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

Flecainide Oral Solution

General Notices

NOTE: This monograph has been developed to cover unlicensed formulations.

Action and use

Class I antiarrhythmic.

DEFINITION

Flecainide Oral Solution is a solution of Flecainide Acetate in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements. Where appropriate, the oral solution also complies with the requirements stated under Unlicensed Medicines.

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.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 190 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

(Piperidin-2-yl)methanamine (Impurity B)

Carry out the method for *thin-layer chromatography*, Appendix III A, protected from light, using the following solutions.

(1) Shake a quantity of the oral solution with sufficient *methanol* to produce a solution containing 0.1% w/v of Flecainide Acetate, centrifuge and use the supernatant liquid.
(2) 0.005% w/v of *flecainide impurity B EPCRS* in *methanol*.
(3) 10 volumes of a 0.1% w/v solution of *flecainide acetate BPCRS* in *methanol* and 1 volume of a 0.05% w/v solution of *flecainide impurity B EPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.

(c) Apply 10 µL of solution (1) and solution (3) and 1 µL of solution (2).
(d) Develop the plate to 10 cm.
(e) After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm)* to determine the position of the spot due to flecainide. Spray the plate with a freshly prepared 0.2% w/v solution of *ninhydrin* in *absolute ethanol*, heat the plate at 105° for approximately 5 minutes and examine immediately.

MOBILE PHASE

A freshly prepared mixture of 5 volumes of *concentrated ammonia* and 95 volumes of *acetone*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

LIMITS

In the chromatogram obtained with solution (1) any bluish-purple spot corresponding to (piperidin-2-yl)methanamine (flecainide impurity B) is not more intense than the spot in the chromatogram obtained with solution (2) (0.5%).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 29 volumes of *acetonitrile* and 71 volumes of *water*.

(1) Dilute a quantity of the oral solution to contain 0.1% w/v of Flecainide Acetate.
(2) Dilute 1 volume of solution (1) to 100 volumes and further dilute 1 volume to 5 volumes.
(3) 0.01% w/v each of *flecainide acetate BPCRS* and *flecainide impurity A EPCRS*.
(4) Dilute 1 volume of solution (2) to 2 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use 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) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for nine times the retention time of the principal peak.

MOBILE PHASE

5 volumes of 1M *tetrabutylammonium hydroxide*, 10 volumes of *glacial acetic acid*, 290 volumes of *acetonitrile* and 710 volumes of *water*; adjust the pH of the mixture to 5.8 using 18M *ammonia*.

When the chromatograms are recorded under the prescribed conditions, the relative retention of impurity A with reference to flecainide (retention time, about 4 minutes) is about 1.7.

SYSTEM SUITABILITY

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

LIMITS

In the chromatogram obtained with solution (1):

the area of any *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 *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 peaks which elute before the peak due to flecainide and any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 29 volumes of *acetonitrile* and 71 volumes of *water*.

(1) Dilute a quantity of the oral solution to contain 0.1% w/v of Flecainide Acetate.
(2) 0.1% w/v of *flecainide acetate BPCRS*.
(3) 0.01% w/v each of *flecainide acetate BPCRS* and *flecainide impurity A EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to flecainide and flecainide impurity A is at least 3.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{20}F_6N_2O_3,C_2H_4O_2$ in the oral solution using the declared content of $C_{17}H_{20}F_6N_2O_3,C_2H_4O_2$ in *flecainide acetate BPCRS*.

IMPURITIES

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