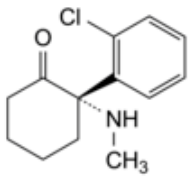
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ketamine Hydrochloride

General Notices

(Ph. Eur. monograph 1020)



and enantiomer , HCl

$C_{13}H_{17}Cl_2NO$ 274.2 *1867-66-9*

Action and use

Intravenous general anaesthetic

Preparations

Ketamine Injection

Ketamine Nasal Spray

Ketamine Oral Solution

Ph Eur

DEFINITION

(2*RS*)-2-(2-Chlorophenyl)-2-(methylamino)cyclohexanone 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 and in methanol, soluble in ethanol (96 per cent).

mp

About 260 °C, with decomposition.

IDENTIFICATION

A. Optical rotation (see Tests).
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *ketamine hydrochloride CRS*.

C. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S

Dissolve 10.0 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

pH (*2.2.3*)

3.5 to 4.1.

Dilute 10 mL of solution S to 20 mL with *carbon dioxide-free water R*.

Optical rotation (*2.2.7*)

-0.2° to + 0.2°.

Dilute 2.5 mL of solution S to 25.0 mL with *water R*.

Related substances

Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use.*

Test solution Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a) Dissolve 5 mg of *ketamine impurity A CRS* in the mobile phase and dilute to 10.0 mL with the mobile phase (using ultrasound if necessary). To 1.0 mL of the solution, add 0.5 mL of the test solution and dilute to 100.0 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 10.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.125 m, Ø = 4.0 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Dissolve 0.95 g of *sodium hexanesulfonate R* in 1 L of a mixture of 25 volumes of *acetonitrile R1* and 75 volumes of *water R* and add 4 mL of *acetic acid R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 215 nm.

Injection 20 µL.

Run time 10 times the retention time of ketamine.

Relative retention With reference to ketamine (retention time = about 3 min): impurity A = about 1.6; impurity B = about 3.3; impurity C = about 4.6.

System suitability Reference solution (a):

— *resolution*: minimum 1.5 between the peaks due to ketamine and impurity A.

Limits:

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

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

— *total*: not more than 2.5 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 (b) (0.05 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 3 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 50 mL of *methanol R* and add 1.0 mL of *0.1 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.

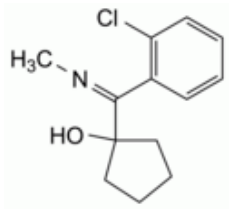
1 mL of *0.1 M sodium hydroxide* is equivalent to 27.42 mg of $C_{13}H_{17}Cl_2NO$.

STORAGE

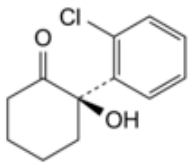
Protected from light.

IMPURITIES

Specified impurities *A, B, C.*

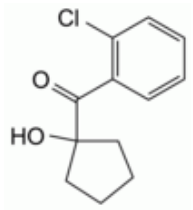


A. 1-(2-chloro-*N*-methylbenzimidoyl)cyclopentanol,



and enantiomer

B. (2*RS*)-2-(2-chlorophenyl)-2-hydroxycyclohexanone,



C. (2-chlorophenyl)(1-hydroxycyclopentyl)methanone.

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