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

Betahistine Dihydrochloride Tablets

General Notices

Action and use

Histamine H_1 receptor agonist; histamine H_3 receptor antagonist; treatment of vertigo, tinnitus, and hearing loss associated with Ménière's disease.

DEFINITION

Betahistine Dihydrochloride Tablets contain Betahistine Dihydrochloride.

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

Content of betahistine dihydrochloride, $C_8H_{12}N_2,2HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the powdered tablets containing 5 mg of Betahistine Dihydrochloride with 100 mL of *water* and filter. The *light absorption*, Appendix II B, in the range 230 to 350 nm exhibits a maximum at about 260 nm, a less well-defined maximum at about 267 nm and a shoulder at about 256 nm.
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

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.0009% w/v of Betahistine Dihydrochloride at the maximum at 260 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0009% w/v solution of *betahistine dihydrochloride BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of betahistine dihydrochloride, $C_8H_{12}N_2,2HCl$, in the medium from the absorbances obtained and using the declared content of $C_8H_{12}N_2,2HCl$ in *betahistine dihydrochloride BPCRS*.

LIMITS

The amount of betahistine dihydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

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

(1) To a quantity of the powdered tablets containing 32 mg of Betahistine Dihydrochloride, add 50 mL of the mobile phase and shake for 10 minutes. Dilute with sufficient mobile phase to produce 100 mL, mix, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 20 volumes with the mobile phase and further dilute 1 volume of the resulting solution to 25 volumes with the same solvent.
(3) 0.000032% w/v of *2-vinylpyridine* (impurity A) in *acetonitrile*.
(4) 0.00064% w/v each of *N-methyl-2-(pyridin-2-yl)-N-[2-(pyridine-2-yl)ethyl]ethanamine trihydrochloride BPCRS* (impurity C) and *betahistine dihydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped extra-dense bonded octadecylsilyl silica gel for chromatography* (5 µm) (Zorbax XDB Eclipse is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for four times the retention time of betahistine.

MOBILE PHASE

Dissolve 0.4 g of *hexylamine* in 600 mL of a solution containing 0.46% w/v of *sodium dihydrogen orthophosphate monohydrate* and 0.27% w/v of *sodium dodecyl sulfate*, add 400 mL of *acetonitrile*, mix and adjust the pH to 3.5 using *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to betahistine and impurity C is at least 3.0.

CALCULATION OF IMPURITIES

For impurity C, use the concentration of impurity C in solution (4).

For impurity A, use the concentration of impurity A in solution (3).

For each unspecified impurity, use the concentration of betahistine dihydrochloride in solution (2).

For the reporting threshold, use the concentration of betahistine dihydrochloride in solution (2).

For peak identification, use solutions (3) and (4).

Betahistine retention time: about 3 minutes.

Relative retention: impurity A, about 0.7 and impurity C, about 2.1.

LIMITS

— impurity C: not more than 2.0%;

— impurity A: not more than 0.2%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 2.0%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) To a quantity of the powdered tablets containing 32 mg of Betahistine Dihydrochloride, add 50 mL and shake for 10 minutes. Dilute to produce 100 mL, mix, centrifuge and use the supernatant liquid.
(2) 0.032% w/v of *betahistine dihydrochloride BPCRS*.
(3) 0.00064% w/v each of *N-methyl-2-(pyridin-2-yl)-N-[2-(pyridine-2-yl)ethyl]ethanamine trihydrochloride BPCRS* and *betahistine dihydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used, with the exception of run time.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to betahistine and impurity C is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_{12}N_2,2HCl$ in the tablets using the declared content of $C_8H_{12}N_2,2HCl$ in *betahistine dihydrochloride BPCRS*.

STORAGE

Betahistine Dihydrochloride Tablets should be protected from light and moisture.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Betahistine Dihydrochloride.