PACKAGE LEAFLET

Package leaflet: Information for the patient

GIAPREZA 2.5 mg/ml concentrate for solution for infusion
angiotensin II

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given 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.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GIAPREZA is and what it is used for

GIAPREZA contains the active substance angiotensin II, a compound normally produced by the body. It makes the blood vessels tighten and become narrower, thus increasing blood pressure.

GIAPREZA is used in an emergency setting to increase blood pressure to normal levels in adult patients with seriously low blood pressure who do not respond to fluids or other medicines that raise blood pressure.

2. What you need to know before you are given GIAPREZA

You must not be given GIAPREZA:
- if you are allergic to angiotensin II or any of the other ingredients of this medicine (listed in section 6).

Your doctor or nurse should be told if any of the above applies to you before this medicine is used.

Warnings and precautions
GIAPREZA has only been tested in people with septic and distributive shock. It has not been tested in other types of shock.

Your doctor or nurse should be told before GIAPREZA is used if you or someone else in your family have a history of blood clots, as this medicine has been associated with the formation of blood clots. As a part of your treatment, you may be given medicine to prevent the formation of blood clots.

When you are first given GIAPREZA, it is expected that your blood pressure will increase. You will be monitored closely to make sure that your blood pressure is at the right level.

Tell your doctor or nurse immediately if you experience a change of colour (redness or paleness), pain, numbness in any of your limbs, or if any of your limbs are cold to the touch, as these could be signs that a blood clot has blocked blood flow to a part of the body.

Elderly
GIAPREZA was tested in a small number of patients more than 75 years of age. There are no dose adjustments needed for patients more than 75 years of age. Your doctor will monitor your blood pressure and adjust your dose as needed.

Impairment of liver or kidneys
There are no dose adjustments needed for patients with impairment of the function of the liver or kidneys. Your doctor will monitor your blood pressure and adjust your dose as needed.

Children and adolescents
GIAPREZA should not be used in children or adolescents under 18 years of age as it has not been studied in these age groups.

Other medicines and GIAPREZA

Your doctor should be told if you are using, have recently used, or might use any other medicines.

A number of medicines may affect the way GIAPREZA works, such as:
- Angiotensin converting enzyme (ACE) inhibitors (medicines used to lower blood pressure, with active substances whose name usually end in -pril). ACE inhibitors may increase to the effect of GIAPREZA.
- Angiotensin II receptor blockers (medicines used to lower blood pressure, with active substances whose names usually end in -sartan) may lessen the effect of GIAPREZA.

Your doctor may already be giving you other medicines used to increase your blood pressure. Adding GIAPREZA to these medicines may require that the doses of the other medicines be lowered.

Pregnancy, breast-feeding and fertility
Your doctor should be told if you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby before this medicine is given.

There is limited information about the effects of GIAPREZA during pregnancy. Use of this medicine during pregnancy should be avoided if possible. You will only be given this medicine if the possible benefit is greater than the possible risks.

It is not known whether GIAPREZA can pass into breast milk. Your doctor should be told if you are breast-feeding before this medicine is given.

It is not known whether GIAPREZA can affect fertility.

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per 2.5 mg/1 ml, that is to say essentially ‘sodium-free’.

3. How GIAPREZA is used

GIAPREZA will be given to you in a hospital by a doctor or a nurse. It is first diluted and then given as a drip (infusion) into a vein, supplying a specified dose each minute.

The dose depends on your body weight. The recommended starting rate of GIAPREZA is 20 nanograms (ng) per kilogram of your body weight per minute. After the initial dose, your doctor will adjust the rate as often as every 5 minutes until you achieve your target blood pressure. Your doctor will continue to assess your response and will adjust the dose accordingly up to a maximum of 80 ng per kilogram each minute during the first 3 hours of treatment. The maximum dose after the first 3 hours will be 40 ng per kilogram each minute.

GIAPREZA will be given to you at the lowest dose that helps you to achieve or maintain your blood pressure. In order to minimise the risk of side effects to this medicine, GIAPREZA will be withdrawn as soon as your condition improves.

If you are given more GIAPREZA than you should
GIAPREZA will be given to you by a doctor or a nurse, so it is unlikely you will be given the wrong dose. However, if you have side effects or think you have been given too much GIAPREZA, tell your doctor or nurse straight away. If you have too much GIAPREZA, you may experience high blood pressure. If this occurs, hospital staff will monitor your vital signs and you will be provided with supportive care.

Stopping GIAPREZA treatment
Your doctor will gradually decrease the amount of GIAPREZA you are given over time once your blood pressure has increased to appropriate levels. If GIAPREZA is stopped suddenly or stopped too early, you may experience a decrease in your blood pressure or your condition may worsen.

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

4. Possible side effects

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

Tell your doctor <u>immediately</u> if you experience:
- Pain, redness or pale colour, swelling or coolness to the touch of the skin or limbs, as these may be symptoms of a blood clot in one of your veins. These clots may travel through blood vessels to the lungs causing chest pain and difficulty breathing. If you notice any of these symptoms, seek medical advice immediately. These types of symptoms occur in greater than 1 out of every 10 patients. While not all of these symptoms lead to life-threatening complications, your doctor should be told about them immediately.

Other side effects are:
Very common side effects (may affect more than 1 in 10 people) are:
- Too high blood pressure

Common side effects (may affect up to 1 in 10 people) are:
- Rapid heartbeat
- Poor circulation to your hands, feet, or other bodily areas which can be severe and cause tissue damage.

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: http://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 GIAPREZA

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

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

Store in a refrigerator (2 °C - 8 °C).

The diluted solution should be used immediately. Chemical and physical in-use stability has been demonstrated for 24 hours at room temperature and 2 °C - 8 °C.

Do not use if you notice any signs of visible damage or discolouration.

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 to protect the environment.

6. Contents of the pack and other information

What GIAPREZA contains

- The active substance is angiotensin II acetate. Each ml contains angiotensin II acetate equivalent to 2.5 mg angiotensin II.
  - One vial of 1 ml concentrate for solution for infusion contains 2.5 mg of angiotensin II
  - One vial of 2 ml concentrate for solution for infusion contains 5 mg of angiotensin II
- The other ingredients are mannitol and water for injections adjusted with sodium hydroxide and/or hydrochloric acid (see section 2 under 'Sodium').

What GIAPREZA looks like and contents of the pack

GIAPREZA is presented as a concentrate for solution for infusion (sterile concentrate). The solution is a clear, colourless solution free of any visible particles.

GIAPREZA is supplied in a carton as a 1 x 1 ml, 10 x 1 ml or 1 x 2 ml single use vial. Not all pack sizes may be marketed.

Marketing Authorisation Holder

PAION Deutschland GmbH
Heussstraße 25
52078 Aachen
Germany

Manufacturer

PAION Netherlands B.V.
Vogt 21
6422 RK Heerlen
Netherlands

This leaflet was last revised in 10/2021.

The following information is intended for healthcare professionals only:

Posology and method of administration

GIAPREZA should be prescribed by a physician experienced in the treatment of shock and is intended for use in an acute and hospital setting.

GIAPREZA should only be administered by continuous intravenous infusion under close monitoring of haemodynamics and end-organ perfusion.

Instructions for dilution

1. Inspect each vial for particulate matter prior to dilution.
2. Dilute 1 or 2 ml of GIAPREZA in sodium chloride 9 mg/ml (0.9%) solution for injection to achieve a final concentration of 5,000 ng/ml or 10,000 ng/ml.
3. Diluted solution should be clear and colourless.
4. Discard the vial and any unused portion of the medicinal product after use.

Diluted solution may be stored at room temperature or under refrigeration. Discard prepared solution after 24 hours at room temperature or under refrigeration.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Administration

When initiating GIAPREZA, it is important to closely monitor blood pressure response and adjust dose accordingly.

Once an infusion has been established, the dose may be titrated as frequently as every 5 minutes in steps of up to 15 ng/kg per minute, as needed, depending on the patient's condition and target mean arterial pressure. Approximately one in every four patients experienced transient hypertension with the angiotensin II 20 ng/kg/min starting dose in clinical trials (see section 4.8), thus needing dose down-titration. For critically ill patients, the usual target mean arterial pressure is 65 – 75 mmHg. Do not exceed 80 ng/kg per minute during the first 3 hours of treatment. Maintenance doses should not exceed 40 ng/kg per minute. Doses as low as 1.25 ng/kg per minute may be used.

It is important to administer GIAPREZA at the lowest compatible dose to achieve or maintain adequate arterial blood pressure and tissue perfusion (see section 4.4). The median duration of treatment in clinical trials was 48 hours (range: 3.5 to 168 hours).

In order to minimise the risk of adverse events derived from prolonged vasoconstriction, treatment with GIAPREZA should be withdrawn once underlying shock is sufficiently improved (see section 4.4 and 4.8). Down-titrate by gradual decrements of up to 15 ng/kg per minute, as needed, based on blood pressure in order to avoid hypotension due to abrupt withdrawal (see section 4.4).

Storage conditions

Store in a refrigerator (2 °C - 8 °C). Dilute before use. Administer as a diluted solution.