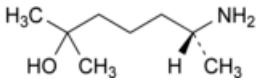
Edition: BP 2025 (Ph. Eur. 11.6 update)

Heptaminol Hydrochloride

General Notices

(Ph. Eur. monograph 1980)



and enantiomer , HCl

$C_8H_{20}ClNO$ 181.7 *543-15-7*

Action and use

Non-selective phosphodiesterase inhibitor; treatment of reversible airways obstruction.

Ph Eur

DEFINITION

(6*RS*)-6-Amino-2-methylheptan-2-ol hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water, soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. To 1 mL of solution S (see Tests) add 4 mL of *water R* and 2 mL of a 200 g/L solution of *ammonium and cerium nitrate R* in *dilute nitric acid R1*. An orange-brown colour develops.
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison heptaminol hydrochloride CRS.

C. Examine the chromatograms obtained in the test for related substances.

Detection Examine in daylight.

Results The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (b).

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 BY_6 (2.2.2, Method II).

Acidity or alkalinity

To 10 mL of solution S add 0.1 mL of methyl red solution R and 0.3 mL of 0.01 M hydrochloric acid. The solution is red. Add 0.6 mL of 0.01 M sodium hydroxide. The solution is yellow.

Related substances

Thin-layer chromatography (2.2.27).

Test solution (a) Dissolve 0.50 g of the substance to be examined in methanol R and dilute to 5.0 mL with the same solvent.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10 mL with methanol R.

Reference solution (a) Dilute 3.0 mL of test solution (a) to 10.0 mL with methanol R. Dilute 1.0 mL of this solution to 50.0 mL with methanol R.

Reference solution (b) Dissolve 0.10 g of heptaminol hydrochloride CRS in methanol R and dilute to 10 mL with the same solvent.

Reference solution (c) Dissolve 10.0 mg of heptaminol impurity A CRS in methanol R and dilute to 5.0 mL with the same solvent.

Reference solution (d) Dilute 1.0 mL of reference solution (c) to 10.0 mL with methanol R.

Reference solution (e) To 2.5 mL of reference solution (c) add 0.5 mL of test solution (b) and dilute to 5 mL with methanol R.

Plate TLC silica gel G plate R.

Mobile phase concentrated ammonia R, dioxan R, 2-propanol R (10:50:50 *V/V/V*).

Application 10 µL; apply test solutions (a) and (b) and reference solutions (a), (b), (d) and (e).

Development Over 2/3 of the plate.

Drying In air.

Detection Expose the plate to iodine vapour for at least 15 h.

System suitability The chromatogram obtained with reference solution (e) shows 2 clearly separated principal spots and the chromatogram obtained with reference solution (a) shows a single principal spot.

Limits In the chromatogram obtained with test solution (a):

— *impurity A*: any spot corresponding to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (d) (0.2 per cent),

— *any other impurity*: any spot, apart from the principal spot and any spot corresponding to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.6 per cent).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4 h.

Sulfated ash (*2.4.14*)

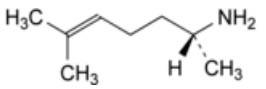
Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.140 g in 50 mL of *alcohol R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 18.17 mg of $C_8H_{20}ClNO$.

IMPURITIES



and enantiomer

A. (2*RS*)-6-methylhept-5-en-2-amine.