

Package Leaflet: Information for the user

Adempas 0.5 mg film-coated tablets

Adempas 1 mg film-coated tablets

Adempas 1.5 mg film-coated tablets

Adempas 2 mg film-coated tablets

Adempas 2.5 mg film-coated tablets

riociguat

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, ask your doctor or pharmacist.
- 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.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- This leaflet has been written as though the person taking the medicine is reading it. If you are giving this medicine to your child, please replace “you” with “your child” throughout.

What is in this leaflet

1. What Adempas is and what it is used for
2. What you need to know before you take Adempas
3. How to take Adempas
4. Possible side effects
5. How to store Adempas
6. Contents of the pack and other information

1. What Adempas is and what it is used for

Adempas contains the active substance riociguat, a guanylate cyclase (sGC)-stimulator. It works by widening the blood vessels that lead from the heart to the lungs.

Adempas is used to treat adults and children with certain forms of pulmonary hypertension, a condition in which these blood vessels become narrowed, making it harder for the heart to pump blood through them and leading to high blood pressure in the vessels. Because the heart must work harder than normal, people with pulmonary hypertension feel tired, dizzy and short of breath.

By widening the narrowed arteries, Adempas improves the ability to carry out physical activity, i.e. to walk further.

Adempas is used in either of two types of pulmonary hypertension:

- **Chronic thromboembolic pulmonary hypertension (CTEPH).**
Adempas tablets are used to treat CTEPH in adult patients. In CTEPH, the blood vessels of the lung are blocked or narrowed with blood clots. Adempas can be used for patients with CTEPH who cannot be operated on, or after surgery for patients in whom increased blood pressure in the lungs remains or returns.
- **Certain types of pulmonary arterial hypertension (PAH).**
Adempas tablets are used to treat PAH in adults and children under 18 years with body weight of at least 50 kg. In PAH, the wall of the blood vessels of the lungs are thickened and the vessels become narrowed. Adempas is only prescribed for certain forms of PAH, i.e. idiopathic PAH (the cause of PAH is unknown), heritable PAH and PAH caused by connective tissue disease. Your doctor will check this. Adempas can be taken alone or together with certain other medicines used to treat PAH.

2. What you need to know before you take Adempas

Do not take Adempas if you:

- take **PDE5 inhibitors** (e.g. sildenafil, tadalafil, vardenafil). These are medicines used to treat high blood pressure in the arteries of the lungs (PAH) or erectile dysfunction.
- have **severe liver problems** (severe hepatic impairment).
- are **allergic** to riociguat or any of the other ingredients of this medicine (listed in section 6).
- are **pregnant**.
- take **nitrates** or **nitric oxide donors** (such as amyl nitrite) in any form, medicines often used to treat high blood pressure, chest pain or heart disease. This also includes recreational drugs called poppers.
- take other medicines, similar to Adempas (**soluble guanylate cyclase stimulators**, such as vericiguat). Ask your doctor if you are not sure.
- have **low blood pressure** (systolic blood pressure: in children aged 6 to < 12 years below 90 mmHg, in patients ≥ 12 years below 95 mmHg) before starting first treatment with this medicine.
- have **increased blood pressure** in your lungs associated with scarring of the lungs, of unknown cause (idiopathic pulmonary pneumonia).

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

Warnings and precautions

Talk to your doctor or pharmacist before taking Adempas if you:

- have recently had serious **bleeding from the lung**.
- have undergone treatment to stop **coughing up blood** (bronchial arterial embolisation).
- take **blood-thinning medicines** (anticoagulants) since this may cause bleeding from the lungs. Your doctor will regularly test your blood and measure blood pressure.
- feel **short of breath**, this can be caused by a build-up of fluid in the lungs. Talk to your doctor if this happens.
- have any symptoms of **low blood pressure** (hypotension) such as dizziness, lightheadedness, or fainting or if you are taking medicines to lower your blood pressure or medicines that cause an increase in urination or if you have problems with your heart or circulation. Your doctor may decide to monitor your blood pressure. If you are older than 65 years, you have an increased risk of developing low blood pressure.
- take medicines used to **treat fungal infections** (e.g. ketoconazole, posaconazole, itraconazole) or medicines for the **treatment of HIV infection** (e.g. abacavir, atazanavir, cobicistat, darunavir, dolutegravir, efavirenz, elvitegravir, emtricitabine, lamivudine, rilpivirine, ritonavir, and tenofovir). Your doctor will monitor your health status and should consider a lower starting dose for Adempas.
- are **on dialysis** or if your **kidneys do not work properly** (creatinine clearance < 30 ml/min) the use of this medicine is not recommended.
- have **moderate liver problems** (hepatic impairment).
- start or stop **smoking** during treatment with this medicine, because this may influence the level of riociguat in your blood.

Children and adolescents

The use of Adempas tablets in children under 6 years and adolescents below 50 kg of weight should be avoided. Efficacy and safety have not been established in the following paediatric populations:

- Children aged < 6 years because of safety concerns.
- Children with PAH with too low blood pressure:
 - aged 6 to < 12 years < 90 mmHg at treatment initiation.
 - aged 12 to < 18 years < 95 mmHg at treatment initiation.
- Children and adolescents with other forms of this disease, i.e. CTEPH, if aged < 18 years old.

Other medicines and Adempas

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, in particular, medicines used for:

- high blood pressure or heart disease (such as **nitrates and amyl nitrite** in any form or other **soluble guanylate cyclase stimulator** (such as **vericiguat**)). You must not take those medicines together with Adempas.
- high blood pressure in the lung vessels (the pulmonary arteries), as you must not take certain medicines (**sildenafil** and **tadalafil**) together with Adempas. Other medicines for high blood pressure in the lung vessels, such as **bosentan** and **iloprost**, can be used with Adempas, but you should still tell your doctor.
- erectile dysfunction (such as **sildenafil, tadalafil, vardenafil**), as you must not take those medicines together with Adempas.
- fungal infections (such as **ketconazole, posaconazole, itraconazole**) or HIV infection (such as **abacavir, atazanavir, cobicistat, darunavir, dolutegravir, efavirenz, elvitegravir, emtricitabine, rilpivirine** or **ritonavir**). Alternative treatment options may be considered. If you already take one of these medicines and start treatment with Adempas, your doctor will monitor your health status and should consider a lower starting dose for Adempas.
- epilepsy (e.g. **phenytoin, carbamazepine, phenobarbitone**).
- depression (**St. John's Wort**).
- preventing rejection of transplanted organs (**ciclosporin**).
- joint and muscular pain (**niflumic acid**).
- cancer (such as **erlotinib, gefitinib**).
- stomach disease or heartburn (**antacids** such as **aluminium hydroxide/magnesium hydroxide**). These medicines should be taken at least 2 hours before or 1 hour after taking Adempas.
- nausea, vomiting (feeling or being sick) (such as **granisetron**).

Smoking

If you smoke, it is recommended that you stop, as smoking may reduce the effectiveness of these tablets. Please tell your doctor if you smoke or stop smoking during treatment. A dose adjustment might be required.

Birth control, pregnancy and breast-feeding

Birth control

Women and female adolescents of childbearing potential must use effective contraception during treatment with Adempas.

Pregnancy

Do not take Adempas during pregnancy. You are also advised to take monthly pregnancy tests. 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 this medicine.

Breast-feeding

If you are breast-feeding or planning to breast-feed, ask your doctor or pharmacist for advice before taking this medicine because it might harm your baby. You should not breast-feed while taking this medicine. Your doctor will decide with you to either stop breast-feeding or to stop taking Adempas.

Driving and using machines

Adempas moderately influences the ability to cycle, drive and use machines. It may cause side effects such as dizziness. You should be aware of the side effects of this medicine before cycling, driving or using machines (see section 4).

Adempas contains lactose

If you have been told by a doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Adempas contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium free”.

3. How to take Adempas

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

Adempas tablets are available for patients aged 6 years and over and weighing at least 50 kg.

Treatment should only be started and monitored by a doctor experienced in the treatment of high blood pressure in lung arteries. During the first weeks of treatment your doctor will need to measure your blood pressure at regular intervals. Adempas is available in different strengths and by checking your blood pressure regularly at the beginning of your treatment, your doctor will ensure that you are taking the appropriate dose.

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 apple sauce, immediately before you take it.

Dose

The recommended starting dose is a 1-mg tablet taken 3 times a day for 2 weeks.

The tablets should be taken 3 times a day, every 6 to 8 hours. They can generally be taken with or without food.

However, if you are prone to having low blood pressure (hypotension), you should not switch from taking Adempas with food to taking Adempas without food because it may affect how you react to this medicine.

During the first weeks of treatment your doctor will need to measure your blood pressure at least every two weeks. Your doctor will increase the dose every 2 weeks to a maximum of 2.5 mg 3 times a day (maximum daily dose of 7.5 mg) unless you experience very low blood pressure. In this case, your doctor will prescribe you Adempas at the highest dose you are comfortable on. The best dose will be selected by your doctor. For some patients lower doses 3 times a day might be sufficient.

Special considerations for patients with kidney or liver problems

Tell your doctor if you have kidney or liver problems. Your doctor may adjust the dose. If you have severe liver problems, do not take Adempas.

65 years or older

If you are 65 years or older your doctor will take extra care in adjusting your dose of Adempas, because you may be at greater risk of low blood pressure.

Special considerations for patients who smoke

Tell your doctor if you start or stop smoking during treatment with this medicine. Your doctor may adjust the dose.

If you take more Adempas than you should

Please contact the doctor if you took more Adempas than you should and if you notice any side effects (see section 4). If your blood pressure drops (which can make you feel dizzy) then you may need immediate medical attention.

If you forget to take Adempas

Do not take a double dose to make up for a forgotten dose. If you miss a dose, continue with the next dose as planned.

If you stop taking Adempas

Do not stop taking this medicine without talking to your doctor first, because this medicine prevents the progression of the disease. If you stop to take this medicine for 3 days or longer, please tell your doctor before restarting taking this medicine.

If you are transitioning between sildenafil or tadalafil and Adempas

You must have a pause between the intake of the previous and the new medicines to avoid interaction:

Switching to Adempas

- Take or give Adempas not earlier than 24 hours after you stop sildenafil.
- Take or give Adempas not earlier than 48 hours after you stop tadalafil for adults and after 72 hours for children.

Switching from Adempas

- Stop taking or giving Adempas a minimum of 24 hours before you start using a PDE5 inhibitor (e.g. sildenafil or tadalafil).

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

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

The most **serious** side effects **in adults** are:

- **coughing up blood** (haemoptysis) (common side effect, may affect up to 1 in 10 people),
- **acute bleeding from the lungs** (pulmonary haemorrhage) may result in coughing up blood, cases with fatal outcomes were observed (uncommon side effect, may affect up to 1 in 100 people).

If this happens, **contact your doctor immediately** as you may need urgent medical treatment.

Overall list of possible side effects:

Very common: may affect more than 1 in 10 people

- headache
- dizziness
- indigestion (dyspepsia)
- swelling of limbs (oedema peripheral)
- diarrhoea
- feeling or being sick (nausea and vomiting)

Common: may affect up to 1 in 10 people

- inflammation of the stomach (gastritis)
- inflammation in the digestive system (gastroenteritis)
- reduction of red blood cells (anaemia) seen as pale skin, weakness or breathlessness
- awareness of an irregular, hard, or rapid heartbeat (palpitation)
- low blood pressure (hypotension)
- nose bleed (epistaxis)
- difficulty breathing through your nose (nasal congestion)
- pain in the stomach, intestine or abdomen (gastrointestinal and abdominal pain)
- heartburn (gastro-oesophageal reflux disease)
- difficulty in swallowing (dysphagia)
- constipation
- bloating (abdominal distension)

Side effects in children

In general, the side effects observed in **children aged 6 to 17 years** treated with Adempas were similar to those observed in adults. The most **frequent** side effects **in children** were:

- **low blood pressure** (hypotension) (may affect more than 1 in 10 people),
- **headache** (may affect up to 1 in 10 people)

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Adempas

Keep this medicine out of the sight and reach of children.

This medicine does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the blister and carton after “EXP”. The expiry date refers to the last day of that month.

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.

6. Contents of the pack and other information

What Adempas contains

- The **active substance** is riociguat.
 - Adempas 0.5 mg film-coated tablets*
Each film-coated tablet contains 0.5 mg riociguat.
 - Adempas 1 mg film-coated tablets*
Each film-coated tablet contains 1 mg riociguat.
 - Adempas 1.5 mg film-coated tablets*
Each film-coated tablet contains 1.5 mg riociguat.
 - Adempas 2 mg film-coated tablets*
Each film-coated tablet contains 2 mg riociguat.
 - Adempas 2.5 mg film-coated tablets*
Each film-coated tablet contains 2.5 mg riociguat.
- The **other ingredients** are:
 - Tablet core:* cellulose microcrystalline, crospovidone (type B), hypromellose 5 cP, lactose monohydrate, magnesium stearate and sodium laurilsulfate (see end of section 2 for further information on lactose).
 - Film-coat:* hydroxypropylcellulose, hypromellose 3 cP, propylene glycol (E 1520) and titanium dioxide (E 171).
 - Adempas 1 mg, 1.5 mg tablets also contains iron oxide yellow (E 172).
 - Adempas 2 mg and 2.5 mg tablets also contains iron oxide yellow (E 172) and iron oxide red (E 172).

What Adempas looks like and contents of the pack

Adempas is a film-coated tablet:

Adempas 0.5 mg film-coated tablets

- *0.5 mg tablet*: white, round, biconvex tablets of 6 mm, marked with the Bayer cross on one side and 0.5 and an “R” on the other side.

Adempas 1 mg film-coated tablets

- *1 mg tablet*: pale yellow, round, biconvex 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

- *1.5 mg tablet*: yellow-orange, round, biconvex tablets of 6 mm, marked with the Bayer cross on one side and 1.5 and an “R” on the other side.

Adempas 2 mg film-coated tablets

- *2 mg tablet*: pale orange, round, biconvex tablets of 6 mm, marked with the Bayer cross on one side and 2 and an “R” on the other side.

Adempas 2.5 mg film-coated tablets

- *2.5 mg tablet*: red-orange, round, biconvex tablets of 6 mm, marked with the Bayer cross on one side and 2.5 and an “R” on the other side.

They are available in packs of:

- 42 tablets: two transparent calendar blisters of 21 tablets each.
- 84 tablets: four transparent calendar blisters of 21 tablets each.
- 90 tablets: five transparent blisters of 18 tablets each.
- 294 tablets: fourteen transparent calendar blisters of 21 tablets each.

Not all pack sizes may be marketed.

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