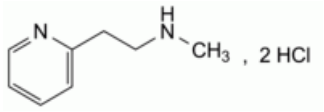
Edition: BP 2025 (Ph. Eur. 11.6 update)

Betahistine Dihydrochloride

General Notices

(Ph. Eur. monograph 1665)



$C_8H_{14}Cl_2N_2$ 209.1 *5579-84-0*

Action and use

Histamine H_1 receptor antagonist; antihistamine.

Preparation

Betahistine Dihydrochloride Tablets

Ph Eur

DEFINITION

N-Methyl-2-(pyridin-2-yl)ethanamine dihydrochloride.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or slightly yellow powder, very hygroscopic.

Solubility

Very soluble in water, soluble in ethanol (96 per cent), practically insoluble in 2-propanol.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Melting point (2.2.14): 150 °C to 154 °C.

B. Infrared absorption spectrophotometry (2.2.24).

Comparison betahistine dihydrochloride CRS.

C. Thin-layer chromatography (2.2.27).

Test solution Dissolve 10 mg of the substance to be examined in 2 mL of ethanol (96 per cent) R.

Reference solution Dissolve 10 mg of betahistine dihydrochloride CRS in 2 mL of ethanol (96 per cent) R.

Plate TLC silica gel GF_{254} plate R.

Mobile phase concentrated ammonia R, ethyl acetate R, methanol R (0.75:15:30 *V/V/V*).

Application 2 µL.

Development Over 2/3 of the plate.

Drying At 110 °C for 10 min.

Detection Examine in ultraviolet light at 254 nm.

Results The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

D. It gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S

Dissolve 5.0 g in carbon dioxide-free water R, and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution B_8 (2.2.2, Method II).

pH (2.2.3)

2.0 to 3.0 for solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 25 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution (a) Dissolve 10 mg of betahistine dihydrochloride CRS and 10 mg of 2-vinylpyridine R in the mobile phase and dilute to 50.0 mL with the mobile phase. Dilute 2.0 mL of the solution to 50.0 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase.

Reference solution (c) Dilute 2.0 mL of reference solution (b) to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 3.0 mm;

— *stationary phase*: base-deactivated end-capped octadecylsilyl silica gel for chromatography R (5 µm).

Mobile phase Dissolve 2.0 g of sodium dodecyl sulfate R in a mixture of 15 mL of a 10 per cent *V/V* solution of sulfuric acid R, 35 mL of a 17 g/L solution of tetrabutylammonium hydrogen sulfate R and 650 mL of water R; adjust to pH 3.3 using dilute sodium hydroxide solution R and mix with 300 mL of acetonitrile R.

Flow rate 1 mL/min.

Detection Spectrophotometer at 260 nm.

Injection 20 µL.

Run time 4 times the retention time of betahistine.

Relative retention With reference to betahistine (retention time = about 7 min): impurity B = about 0.2; impurity A = about 0.3; impurity C = about 3.

System suitability Reference solution (a):

— *resolution*: minimum 3.5 between the peaks due to 2-vinylpyridine and betahistine.

Limits:

— *correction factor*: for the calculation of content, multiply the peak area of impurity B by 0.4;

— *impurities A, B, C*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than 0.5 times of the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent);

— *total*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 80.0 mg in 50 mL of *ethanol (96 per cent) R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Read the volume added to reach the second point of inflexion.

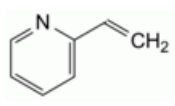
1 mL of *0.1 M sodium hydroxide* is equivalent to 10.46 mg of $C_8H_{14}Cl_2N_2$.

STORAGE

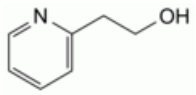
In an airtight container.

IMPURITIES

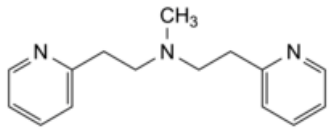
Specified impurities *A, B, C.*



A. 2-ethenylpyridine (2-vinylpyridine),



B. 2-(pyridin-2-yl)ethanol,



C. *N*-methyl-2-(pyridin-2-yl)-*N*-[2-(pyridin-2-yl)ethyl]ethanamine.

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