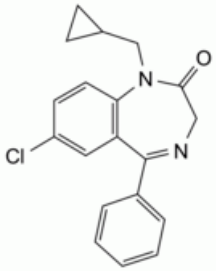
Edition: BP 2025 (Ph. Eur. 11.6 update)

Prazepam

General Notices

(Ph. Eur. monograph 1466)



$C_{19}H_{17}ClN_2O$ 324.8 *2955-38-6*

Action and use

Anxiolytic.

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DEFINITION

7-Chloro-1-(cyclopropylmethyl)-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in methylene chloride, sparingly soluble in anhydrous ethanol.

mp

About 145 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison prazepam CRS.

TESTS

Related substances

Liquid chromatography (2.2.29).

Solvent mixture acetonitrile R1, water for chromatography R (50:50 *V/V*).

Test solution Dissolve 50 mg of the substance to be examined in 25 mL of acetonitrile R1 and dilute to 50.0 mL with water for chromatography R.

Reference solution (a) Dissolve 5 mg of aminochlorobenzophenone R (impurity C) in acetonitrile R1 and dilute to 50.0 mL with the same solvent. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the test solution.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: end-capped extra-dense bonded octadecylsilyl silica gel for chromatography R (1.8 µm);

— *temperature*: 55 °C.

Mobile phase:

— *mobile phase A*: methanol R1, water for chromatography R (5:95 *V/V*);

— *mobile phase B*: methanol R1, acetonitrile R1 (5:95 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 0.5	55	45
0.5 - 6.5	55 → 15	45 → 85
6.5 - 8.5	15	85

Flow rate 2.0 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 2 µL.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity C.

Relative retention With reference to prazepam (retention time = about 3 min): impurity C = about 0.9.

System suitability Reference solution (a):

— resolution: minimum 2.5 between the peaks due to impurity C and prazepam.

Calculation of percentage contents:

— for each impurity, use the concentration of prazepam in reference solution (b).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 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.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 25 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

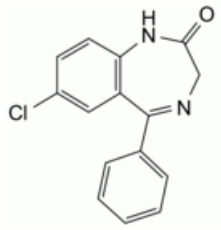
1 mL of *0.1 M perchloric acid* is equivalent to 32.48 mg of $C_{19}H_{17}ClN_2O$.

STORAGE

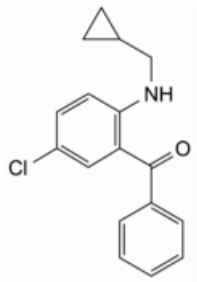
Protected from light.

IMPURITIES

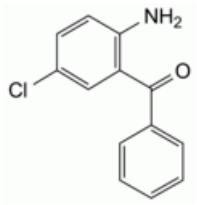
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, D.



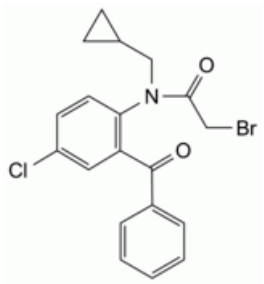
A. 7-chloro-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one (nordazepam),



B. [5-chloro-2-[(cyclopropylmethyl)amino]phenyl]phenylmethanone,



C. (2-amino-5-chlorophenyl)phenylmethanone (aminochlorobenzophenone),



D. *N*-(2-benzoyl-4-chlorophenyl)-2-bromo-*N*-(cyclopropylmethyl)acetamide.

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