

Riociguat (0.5 mg film-coated tablets, 1.0 mg film-coated tablets, 1.5 mg film-coated tablets, 2.0 mg film-coated tablets, 2.5 mg film-coated tablets)

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What *Adempas* is used for

Chronic-thromboembolic pulmonary hypertension (CTEPH, WHO Group 4)

Adempas is used to treat adult patients with CTEPH, a disease where high blood pressure in lung vessels (pulmonary arteries) is caused by fixed blood clots narrowing or blocking 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.

Adempas lowers high blood pressure in the lung vessels and leads to an increase in exercise capacity (will increase a patient's ability to walk further).

Pulmonary arterial hypertension (PAH, WHO Group 1)

Adempas is used to treat adult patients with PAH, a disease characterized by high blood pressure in blood vessels (the pulmonary arteries) that carry blood from the heart to the lungs. 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.

Adempas lowers the high blood pressure in the lung vessels and leads to an increase in exercise capacity (will increase a patient's ability to walk further).

Adempas can be taken alone or together with certain medicines used to treat PAH (endothelin receptor antagonists or prostanoids).

How *Adempas* works

Adempas contains the active substance *riociguat*. *Riociguat* is a soluble guanylate cyclase (sGC)-stimulator. It works by widening the pulmonary arteries (the blood vessels that connect the heart to the lungs), making it easier for the heart to pump blood through the lungs.

Before you use *Adempas*

- *When you must not use it*

Do not take *Adempas*

- if you are **pregnant**.
- if you are taking **nitrates** (medicines used to treat high blood pressure or heart disease) or **nitric oxide donors** (such as amyl nitrite) in any form.
- 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 have increased pressure in your pulmonary circulation associated with scarring of the lungs, of unknown cause (idiopathic pulmonary pneumonia).

If any of these applies to you, **talk to your doctor** and do not take *Adempas*.

Adempas with food and drink

Adempas can be taken with or without food.

Adempas and smoking

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.

Pregnancy and lactation

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*.

- *Before you start use it*

Talk to your doctor or pharmacist before taking *Adempas*:

- 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 had experienced recently serious bleeding from the lung, if you have undergone interventional treatment to stop **coughing up blood** (bronchial arterial embolization). In this case the risk of bleeding from the lungs may be further increased. Inform your doctor if you take medicines used to **prevent blood clots** (anticoagulants). Your doctor will regularly monitor.
- 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.

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

Children and adolescents

Adempas is not recommended for patients under 18 years of age, because there is no information on its use in children and adolescents.

- Taking other medicines

Tell your doctor if you are taking, have recently taken or might take any other medicines:

Do not take :

- **nitric oxide donors** (such as amyl nitrite)
- **nitrates** (medicines used to treat high blood pressure or heart disease)
- PDE-5-inhibitors (such as **sildenafil or tadalafil**), medicines used to treat high blood pressure in the pulmonary arteries (pulmonary arterial hypertension) or male erectile dysfunction (such as **the above or vardenafil**)

Avoid taking:

- medicines used to treat fungal infections (e.g. **ketoconazole, itraconazole**)
- medicine for the treatment of HIV infection (e.g. **ritonavir**)

Use with caution:

- **cyclosporine** (medicine used to prevent rejection of transplanted organs)
- **erlotinib** or **gefitinib** (medicines against cancer)
- **granisetron** (medicine used to treat nausea and vomiting)
- **phenytoin** and **carbamazepine** (antiepileptic medicines), **phenobarbitone** (antiepileptic medicine, sedative), and **St. John's Wort** (herbal treatment for depression)

Take at least 1 hour after Adempas:

- **aluminum hydroxide / magnesium hydroxide** (used to treat stomach disease or heartburn)

How to use Adempas

- How much to use

Adults:

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

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-2.5 mg)).

The recommended starting dose of Adempas in adults is one 1.0 mg tablet, three times daily for 2 weeks.

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 'Possible side effects'*), please contact your doctor.

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. If you may experience any side effects mentioned (*see below section 'Possible side effects'*), please contact your doctor.

Crushed tablets:

If you have difficulty swallowing the whole tablet, talk to your doctor about other ways to take Adempas. The tablet may be crushed and mixed with water or a soft food such as applesauce immediately before you take it.

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 (*see above section 'Other medicines and Adempas'*).

- When to use it

Follow all directions given to you by your doctor and pharmacist carefully. They may differ from the information contained in this leaflet. If you do not understand the instructions on the label, ask your doctor or pharmacist for help.

- How long to use it

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

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

- If you forget to use it

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.

- If you use too much (overdose)

You may experience the side effects mentioned below (see section 'Possible side effects'). Contact your doctor, he or she will treat any symptoms that follow.

While you are using it

- Things you must do

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

Keep this leaflet. You may need to read it again.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

- Things you must not do

This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours. Don't stop taking *Adempas* without talking to your doctor first, because this medicine prevents the development of a serious condition.

- Things to be careful of

Driving and using machines

Dizziness as a common side effect may affect the ability to drive and use machines (see below section 'Possible side effects'). You should be aware of your side effects to *Adempas*, before driving or using machines.

Side effects

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.

The most **common** side effects which may affect more than 1 in 10 people with *Adempas* treatment are **headache, dizziness, indigestion** (dyspepsia), **swelling of limbs** (edema peripheral), **nausea, diarrhea** and **vomiting**.

Other possible side effects are listed below by how likely they are:

- headache
- dizziness
- indigestion (dyspepsia)
- swelling of limbs (edema peripheral)
- nausea
- diarrhea
- vomiting

Common (may affect up to 1 in 10 people)

- Inflammation in the digestive system (gastroenteritis)
- Decreased number of red blood cells (anemia incl. respective laboratory parameters)
- Fast or irregular heart beats (palpitations)
- Low blood pressure (hypotension)
- Coughing of blood (hemoptysis)
- Nosebleed (epistaxis)
- Congestion in the nose (nasal congestion)
- Inflammation of the stomach (gastritis)
- Heartburn (gastroesophageal reflux disease)
- Difficulty in swallowing (dysphagia)
- Pain in stomach and bowels (gastrointestinal and abdominal pain)
- Constipation
- Bloating (abdominal distension)

Uncommon (may affect up to 1 in 100 people)

- **bleeding from the lungs** (pulmonary hemorrhage)

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website npra.moh.gov.my (Public → Reporting Medicinal Problems / Side Effects / AEFI).

Storage and Disposal of *Adempas*

- Storage

Keep this medicine out of the sight and reach of children. Store below 30 °C.

Do not use this medicine after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

- Disposal

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Product Description

- What it looks like

Adempas 0.5 mg film-coated tablets: White, tablets of 6 mm marked with the Bayer cross on one side and 0.5 and an "R" on the other side.

Adempas 1.0 mg film-coated tablets: Pale yellow, tablets of 6 mm marked with the Bayer cross on one side and 1 and an "R" on the other side.

Adempas 1.5 mg film-coated tablets: Yellow-orange, tablets of 6 mm marked with the Bayer cross on one side and 1.5 and an "R" on the other side.

Adempas 2.0 mg film-coated tablets:

Pale orange, tablets of 6 mm marked with the Bayer cross on one side and 2 and an “R” on the other side.

D-51368 Leverkusen
Germany

Adempas 2.5 mg film-coated tablets:
Red-orange, tablets of 6 mm marked with the Bayer cross on one side and 2.5 and an “R” on the other side.

Product Registration Holder

Bayer Co.(Malaysia) Sdn Bhd
B-19-1 & B-19-2, The Ascent Paradigm,
No. 1, Jalan SS 7/26A, Kelana Jaya,
47301 Petaling Jaya, Selangor.

- **Ingredients**

-Active ingredients

The active substance is *riociguat*.
Each film-coated tablet contains either
0.5 mg, 1.0 mg, 1.5 mg, 2.0 mg,
2.5 mg *riociguat*.

Date of revision

29/03/2018

Serial number:

NPRA (R1/2) 07062018/074

- Inactive ingredients

Tablet core:

- cellulose microcrystalline
- crospovidone
- hypromellose 5cP
- lactose monohydrate
- magnesium stearate
- sodium laurilsulfate

Film coat:

0.5 mg tablets:

- hydroxypropylcellulose
- hypromellose 3cP
- propylene glycol
- titanium dioxide (E 171)

1.0 mg, 1.5 mg tablets:

- hydroxypropylcellulose
- hypromellose 3cP
- propylene glycol
- titanium dioxide (E 171)
- ferric oxide yellow (E 172)

2.0 mg and 2.5 mg tablets:

- hydroxypropylcellulose
- hypromellose 3cP
- propylene glycol
- titanium dioxide (E 171)
- ferric oxide red (E 172)
- ferric oxide yellow (E 172)

- MAL number(s):

MAL14115019ARZ
MAL14115022ARZ
MAL14115020ARZ
MAL14115023ARZ
MAL14115021ARZ

Manufacturer

Bayer AG