
- Nasal congestion
- Nosebleeds
- Difficulty swallowing
- Abdominal swelling
- Edema (Swelling in feet)

A reduction in blood pressure throughout the body may occur because riociguat relaxes blood vessels (arteries) throughout the body. Caution must be used in patients taking blood pressure medicines, medicines that might interact with riociguat, or if they have low blood pressure. Caution is also needed in patients with dehydration, left-sided heart diseases and certain abnormalities of the body's nervous system function.

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As for all medicines, notify your doctor immediately of serious side effects or symptoms that might be due to riociguat.

HOW ARE SIDE EFFECTS OF RIOCIQUAT MONITORED?

No regular blood work for side effects is required.

Blood pressure monitoring when you start riociguat is necessary. It should be checked about every 2 weeks to help your doctor decide the best dose riociguat to take.

If you experience any of the symptoms mentioned in the previous section, you should promptly notify your physician.

WHAT ARE CONSIDERATIONS FOR USE OF RIOCIQUAT IN SPECIAL POPULATIONS?

Riociguat can cause serious birth defects if taken during pregnancy. Females must not be pregnant when starting riociguat or become pregnant during treatment. For this reason, females who can become pregnant must have regular testing to insure they are not pregnant, or become pregnant during therapy or within one month of stopping riociguat. It is recommended that two acceptable means of birth control be used during these times. It is not known if riociguat passes into breast milk. Nursing mothers should not use this drug.

Patients with severe liver disease should not take riociguat.

Patients with severe kidney dysfunction or if they are on dialysis should not take riociguat.

The safety and effectiveness of riociguat in pediatric patients has not been established.

Riociguat may cause buildup of fluid in the lungs in patients with: pulmonary veno-occlusive disease. If this occurs, patients may need to stop taking riociguat.

COULD A PATIENT BE ALLERGIC TO RIOCIQUAT?

This is possible, but not likely.

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

Riociguat should not 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.

Riociguat interacts with liver enzymes called CYP3A, P-gp and BCRP in the liver. Some medicines like ketoconazole, itraconazole or medicines called protease inhibitors (which are prescribed for some patients with human immunodeficiency virus, HIV or AIDS) among others can also interact with these enzymes and cause levels of riociguat to be higher. Patients taking these medicines can have more side effects especially low blood pressure and may need different doses of riociguat and/or more careful monitoring of blood pressure when taking these medicines.

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Riociguat does not affect warfarin levels.

Although a slight drug interaction has been demonstrated with riociguat and bosentan, dose adjustments are presently not recommended for either drug.

Antacids containing magnesium or aluminum hydroxide (such as Maalox® or Mylanta®) can keep riociguat from being absorbed once taken. Antacids like this should not be taken within an hour of taking riociguat.

MISCELLANEOUS CONSIDERATIONS:

SMOKING AND RIOCIQUAT

Smoking can decrease the amount of riociguat in the body. Adjustments of dosing may be needed during smoking or if you stop smoking while taking riociguat.

DOSE INTERRUPTION

If riociguat is not taken for 3 days or more once you have started taking the medicine, your doctor will likely decrease the dose of medicine to the original starting doses and then slowly increase to the maximum dose as tolerated.

CAN MEN AND WOMEN TAKE RIOCIQUAT?

Yes, studies have evaluated riociguat in both men and women, and no differences in side effects have been reported between genders.