PART III: CONSUMER INFORMATION

PrADEMPAS®

Riociguat Tablets

This leaflet is Part 3 of a three-part "Product Monograph" published when ADEMPAS was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ADEMPAS. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ADEMPAS is indicated to treat adult patients with:

- CTEPH (Chronic Thromboembolic Pulmonary Hypertension) (WHO Group 4).

CTEPH is a disease where high blood pressure occurs in lung vessels (pulmonary arteries) which is caused by fixed blood clots hindering the blood flow. High pulmonary blood pressure in the lung vessels means that the heart needs to work harder to pump blood through the lungs. This causes people to feel tired, dizzy and short of breath.

ADEMPAS is intended for use in patients with CTEPH who cannot be operated (inoperable CTEPH) or in patients with persistent or recurrent high pulmonary blood pressure after surgical treatment.

- PAH (Pulmonary Arterial Hypertension) (WHO Group 1)

PAH is a disease where high blood pressure occurs in lung vessels (pulmonary arteries). In patients with PAH, these arteries get narrower, so the heart has to work harder to pump blood through them. This causes people to feel tired, dizzy and short of breath.

What it does:

CTEPH (WHO Group 4):

ADEMPAS contains riociguat, which is a soluble guanylate cyclase (sGC)-stimulator. It works by dilating the pulmonary arteries (the blood vessels that connect the heart to the lungs), lowering the high blood pressure and making it easier for the heart. This leads to an increase in exercise capacity (will increase a patient's ability to walk further) and an improvement of Functional Class (a World Health Organization measure of symptom severity and impact on daily activities).

PAH (WHO Group 1):

ADEMPAS contains riociguat, which is a soluble guanylate cyclase (sGC)-stimulator. It works by dilating the pulmonary arteries (the blood vessels that connect the heart to the lungs), lowering the high blood pressure and making it easier for the heart. This leads to an increase in exercise capacity (will increase a patient's ability to walk further), an improvement of Functional Class (a World Health Organization measure of symptom severity and impact on daily activities) and delayed clinical worsening in patients with PAH.

When it should not be used:

- if you are hypersensitive (allergic) to ADEMPAS or any other ingredients in the tablet.
- if you are pregnant or planning to become pregnant.
- If you are breast-feeding or plan to breast-feed.
- if you are taking **sildenafil (VIAGRA, REVATIO), tadalafil (CIALIS, ADCIRCA), vardenafil (LEVITRA, STAXYN)**, **nitrates** (medicines used to treat high blood pressure or heart disease) or **nitric oxide donors** (such as amyl nitrite) in any form.
- if you have increased pressure in your pulmonary circulation associated with scarring of the lungs, of unknown cause (idiopathic pulmonary pneumonia).

What the medicinal ingredient is:

Riociguat.

What the nonmedicinal ingredients are:

Cellulose microcrystalline, crospovidone, hypromellose 5cP, lactose monohydrate, magnesium stearate, sodium laurilsulfate. The film-coating is composed of ferric oxide red, ferric oxide yellow, hydroxypropylcellulose, hypromellose 3cP, propylene glycol, titanium dioxide.

What dosage forms it comes in:

Film-coated tablets: 0.5 mg (white), 1 mg (pale yellow), 1.5 mg (yellow-orange), 2 mg (pale orange), 2.5 mg (red-orange).

WARNINGS AND PRECAUTIONS

BEFORE you use ADEMPAS talk to your doctor or pharmacist if you have or have had any of the following conditions:

- if you take PDE-5-inhibitors (such as sildenafil or tadalafil) used to **treat high blood pressure in the pulmonary arteries** (pulmonary arterial hypertension) or **male erectile dysfunction** (such as the above or vardenafil).
- if you feel **short of breath** during treatment with ADEMPAS, this can be caused by a build-up of fluid in the lungs (pulmonary veno-occlusive disease). Talk to your doctor.
- if you have recently experienced serious bleeding from the lung, or if you have undergone interventional treatment to stop **coughing up blood** (bronchial arterial embolization). In these cases the risk of bleeding from the lungs may increase further. Inform your doctor if you take medicines used to **prevent blood clots** (anticoagulants). You will be regularly monitored by your doctor.
- if you have **problems with your heart, circulation** or are on antihypertensive therapy.
- if you take medicines used to **treat fungal infections** (e.g. ketoconazole, itraconazole), or medicines for the **treatment of HIV infection** (e.g. ritonavir).
- if you take **medicines against cancer** called tyrosine kinase inhibitors (e.g. erlotinib, gefitinib) or cyclosporine a medicine used to **prevent rejection of transplanted organs**. In this case your doctor will have to check your blood pressure regularly.
- ADEMPAS is not recommended for patients under 18 years of age, because there is no information on its use in children and adolescents.
- Do not take ADEMPAS during pregnancy. If there is a chance you could become pregnant, use reliable forms of contraception while you are taking ADEMPAS. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking ADEMPAS.
- If you are breast-feeding, ask your doctor or pharmacist for advice before taking ADEMPAS because it might harm your baby. A decision must be made whether to discontinue breast feeding or to stop therapy with ADEMPAS.

If you have the following conditions:

- **low blood pressure** (<95 mm Hg) at the beginning of treatment
- **severe liver problems** (hepatic impairment, Child Pugh C)
- **severe kidney problems** (creatinine clearance <15 mL/min or if you are **on dialysis**)

the use of ADEMPAS is not recommended, as there are no studies on the use of ADEMPAS in patients with these conditions.

INTERACTIONS WITH THIS MEDICATION

Drug-drug interaction:

Drugs that may interact with ADEMPAS include:

- **nitric oxide donors** (such as amyl nitrite)
- **nitrates** (medicines used to treat high blood pressure or heart disease)
- PDE-5-inhibitors, [such as sildenafil (VIAGRA, REVATIO) or tadalafil (CIALIS, ADCIRCA)] medicines used to treat high blood pressure in the pulmonary arteries (pulmonary arterial hypertension) or male erectile dysfunction [such as the above or vardenafil (LEVITRA, STAXYN)]
- medicines used to treat fungal infections (e.g. **ketoconazole, itraconazole**)
- medicine for the treatment of HIV infection (e.g. **ritonavir**)
- **cyclosporine** (medicine used to prevent rejection of transplanted organs)
- **erlotinib (TARCEVA)** or **gefitinib (IRESSA)** (medicines against cancer)
- **granisetron** (medicine used to treat nausea and vomiting)
- **phenytoin** and **carbamazepine** (antiepileptic medicines), **phenobarbitone** (antiepileptic medicine, sedative)
- **quinidine** (antiarrhythmic, antimalarial agent)
- **carvedilol** (for the treatment of heart failure and hypertension)

Drug-herb interaction:

- **St. John´s Wort** (herbal treatment for depression)

Drug-food interaction:

- ADEMPAS contains **lactose**. If you have been told by any doctor that you have an intolerance to some sugars, inform your doctor before taking this medicinal product.

Drug-lifestyle interaction:

If you **smoke**, it is recommended that you stop, as smoking may reduce the efficacy of ADEMPAS. Contact your doctor if you stop or start smoking during treatment as a dose adjustment might be required.

See also ABOUT THIS MEDICATION: When it should not be used, and SIDE EFFECTS AND WHAT TO DO ABOUT THEM.

PROPER USE OF THIS MEDICATION

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Treatment should only be initiated and monitored by a doctor experienced in the treatment of CTEPH or PAH.

Usual adult dose:

During the first weeks of treatment your doctor will need to measure your blood pressure at least every two weeks. This is required to decide on the correct dose of your medication (ADEMPAS is available in different strengths (0.5 mg to 2.5 mg)).

Initial treatment dose:

- Starting at one 1 mg tablet, three times daily for 2 weeks. Your physician may have prescribed 0.5 mg 3 times daily for 2 weeks, depending on your health status.
- Tablets should be taken three times a day, approximately 6 to 8 hours apart, with or without food.
- Your doctor will increase the strength of your tablet every 2 weeks to a maximum of 2.5 mg three times a day (maximum daily dose of 7.5 mg) unless you experience any side effects or very low blood pressure. If you may experience any side effects mentioned *(see below section 'SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM')*, contact your doctor.

Maintenance dose:

Your doctor will continue to prescribe you ADEMPAS at the highest dose you are comfortable on unless you experience any side effect or very low blood pressure, symptoms like dizziness and fainting.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

You may experience the side effects mentioned below (*see section 'SIDE EFFECTS WHAT TO DO ABOUT THEM'*).

Contact your doctor, he or she will treat any symptoms that follow.

Missed dose:

Do not take a double dose to make up for a forgotten dose. If a dose is missed, treatment should be continued with the next dose as planned.

Stopped treatment:

Don't stop taking ADEMPAS without talking to your doctor first, because this medicine prevents the development of a serious condition.

In case treatment has to be interrupted for 3 days or more, please contact your doctor before restart of treatment.

Special considerations for patients with liver or kidney problems:

You should tell your doctor if you have liver or kidney problems. Your dose may need to be adjusted.

If you have severe liver problems (hepatic impairment, Child Pugh C) or severe kidney problems (creatinine clearance <15 mL/min or if you are on dialysis) you should not take ADEMPAS, as there are no data on the use of ADEMPAS in patients with these conditions.

65 years or older:

If you are 65 years or older your doctor will take extra care in adjusting your dose of ADEMPAS.

Other medicines:

Medicines used to treat stomach disease or heartburn, such as aluminum hydroxide/magnesium carbonate should be taken at least 1 hour after ADEMPAS.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, this medicine can cause side effects, although not everybody gets them. The most **serious** side effects are **coughing up blood** (hemoptysis) and **bleeding from the lungs** (pulmonary hemorrhage); cases with fatal outcome were observed.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / Effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Very common	Headache, dizziness	✓		
	Indigestion	✓		
	Swelling of limbs (edema peripheral)	✓		
	Nausea		✓	
	Diarrhea		✓	
	Vomiting		✓	
Common	Pain in stomach and bowels (gastrointestinal or abdominal pain), bloating, constipation or heartburn (gastroesophageal reflux disease)	✓		
	Reduction in red blood cells which can make your skin pale and cause weakness, tiredness, dizziness, headache, breathlessness, unusually fast heartbeat, or chest pain		✓	
	Unusually fast or irregular heartbeats (palpitations)		✓	
	Low blood pressure (lightheaded-ness, dizziness)		✓	
	Coughing up blood (mild to moderate)		✓	
	Nosebleed lasting more than 5 minutes		✓	
	Congestion in the nose (nasal congestion)		✓	
	Difficulty in swallowing		✓	
Uncommon	Bleeding from the lung/coughing up blood (severe)			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / Effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Unknown	Allergic reactions (symptoms like sudden wheeziness and chest pain or tightness; or swelling of eyelids, face, lips, tongue or throat.)			✓

This is not a complete list of side effects. For any unexpected effects while taking ADEMPAS, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of reach and sight of children. Store at room temperature between 15°C and 30°C. Do not use after the expiry date stated on the label.

REPORTING SUSPECTED SIDE EFFECTS

Canada Vigilance Program

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at www.healthcanada.gc.ca/medeffect

Call toll-free at 1-866-234-2345

Complete a Canada Vigilance Reporting Form and:

- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of the side effect, please contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at
1-800-265-7382 or canada.medinfo@bayer.com.

This document plus the full Product Monograph, prepared for health professionals can be found at:
http://www.bayer.ca or by contacting the manufacturer at the above-mentioned phone number and email address.

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