Adempas[®] 0.5 mg Adempas[®] 1 mg Adempas[®] 1.5 mg Adempas[®] 2.5 mg Adempas[®] 2 mg **Film-coated Tablets**

Each tablet contains: Riociguat 0.5 mg Riociauat 1 ma Riociguat 1.5 mg Riociquat 2 mg Riociguat 2.5 mg Respectivelv

Inactive and allergenic ingredients in the preparation: see section 6 "Further Information" and section 2 "Important information regarding some of the ingredients of the medicine".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

The medicine is not intended for children and adolescents under 18 years of age.

Patient safety information card

In addition to the leaflet. Adempas comes with a patient safety information card, regarding potential harm to an unborn baby.

This card contains important safety information that you should know before starting and during treatment with Adempas. Read the patient safety information card and patient leaflet before commencing use of the preparation. Keep the card and leaflet for further reference, if necessary.

Do not take Adempas if you are pregnant, since the use of this medicine may harm the unborn baby (see in section 2, "Pregnancy and breastfeeding"). If you are a woman of child-bearing age and may become pregnant, perform a pregnancy test before starting treatment with Adempas and routinely every month while taking the medicine, as well as one month after completing treatment. Confirm a negative result with every pregnancy test. You must use a reliable contraceptive while using Adempas, as well as for one additional month after completing treatment (see "Pregnancy and breastfeeding" in section 2)

1) WHAT IS THE MEDICINE INTENDED FOR?

Adempas is intended to treat either one of two types of pulmonary hypertension detailed below.

Pulmonary hypertension is a condition in which blood vessels in the lungs become narrow, making it harder for the heart to pump blood through them, resulting in increased blood pressure in these vessels. Because the heart must work harder than normal in this state, people with pulmonary hypertension feel tired, dizzy and short of breath. By widening the narrowed arteries in the lungs, Adempas leads to an improvement in your ability to carry out physical activity.

Adempas is intended to treat either of the following two types of pulmonary hypertension: 1. Chronic thromboembolic pulmonary hypertension (CTEPH):

In this condition, a blood clot is blocking or narrowing the blood vessels of the lungs. Adempas can be used to treat people who suffer from CTEPH and cannot be operated on, or who have undergone surgery but their pulmonary hypertension has remained unchanged or returned

 Certain types of pulmonary arterial hypertension (PAH): In PAH, the walls of the blood vessels of the lungs thicken and the blood vessels become narrow. Adempas can be used to treat certain forms of PAH, such as idiopathic PAH (the cause of the disease is unknown), heritable PAH and PAH caused by connective tissue disease. Your doctor will check this. Adempas can be taken alone or together with other medicines used to treat PAH

Therapeutic group: Adempas belongs to a group of medicines called guanylate cyclase stimulators and acts by widening the pulmonary arteries (blood vessels that connect the heart to the lungs). Widening of the pulmonary arteries makes it easier for the heart to pump blood through the lungs.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:

• You are sensitive (allergic) to riociguat or to any of the additional ingredients contained in the medicine.

For the list of inactive ingredients, see section 6 "Further Information". You are taking certain medicines to treat pulmonary arterial hypertension or to treat erectile dysfunction, called phosphodiesterase-5 (PDE-5) inhibitors,

e.g., sildenafil, tadalafil, vardenafil You suffer from severe liver problems (severe hepatic failure,

Child Pugh C). You are pregnant.

 You are taking medicines to treat hypertension, chest pains or heart disease called nitrates or nitric oxide donors in any form, such as amyl nitrite. This also includes preparations (recreational drugs) intended to alter the state of consciousness, called poppers.

You are taking other soluble guanylate cyclase stimulators. Ask your doctor if you are not sure.

• You suffer from low blood pressure before commencing treatment (systolic blood pressure [peak pressure during ventricular contraction] less than 95

You suffer from high blood pressure in the pulmonary circulation associated with scarring of the lungs, caused by a lung disease called idiopathic interstitial pneumonia (a noninfectious lung inflammation, with no known cause).

If any of these apply to you, consult the doctor and do not take Adempas. Special warnings regarding use of the medicine:

Before using Adempas, tell the doctor if:

• You have recently suffered from serious bleeding from the lungs, or if you have undergone treatment to stop coughing up blood (bronchial arterial embolisation)

• You take **blood-thinning medicines** (anticoagulants), since this may cause bleeding from the lungs. The doctor will monitor your condition regularly. • You feel shortness of breath during treatment with Adempas, which can be caused by a build-up of fluid in the lungs. Consult your doctor if this happens to you.

You experience 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.

 You 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 reduced starting dose for Adempas.

Your kidneys do not function properly (creatinine clearance of less than 30 ml/min) or you are on dialysis. Use of Adempas is not recommended under these conditions.

You suffer from moderate liver failure (moderate hepatic failure. Child Pugh

You started or stopped smoking during treatment with Adempas, because this may influence the blood level of the active ingredient riociguat.

Adempas is intended to treat certain types of pulmonary arterial hypertension (see section 1 "What Is The Medicine Intended For?"). There is no experience with use of Adempas for other types of pulmonary arterial hypertension and it is therefore not recommended in these cases. The doctor will check if treatment with Adempas is suitable for you.

Smoking

If you smoke, it is recommended that you stop, since smoking may reduce the effectiveness of Adempas. Tell your doctor if you smoke or stop smoking during the treatment.

Children and adolescents

Avoid using Adempas in children and adolescents (below 18 years of age) because the safety and effectiveness in this population have not been established.

Drug interactions

If you are taking, or have recently taken, or may take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular, inform the doctor or pharmacist if vou are takina:

- Medicines to treat hypertension or heart disease (such as nitrates and amy nitrite in any form or other soluble guanylate cyclase stimulators). Do not take them together with Adempas.
- Medicines to treat pulmonary (arterial) hypertension, as certain medicines (such as sildenafil and tadalafil) should not be taken together with Adempas. Other medicines to treat pulmonary arterial hypertension, such as bosentan
- and iloprost, can be taken, but you should tell the doctor that you are taking
- them. • Medicines to treat erectile dysfunction (such as sildenafil, tadalafil, vardenafil), as they should not be taken together with Adempas.
- Medicines to treat fungal infections (such as ketoconazole, posaconazole itraconazole) or medicines for treatment of or HIV infection (such as abacavir atazanavir, cobicistat, darunavir, dolutegravir, efavirenz, elvitegravir, emtricitabine, rilpivirine or ritonavir) because 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 reduced starting dose for Adempas. Medicines to treat epilepsy (such as phenytoin, carbamazepine, phenobarbitone).
- Medicines to treat depression (St. John's wort).
- Medicines used to prevent rejection of transplanted organs (ciclosporin). Medicines to treat muscular and joint pains (niflumic acid).
- Medicines to treat cancer (such as erlotinib, gefitinib).
- · Medicines to treat stomach ailment or heartburn (antacids such as aluminum
- hydroxide/magnesium hydroxide): take these medicines at least two hours before or one hour after taking Adempas. Medicines to treat nausea, vomiting (such as granisetron)

Use of the medicine and food

Adempas can be swallowed with or without food. However, if you are prone to low blood pressure, do not switch from taking Adempas with food to taking Adempas without food, since this may affect your response to the medicine

Pregnancy and breastfeeding

Pregnancy: Adempas may cause harm to unborn babies in a pregnancy that began before or during treatment.

Do not take Adempas if you are pregnant or are planning to become pregnant.

If you are a woman of child-bearing age and may become pregnant, talk to your doctor about your monthly period.

Your doctor will ask you to perform a pregnancy test before starting treatment with Adempas and routinely every month while taking the medicine and one month after completing treatment. Confirm a negative result with every pregnancy test.

You must use a reliable contraceptive while using Adempas, as well as for one additional month after completing treatment.

Your doctor or gynecologist will guide you regarding reliable contraceptive methods while using Adempas:

• One very effective contraceptive (e.g., intrauterine device or tubal ligation) • Or a combination of two contraceptive methods (e.g., hormonal contraceptive and barrier contraceptive [e.g., diaphragm, contraceptive sponge or that your partner also uses a condom] or two barrier contraceptives).

Consult your doctor regarding use of these two contraceptive options. If a vasectomy is your partner's chosen method of contraception, you must also use a hormonal or barrier contraceptive.

Inform your doctor immediately if you become pregnant while using Adempas, if you think you may be pregnant or if you are planning to become pregnant in the near future.

4) SIDE EFFECTS

from any of them.

to 1 user in 100).

Additional side effects:

- indigestion (dyspepsia)

- nausea or vomiting

shortness of breath

to 1 user in

headache

- dizziness

- diarrhea

nosebleed

- constipation

temperature.

Tablet coating

on the other side.

on the other side.

on the other side

on the other side.

and "R" on the other side.

Adempas 0.5 mg - 42 tablets

Adempas 1.5 mg - 42 tablets

Adempas 2.5 mg - 84 tablets

Hasharon 4527702.

Ministry of Health:

Adempas 1 mg -

Adempas 2 mg -

Adempas 0.5 mg -

Adempas 1.5 mg -

Adempas 2.5 mg -

Adempas 2 mg - 42, 84 tablets

Not all pack sizes may be marketed.

Adempas 1 mg - 42 tablets

alvcol.

coating

The most serious side effects are:

you may need urgent medical treatment.

- swelling of limbs (peripheral edema)

- inflammation of the stomach (gastritis)

- pain in the stomach, intestine or abdomen

- heartburn (gastro-esophageal reflux disease)

5) HOW SHOULD THE MEDICINE BE STORED?

- low blood pressure (hypotension)

- difficulty in swallowing (dysphagia)

- bloating (abdominal distension)

Reporting side effects

https://sideeffects.health.gov.il

6) FURTHER INFORMATION

As with any medicine, use of Adempas may cause side effects in some users

Do not be alarmed when reading the list of side effects. You may not suffer

- coughing up blood (hemoptysis) (common side effect, which may affect up

- acute bleeding from the lungs that may cause coughing up blood, and fatal outcomes have been observed (uncommon side effect, which may affect up

If you suffer from the effects listed above, refer to a doctor immediately, as

- reduction of red blood cells (anemia), whose signs are: pallor, weakness or

If a side effect occurs, if one of the side effects worsens, or if you suffer

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

• Avoid poisoning! This medicine, and any other medicine. should be kept in

a safe place out of the reach and sight of children and/or infants in order to

avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

• No special storage conditions. It is recommended to store at room

• Do not dispose of medicines in the wastewater or household waste bin.

Consult a pharmacist about how to dispose of medicines you no longer need This will help protect the environment.

Lactose monohydrate, cellulose microcrystalline, crospovidone, hypromellose

Hydroxypropylcellulose, titanium dioxide, hypromellose 3 cP, propylene

Adempas 1 mg, Adempas 1.5 mg, Adempas 2 mg and Adempas 2.5 mg also contain ferric oxide yellow in the tablet coating.

Adempas 2 mg and Adempas 2.5 mg also contain ferric oxide red in the tablet

Adempas 0.5 mg: film-coated, white, round and biconvex tablets. Their

diameter is 6 mm and they are marked "Bayer" on one side and 0.5 and "R

Adempas 1 mg: film-coated, light yellow, round and biconvex tablets. Their diameter is 6 mm and they are marked "Bayer" on one side and 1 and "R"

Adempas 1.5 mg: film-coated, yellow-orange, round and biconvex tablets. Their diameter is 6 mm and they are marked "Bayer" on one side and 1.5

· Adempas 2 mg: film-coated, light orange, round and biconvex tablets. Their

diameter is 6 mm and they are marked "Bayer" on one side and 2 and "R

Adempas 2.5 mg: film-coated, red-orange, round and biconvex tablets. Their diameter is 6 mm and they are marked "Bayer" on one side and 2.5 and "R"

• Registration Holder and Address: Bayer Israel, Ltd., 36 Hacharash Street, Hod

• Registration numbers of the medicine in the National Drug Registry of the

ADEM CTAB PL SH 170322

• In addition to the active ingredient, the medicine also contains:

What the medicine looks like and the contents of the package

The tablets are provided in trays (blisters) in packs of:

• Manufacturer and Address: Bayer AG, Leverkusen, Germany.

153 76 34132 00/01

153 77 34137 00/01

153 78 34138 00/01

153 79 34139 00/01

153 80 34150 00/01

• Revised in January 2022 according to MOH guidelines.

5 cP. magnesium stearate, sodium laurilsulphate.

from a side effect not mentioned in this leaflet, consult the doctor.

Very common side effects - effects that occur in more than 1 in 10 users

Common side effects - effects that occur in up to one in 10 users

- awareness of an irregular, strong or rapid heartbeat (palpitations)

- inflammation in the digestive system (gastroenteritis)

- difficulty breathing through the nose (nasal congestion)

Breastfeeding:

BAYER E R

If you are breastfeeding or planning to breastfeed, consult the doctor or pharmacist before starting Adempas treatment, for fear of harming the baby. Do not breastfeed while using this medicine. The doctor will decide if you should stop breastfeeding or stop treatment with Adempas.

Driving and operating machinery

Adempas has a moderate influence on the ability to drive and operate machines. Adempas may cause side effects such as dizziness. You must be aware of the possible side effects that may be caused by use of this medicine before driving and operating machinery (see section 4 "Side

Effects") Important information regarding some of the ingredients of the

Adempas contains lactose and sodium.

If you have been told by a doctor that you have an intolerance to certain sugars. tell the attending doctor before starting treatment.

Adempas contains less than 1 mmol sodium (23 mg) in each tablet and is therefore considered to be essentially "sodium-free".

3) HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation in accordance with the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.

Commencement of treatment with Adempas and follow-up will be performed by a doctor specializing in pulmonary hypertension secondary to chronic thromboembolic events or treatment of pulmonary hypertension. In the first weeks of treatment the doctor will measure your blood pressure at regular time intervals. Adempas is available in different doses; your doctor will ensure that you take the most appropriate dose for you by monitoring your blood pressure regularly at the beginning of treatment.

 The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

Start with one tablet at a dosage of 1 mg, 3 times a day, for two weeks. Take the tablets 3 times a day at intervals of approximately 6-8 hours between doses. Your doctor will increase the dosage every two weeks until reaching a maximal dose of 2.5 mg, 3 times a day (maximal daily dose of 7.5 mg), unless you experience side effects or very low blood pressure. In such a case, your doctor will prescribe Adempas for you at the highest dosage that suits you. For some patients, low doses 3 times a day might be sufficient. The dose most suitable for you will be determined by the doctor.

Special considerations for patients with liver or kidney problems

Tell the doctor if you are suffering from liver or kidney problems. There may be a need to adjust your dosage. If you are suffering from severe liver problems (Child Pugh C), do not take Adempas.

Age 65 and over

If you are 65 years of age or older, the attending doctor will exercise extra caution when determining the Adempas dosage, since you may be at a higher risk of low blood pressure. Special considerations for smoking patients

You must tell the doctor if you start or stop smoking during the course of treatment with Adempas. There may be a need to adjust the dosage for you.

Crushing 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.

Do not exceed the recommended dose.

Tests and follow-up

During the first weeks of treatment, your doctor will measure blood pressure at regular time intervals.

Since Adempas is available in a number of dosages, routine blood pressure measurements at the beginning of treatment will help the doctor confirm that you are receiving the suitable dosage.

Pregnancy tests for women of child-bearing age

If you are a woman of child-bearing age and may become pregnant, your doctor will ask you to perform a pregnancy test before starting treatment with Adempas and routinely every month while taking the medicine as well as one month after completing treatment. Confirm a negative result with every pregnancy test.

If you accidentally took a higher dosage and you experience any side effects (see section 4 "Side Effects"), refer to a doctor. If your blood pressure drops (which can cause you to feel dizzy), seek immediate medical attention. If you took an overdose or if a child has accidentally swallowed the medicine,

immediately refer to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

dose to compensate for the missed dose. Take the next dose at the usual

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist, since Adempas prevents

progression of the disease. If you stop taking the medicine for 3 or more days, refer to the doctor before you resume treatment with Adempas.

If you stop taking sildenafil, wait at least 24 hours before taking Adempas.

• If you stop taking tadalafil, wait at least 48 hours before taking Adempas.

• If you switch from Adempas to a phosphodiesterase-5 inhibitor (PDE-5), e.g.,

Do not take medicines in the dark! Check the label and the dose

If you have further questions regarding use of the medicine, consult the

sildenafil or tadalafil, wait at least 24 hours from the last dose of Adempas

Adhere to the treatment regimen as recommended by the doctor.

Transitioning between sildenafil or tadalafil and Adempas:

each time you take medicine. Wear glasses if you need them.

If you forget to take the medicine If you forget to take the medicine at the required time, do not take a double

Stopping treatment with Adempas

before taking the PDE-5.

doctor or pharmacist.

time