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Pyridostigmine Tablets

General Notices

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

EAG/Panel/Working Party	Medicinal Chemicals 2
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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Related substances** Impurity B limit tightened, aligned with UK licenses

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Action and use

Cholinesterase inhibitor.

DEFINITION

Pyridostigmine Tablets contain Pyridostigmine Bromide.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of pyridostigmine bromide, $C_9H_{13}BrN_2O_2$

92.5 to 107.5% of the stated amount.

IDENTIFICATION

A. Triturate a quantity of the powdered tablets containing 0.1 g of Pyridostigmine Bromide with two 5 mL quantities of *water* and filter. Dilute the filtrate with *water* to contain 0.005% w/v of

Pyridostigmine Bromide. The *light absorption* of the resulting solution, Appendix II B, exhibits a maximum at 270 nm. Reserve the filtrate for use in tests B and C.

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

(1) Dilute 1 volume of the filtrate obtained in test A to 10 volumes with *methanol*.

(2) 0.1% w/v of *pyridostigmine bromide EPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel G*.

(b) Use the mobile phase as described below.

(c) Apply 10 µL of each solution.

(d) Develop the plate to 20 cm.

(e) After removal of the plate, dry in air and spray with *dilute potassium iodobismuthate solution*.

MOBILE PHASE

5 volumes of *water*, 10 volumes of *formic acid*, 35 volumes of *methanol* and 50 volumes of *chloroform*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

C. The filtrate obtained in test A yields the reactions characteristic of *bromides*, Appendix VI.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of powdered tablets containing 0.1 g of Pyridostigmine Bromide with 100 mL of a mixture of 30 volumes of *acetonitrile* and 70 volumes of *water* for 30 minutes and filter through a glass fibre filter (Whatman GF/C is suitable).

(2) Dilute 3 volumes of solution (1) to 100 volumes with a mixture of 30 volumes of *acetonitrile* and 70 volumes of *water*.

(3) Dilute 1 volume of solution (1) to 250 volumes with a mixture of 30 volumes of *acetonitrile* and 70 volumes of *water*.

(4) 0.0005% w/v each of *pyridostigmine impurity A EPCRS* and *pyridostigmine bromide EPCRS* in the mobile phase.

(5) Dilute 1 volume of solution (3) to 10 volumes with a mixture of 30 volumes of *acetonitrile* and 70 volumes of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS C18 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 1.1 mL per minute.

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(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to continue for at least twice the retention time of the peak due to pyridostigmine.

MOBILE PHASE

30 volumes of *acetonitrile* and 70 volumes of a 0.43% w/v solution of *sodium dodecyl sulfate*, previously adjusted to pH 2.0 with *orthophosphoric acid*.

Use the chromatogram obtained with solution (4) to identify the peak due to impurity A. When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to pyridostigmine (retention time about 32 minutes) are: impurity B, about 0.75; impurity A, about 0.92.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity A and pyridostigmine is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (3%);

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.4%);

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 (3) (0.4%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.04%).

ASSAY

Weigh and powder 20 tablets. Shake a quantity of the powdered tablets containing 0.15 g of Pyridostigmine Bromide with 50 mL of *water* for 30 minutes, filter, wash the residue with *water* and add sufficient *water* to produce 250 mL. Dilute 5 mL to 100 mL with *water* and measure the *absorbance* of the resulting solution at the maximum at 270 nm, Appendix II B. Calculate the content of $C_9H_{13}BrN_2O_2$ taking 186 as the value of A(1%, 1 cm) at the maximum at 270 nm.

STORAGE

Pyridostigmine Tablets should be protected from light.

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IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and B listed under Pyridostigmine Bromide.

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