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

Flecainide Injection

General Notices

Action and use

Class I antiarrhythmic.

DEFINITION

Flecainide Injection is a sterile solution of Flecainide Acetate in Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of flecainide acetate, $C_{17}H_{20}F_6N_2O_3,C_2H_4O_2$

95.0 to 105.0% of the stated amount.

CHARACTERISTICS

A clear, colourless or almost colourless solution.

IDENTIFICATION

A. The *light absorption*, Appendix II B, of the solution obtained in the Assay in the range 230 nm to 350 nm exhibits a maximum at 296 nm.
B. In the test for (Piperidin-2-yl)methanamine, examine the chromatograms under *ultraviolet light (254 nm)* before spraying. The principal spot in the chromatogram obtained with solution (2) corresponds to that in the chromatogram obtained with solution (3).

TESTS

Acidity

pH, 5.0 to 6.5, Appendix V L.

(Piperidin-2-yl)methanamine

Carry out the method for *thin-layer chromatography*, Appendix III A, using a silica gel F_{254} precoated plate (Merck plates are suitable) and a mixture of 2 volumes of *methanol*, 5 volumes of 18M *ammonia*, 100 volumes of *acetone* and 100 volumes of *dichloromethane* as the mobile phase but allowing the solvent front to ascend 10 cm above the line of application. Apply separately to the plate 1 µL of solution (1) and 5 µL of each of solutions (2) and (3). Solution (1) contains 0.025% w/v of *flecainide acetate impurity B EPCRS* [(piperidin-2-yl)methanamine] in *methanol*. For solution (2) dilute the injection, if necessary, with *methanol* to contain 1% w/v of flecainide acetate. Solution (3) contains 1% w/v of *flecainide*

acetate BPCRS in *methanol*. After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm)* (for Identification test B). Spray the plate with a freshly prepared 0.2% w/v solution of *ninhydrin* in *methanol*, heat the plate at 105° for approximately 5 minutes and examine immediately. In the chromatogram obtained with solution (2) any bluish-purple spot corresponding to (piperidin-2-yl)methanamine is not more intense than the spot in the chromatogram obtained with solution (1) (0.5%).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Solution (1) is the injection diluted, if necessary, with a mixture of 29 volumes of *acetonitrile* and 71 volumes of *water* to contain 1.0% w/v of flecainide acetate. For solution (2) dilute 1 volume of solution (1) to 100 volumes with a mixture of 29 volumes of *acetonitrile* and 71 volumes of *water* and further dilute 1 volume of this solution to 5 volumes with the same solvent mixture. Solution (3) contains 0.01% w/v of each of *flecainide acetate BPCRS* and *flecainide impurity A EPCRS* in a mixture of 29 volumes of *acetonitrile* and 71 volumes of *water*.

The chromatographic procedure may be carried out using (a) a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Zorbax C8 is suitable), (b) as the mobile phase with a flow rate of 2 mL per minute a mixture of 5 volumes of 1M *tetrabutylammonium hydroxide*, 10 volumes of *glacial acetic acid*, 290 volumes of *acetonitrile* and 710 volumes of *water*, the mixture adjusted to pH 5.8 using 18M *ammonia*, and (c) a detection wavelength of 254 nm.

Inject 20 µL of each solution. The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks corresponding to flecainide and flecainide impurity A is at least 3.5.

For solution (1) allow the chromatography to proceed for nine times the retention time of the principal peak. In the chromatogram obtained with solution (1) the area of any *secondary peak* is not greater than the area of the peak in the chromatogram obtained with solution (2) (0.2%) and the sum of the areas of any such peaks is not greater than two and a half times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%). Disregard any peak with an area less than 0.05 times the area of the peak in the chromatogram obtained with solution (2) (0.01%).

ASSAY

Dilute the injection with a 0.2% v/v solution of *lactic acid* to produce a solution containing 0.01% w/v of flecainide acetate and measure the *absorbance* of the resulting solution at the maximum at about 296 nm, Appendix II B, using a 0.2% v/v solution of *lactic acid* in the reference cell. Calculate the content of $C_{17}H_{20}F_6N_2O_3,C_2H_4O_2$ in the injection from the *absorbance* obtained with a solution containing 0.01% w/v of *flecainide acetate BPCRS* in a 0.2% v/v solution of *lactic acid* and using the declared content of $C_{17}H_{20}F_6N_2O_3,C_2H_4O_2$ in *flecainide acetate BPCRS*.

STORAGE

Flecainide Injection should not be allowed to freeze.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B and D stated under Flecainide Acetate.