Edition: BP 2025 (Ph. Eur. 11.6 update)

Amiodarone Infusion

General Notices

Amiodarone Intravenous Infusion

Action and use

Potassium channel blocker; class III antiarrhythmic.

DEFINITION

Amiodarone Infusion is a sterile solution containing Amiodarone Hydrochloride. It is prepared by diluting Amiodarone Sterile Concentrate with a suitable diluent in accordance with the manufacturer's instructions.

The infusion complies with the requirements stated under Parenteral Preparations.

AMIODARONE STERILE CONCENTRATE

DEFINITION

Amiodarone Sterile Concentrate is a sterile solution of Amiodarone Hydrochloride in a suitable diluent.

The concentrate complies with the requirements for Concentrates for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

Content of amiodarone hydrochloride, $C_{25}H_{29}I_2NO_3,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Extract a volume of the concentrate containing 0.3 g of Amiodarone Hydrochloride with three 25-mL quantities of *dichloromethane*. Dry the combined extracts over *anhydrous sodium sulfate*, filter and evaporate to dryness. To the residue add 2 mL of 1M *sodium hydroxide* and extract with 25 mL of *ether*. Dry the extract over *anhydrous sodium sulfate*, filter and evaporate to dryness. Dry the residue obtained under reduced pressure over *phosphorus pentoxide* and dissolve in 2.5 mL of *dichloromethane*. The *infrared absorption spectrum* of the resulting solution, Appendix II A, is concordant with the *reference spectrum* of amiodarone *(RS 008)*.
B. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the peak in the chromatogram obtained with solution (2).

TESTS

Colour of solution

Not more intense than *reference solution* BY_4 or GY_4, Appendix IV B, Method II.

Iodides

Prepare a solution containing 1 volume *nitric acid*, 20 volumes of *water* and 80 volumes of *methanol* (solution A).

(1) Add 5.0 mL of a solution containing 0.0052% w/v of *potassium iodide* to a volume of the sterile concentrate containing 0.40 g of Amiodarone Hydrochloride and dilute to 50 mL with solution A.
(2) Dilute 10.0 mL of a solution containing 0.0052% w/v of *potassium iodide* to 50 mL with solution A.

Titrate solutions (1) and (2) with *0.001M silver nitrate VS* and determine the end point for each potentiometrically using a combined silver electrode. The volume used for the titration of solution (1) is not more than the volume required for the titration of solution (2) (500 ppm).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *acetonitrile (50%)*.

(1) Dilute a volume of the concentrate containing 50 mg of Amiodarone Hydrochloride to 20 mL.
(2) Dilute 1 volume of solution (1) to 500 volumes.
(3) 0.004% w/v of *amiodarone impurity D BPCRS*.
(4) 0.0005% w/v each of *amiodarone impurity D BPCRS* and *amiodarone impurity E EPCRS*.
(5) 0.1% w/v of *benzyl alcohol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 240 nm.
(f) Inject 10 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 1.5 times the retention time of amiodarone.

MOBILE PHASE

Buffer solution pH 4.9. To 800 mL of *water*, add 3 mL of *glacial acetic acid*, adjust to pH 4.9 with *dilute ammonia R1* and dilute to 1000 mL with *water*.

30 volumes of *methanol*, 40 volumes of *acetonitrile* and 30 volumes of buffer solution pH 4.9.

When the chromatograms are recorded under the prescribed conditions the retention times relative to amiodarone (retention time about 24 minutes) are impurity D, about 0.3 and impurity E, about 0.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity D and impurity E is at least 3.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (1.6%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak due to benzyl alcohol and any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *acetonitrile (50%)*.

(1) Dilute a volume of the concentrate containing 50 mg of Amiodarone Hydrochloride to 100 mL.
(2) 0.05% w/v of *amiodarone hydrochloride BPCRS*.
(3) 0.0005% w/v each of *amiodarone impurity D BPCRS* and *amiodarone impurity E EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity D and impurity E is at least 3.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{25}H_{29}I_2NO_3$,HCl in the infusion using the declared content of $C_{25}H_{29}I_2NO_3$,HCl in *amiodarone hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those under Amiodarone Hydrochloride.

STORAGE

Amiodarone Sterile Concentrate should be protected from light.