GIAPREZA®
(Angiotensin II)
onzentrat zur Herstellung einer Infusionslösung

Giapreza Prescribing Information

Product name and active ingredients:
Giapreza 2.5 mg/ml concentrate for solution for infusion

Indications: the treatment of refractory hypotension in adults with septic or other distributive shock who remain hypotensive despite adequate volume restitution and application of catecholamines and other available vasopressor therapies

- **Dosing an 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. The recommended starting dosage is 20 nanograms (ng)/kg per minute via continuous intravenous infusion. Giapreza must be diluted in sodium chloride 9 mg/ml (0.9%) solution for injection prior to use. One or two millilitres of Giapreza must be diluted 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. Preparation of diluted solution:

ng/kg KG/min	Vial strenght	Withdraw amount (ml)	Infusion bag size (ml)	Final concentration (ng/ml)
No	2.5 mg/ml	1	500	5,000
Yes	2.5 mg/ml	1	250	10,000
Yes	5 mg/2 ml	2	500	10,000

- When initiating Giapreza, it is important to closely monitor blood pressure response and adjust dose accordingly. Concurrent venous thromboembolism (VTE) prophylaxis should be used unless contraindicated during treatment with Giapreza. 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 1 in 4 patients experienced transient hypertension with the angiotensin II 20 ng/kg per minute starting dose in clinical trials, 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. 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order to minimise the risk of adverse events derived from prolonged vasoconstriction, treatment with Giapreza should be withdrawn once underlying shock is sufficiently improved. 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. Elderly: there are limited efficacy and safety data in patients > 75 years. No special dose adjustment is required in patients over 75 years. As for other age groups, it is important to closely monitor blood pressure response and adjust dose accordingly. Renal or hepatic impairment: no special dose adjustment required. As for other patient populations, it is important to closely monitor blood pressure response and adjust dose accordingly. Paediatric population: the safety and efficacy in children less than 18 years old has not yet been established. No data are available.

- **Method of administration:** Giapreza should only be administered by continuous intravenous infusion under close monitoring of haemodynamics and end-organ perfusion. For intravenous use only after dilution. Giapreza is recommended to be administered via a central venous line.

- **Contraindications:** Hypersensitivity to angiotensin II or excipients (mannitol, water for injections, sodium hydroxide, hydrochloric acid.)

- **Warnings and precautions:** The clinical experience with Giapreza is limited to septic or other distributive shock. Giapreza is not recommended in other types of shock (e.g. cardiogenic shock, etc) as patients with non-distributive shocks were excluded from clinical trials. Thromboembolic events: have been reported with the use of angiotensin II in clinical trials. The major imbalance compared to placebo was in venous thromboembolism (6.1% vs 0%). Concurrent venous thromboembolism prophylaxis (VTE) should be used unless contraindicated during treatment with Giapreza. Non-pharmacologic VTE prophylaxis may be considered where pharmacologic prophylaxis is contraindicated. Peripheral ischaemia: has been reported with the use of angiotensin II. It is important to administer Giapreza at the lowest compatible dose to achieve or maintain adequate mean arterial pressure and tissue perfusion. Withdrawal of therapy: Giapreza should be gradually decreased since patients may experience hypotension or worsening of the underlying diagnosis of shock on abrupt withdrawal or premature discontinuation. Sodium content: Giapreza contains less than 1 mmol sodium (23 mg) per 2.5 mg/ml, that is to say essentially 'sodium-free'.

- **Interactions:** Concomitant administration with other vasopressors may have an additive effect on mean arterial pressure (MAP). The addition of Giapreza may require a reduction in doses of other vasopressors. Patients who have recently received angiotensin converting enzyme (ACE) inhibitors may be more sensitive to Giapreza's action with an increased response. Patients who have recently received angiotensin II receptor blockers (ARBs) may be less sensitive to Giapreza's actions with a reduced response

- **Side effects:** Very common (≥ 1/10): thromboembolic events, transient hypertension. Common (≥ 1/100 to < 1/10): tachycardia, peripheral ischaemia.

- Consult the Summary of Product Characteristics regarding a full list of side effects.

- **Marketing Authorization Holder:** PAION Pharma GmbH, Heussstraße 25, 52078 Aachen, Germany.

- **Marketing Authorization Numbers:** EU/1/19/1384/001, EU/1/19/1384/002, and EU/1/19/1384/003. Date of First Authorization: 23 August 2019.

- **Date of Last Renewal:** 16 May 2024. Job Code: EU-RH-0067