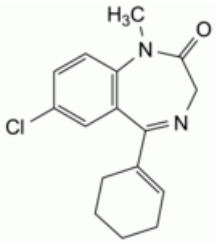
Edition: BP 2025 (Ph. Eur. 11.6 update)

Tetrazepam

General Notices

(Ph. Eur. monograph 1738)



$C_{16}H_{17}ClN_2O$ 288.8 *10379-14-3*

Action and use

Benzodiazepine; hypnotic.

Ph Eur

DEFINITION

7-Chloro-5-(cyclohex-1-enyl)-1-methyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

Content

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

CHARACTERS

Appearance

Light yellow or yellow crystalline powder.

Solubility

Practically insoluble in water, freely soluble in methylene chloride, soluble in acetonitrile.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison Ph. Eur. reference spectrum of tetrazepam.

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 25.0 mg of the substance to be examined in acetonitrile R and dilute to 25.0 mL with the same solvent.

Reference solution (a) Dissolve 5.0 mg of the substance to be examined and 5.0 mg of tetrazepam impurity C CRS in acetonitrile R and dilute to 10.0 mL with the same solvent. Dilute 1.0 mL of the solution to 10.0 mL with acetonitrile R.

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

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

Mobile phase:

— *mobile phase A*: mix 40 volumes of acetonitrile R and 60 volumes of a 3.4 g/L solution of potassium dihydrogen phosphate R;

— *mobile phase B*: acetonitrile R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 35	100	0
35 - 40	100 → 55	0 → 45
40 - 50	55	45

Flow rate 1.5 mL/min.

Detection A spectrophotometer at 229 nm.

Injection 20 µL.

System suitability Reference solution (a):

— resolution: minimum 2.0 between the peaks due to tetrazepam and to impurity C.

Limits:

— *any impurity*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 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).

Chlorides (2.4.4)

Maximum 100 ppm.

Dissolve 0.750 g in 10 mL of methylene chloride R and add 15 mL of water R. Shake and separate the 2 layers. Dilute 10 mL of the aqueous layer to 15 mL with water R.

Loss on drying (*2.2.32*)

Maximum 0.5 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

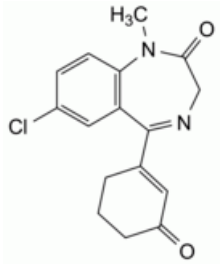
Dissolve 0.230 g in 50.0 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 28.88 mg of $C_{16}H_{17}ClN_2O$.

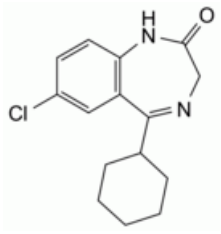
STORAGE

Protected from light.

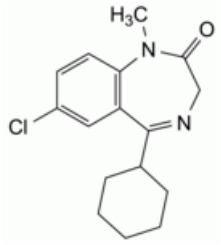
IMPURITIES



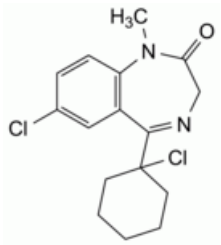
A. 7-chloro-1-methyl-5-(3-oxocyclohex-1-enyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one,



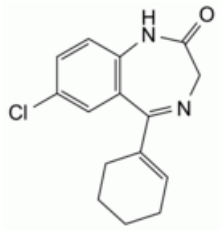
B. 7-chloro-5-cyclohexyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one,



C. 7-chloro-5-cyclohexyl-1-methyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one,



D. 7-chloro-5-(1-chlorocyclohexyl)-1-methyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one,



E. 7-chloro-5-(cyclohex-1-enyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

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