22 APRIL 2024

Potentially Low Fill Vials of GIAPREZA® (Angiotensin II) 2.5mg/ml concentrate for solution for infusion: Important information regarding instructions for use

Dear Healthcare professional,

PAION Deutschland GmbH in agreement with the European Medicines Agency and the <National Competent Authority > would like to inform you of the following:

Summary

- **PAION Deutschland GmbH has been notified by the Supplier of GIAPREZA® (Giapreza 2.5 mg/ml concentrate for solution for infusion) with 2.5mg Angiotensin II /vial) that several hospitals in the United States, have identified low fill vials of GIAPREZA® (Angiotensin II) Product Lot 2457-116 corresponding to Product Batches: 23GPZ001, 23GPZ002, 23GPZ003, 23GPZ004, 23GPZ005, 23GPZ006 and 23GPZ008 in Europe, one or more of which have been supplied to your health institution.**
- **It has been reported that when the contents of a vial are withdrawn into a syringe the volume is less than the 1 mL volume defined in the Product Information.**
- **We have determined that patient safety is not impacted since the product is dosed as "titrate to effect".**
- **Should you identify a vial with less than 1 ml volume,**
  - preferably discard the vial and use another new vial or
  - alternatively dilute the lower withdrawn volume from the 2.5 mg/mL solution using a matching volume of normal saline (0.9% sodium chloride) to achieve the desired concentration of 5,000 ng/ml or 10,000 ng/ml.
- **Out of an abundance of caution, PAION Deutschland GmbH (PAION), is notifying health care providers and will replace any impacted vials found to have less than 1 mL volume, if requested (For product replacement, see Annex 1 below for instructions).**
- **Please be aware that low fill vial have not been reported in EU so far.**

Background – Instructions for Use

GIAPREZA® (Giapreza 2.5 mg/ml concentrate for solution for infusion with 2.5mg Angiotensin II/vial), a vasoconstrictor used for 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. The recommended starting dosage of GIAPREZA 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 millilitre 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 (using 500 ml infusion bag size) or 10,000 ng/ml (using 250 ml infusion bag size).

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

PAION received information from the GIAPREZA supplier that there were several reports of low fill vials notified by some hospitals in the United States. All of these reports relates to Product lot 2457-116 which was released in Europe as Product Batches 23GPZ001, 23GPZ002, 23GPZ003, 23GPZ004, 23GPZ005, 23GPZ006 and 23GPZ008. One of these batches has been supplied to your health institution. It has been reported that when the contents of a vial are withdrawn into a syringe the volume is less than the 1 mL volume defined in Product Information.

PAION wants to emphasize important information:

- This notification only applies to GIAPREZA® (Angiotensin II) 2.5mg/vial from the Product Batches 23GPZ001, 23GPZ002, 23GPZ003, 23GPZ004, 23GPZ005, 23GPZ006 and 23GPZ008.
- These vials are still acceptable to use as GIAPREZA® must be diluted in a normal saline (0.9% sodium chloride) infusion bag to achieve the desired final concentration of 5,000 ng/ml or 10,000 ng/ml.
- Please carefully monitor the volume withdrawn from each vial.
- Should you identify a vial with less than 1 ml volume,
  - preferably discard the vial and use another new one **or**
  - alternatively dilute the lower withdrawn volume from the 2.5 mg/mL solution using a matching volume of normal saline (0.9% sodium chloride) to achieve the desired concentration of 5,000 ng/ml or 10,000 ng/ml.
- It has been determined that patient safety is not impacted since the product is dosed as "titrate to effect".

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of GIAPREZA in accordance with the national spontaneous reporting system *<include the details (e.g. name, postal address, fax number, web address) on how to access the national spontaneous reporting system>.*

GIAPREZA is subject to additional monitoring as it contains a new active substance (Angiotensin II).

Company contact point

Medical Information at PAION Deutschland GmbH

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52078 Aachen

Germany

medinfo@paion.com

Annexes

ANNEX 1: Replacement Directions

PAION will provide a replacement for any impacted GIAPREZA vials. For product replacement, please contact

Supply Chain at Paion Deutschland GmbH
Heussstraße 25
52078 Aachen
Germany

Email: SC@paion.com

Phone: +49 241 4453 0