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Amitripyline Oral Solution

Details for the public consultation of this monograph are as follows:

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Deadline for Comment	31st March 2019
Target Publication Date (subject to change)	BP 2020
Notes:	New monograph

Action and use

Monoamine reuptake inhibitor; tricyclic antidepressant.

DEFINITION

Amitriptyline Oral Solution is a solution of Amitriptyline Hydrochloride in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of Amitriptyline Hydrochloride, $C_{20}H_{23}N,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for thin-layer chromatography, Appendix III A, using the following solutions.
(1) Dilute a quantity of the oral solution containing 50 mg of Amitriptyline Hydrochloride to 25 mL with a mixture of 1 volume of 2M *hydrochloric acid* and 9 volumes of *ethanol (96%)*.
(2) 0.2% w/v of *amitriptyline hydrochloride BPCRS* in 1 volume of 2M *hydrochloric acid* and 9 volumes of *ethanol (96%)*.
(3) 0.4% w/v of *amitriptyline hydrochloride BPCRS* and 0.4% w/v of *notriptyline hydrochloride BPCRS* in 1 volume of 2M *hydrochloric acid* and 9 volumes of *ethanol (96%)*.

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 2 µL of each solution.
(d) Develop the plate to 15 cm.

(e) After removal of the plate, dry in air and examine immediately under *ultraviolet light (254 nm)*.

MOBILE PHASE

5 volumes of *diethylamine*, 15 volumes of *ethyl acetate* and 85 volumes of *cyclohexane*.

SYSTEM SUITABILITY

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

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, 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

ACIDITY

pH, 2.5 to 3.5, Appendix V L.

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in the mobile phase

(1) Dilute a quantity of the oral solution containing 50 mg of Amitriptyline Hydrochloride to 50 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.001% w/v of *amitriptyline hydrochloride BPCRS*, 0.001% w/v of *cyclobenzaprine hydrochloride BPCRS* and 0.002% w/v of *dibenzosuberone BPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column 15 cm × 4.6 mm packed with *end-capped polar embedded octadecylsilyl amorphous organosilica polymer* (5 µm) (Waters X-Terra RP 18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for 3.5 times the retention time of amitriptyline for solution (1)

MOBILE PHASE

35 volumes of *acetonitrile* and 65 volumes of *dipotassium hydrogen orthophosphate*, previously adjusted to pH 7.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to amitriptyline (retention time about 12 minutes) are: impurity B, about 0.9 and impurity A, about 2.7.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between cyclobenzaprine and amitriptyline is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the peak due to dibenzosuberone in the chromatogram obtained with solution (3) (0.2%);

the area of any peak corresponding to impurity B is not greater than 0.2 times the area of the peak due cyclobenzaprine in the chromatogram obtained with solution (3) (0.2%);

the area of any *secondary peak* is not greater than 0.4 times 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 the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than half 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 the mobile phase.

(1) Dilute a quantity of the oral solution containing 10 mg of Amitriptyline Hydrochloride to 100 mL.
(2) 0.01% w/v of *amitriptyline hydrochloride BPCRS*.
(3) 0.001% w/v of *amitriptyline hydrochloride BPCRS*, 0.001% w/v of *cyclobenzaprine hydrochloride BPCRS* and 0.002% w/v of *dibenzosuberone BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure 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 cyclobenzaprine and amitriptyline is at least 2.0.

DETERMINATION OF CONTENT

Determine the weight per mL of the Oral Solution, Appendix V G, and calculate the content of $C_{20}H_{23}N$,HCl weight in volume, using the declared content of $C_{20}H_{23}N$,HCl in *amitriptyline hydrochloride BPCRS*.

STORAGE

Amitriptyline Oral Solution should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under *Amitriptyline Hydrochloride*.