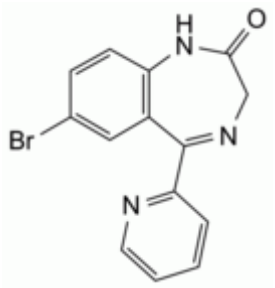
Edition: BP 2024 (Ph. Eur. 11.3 update)

Bromazepam

General Notices

(Ph. Eur. monograph 0879)



$C_{14}H_{10}BrN_3O$ 316.2 *1812-30-2*

Action and use

Benzodiazepine.

Ph Eur

DEFINITION

7-Bromo-5-(pyridin-2-yl)-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 yellowish, crystalline powder.

Solubility

Practically insoluble in water, slightly soluble or sparingly soluble in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison bromazepam CRS.

TESTS

Related substances

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

Solvent mixture Mix 1 volume of acetonitrile R and 8 volumes of methanol R.

Test solution Dissolve 10.0 mg of the substance to be examined in 9 mL of the solvent mixture. Dilute to 20.0 mL with an 11.33 g/L solution of potassium dihydrogen phosphate R previously adjusted to pH 7.0 with a 100 g/L solution of potassium hydroxide R.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve 5 mg of bromazepam for system suitability A CRS (containing impurities A and C) in 5 mL of the solvent mixture. Dilute to 10 mL with an 11.33 g/L solution of potassium dihydrogen phosphate R previously adjusted to pH 7.0 with a 100 g/L solution of potassium hydroxide R.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: end-capped extra-dense bonded octadecylsilyl silica gel for chromatography R (3.5 µm);

— *temperature*: 50 °C.

Mobile phase Mix 5 volumes of acetonitrile for chromatography R, 45 volumes of methanol R1 and 50 volumes of an 11.33 g/L solution of potassium dihydrogen phosphate R previously adjusted to pH 7.0 with a 100 g/L solution of potassium hydroxide R.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 20 µL.

Run time 4 times the retention time of bromazepam.

Identification of impurities Use the chromatogram supplied with *bromazepam for system suitability A CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and C.

Relative retention With reference to bromazepam (retention time = about 5 min): impurity A = about 1.5; impurity C = about 1.6.

System suitability Reference solution (b):

— *resolution*: minimum 1.2 between the peaks due to impurities A and C.

Calculation of percentage contents:

— for each impurity, use the concentration of bromazepam in reference solution (a).

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 0.2 per cent, determined on 1.000 g by drying *in vacuo* at 80 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 20 mL of *anhydrous acetic acid R*. Add 50 mL of *acetic anhydride 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 31.62 mg of $C_{14}H_{10}BrN_3O$.

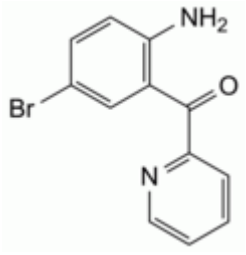
STORAGE

Protected from light.

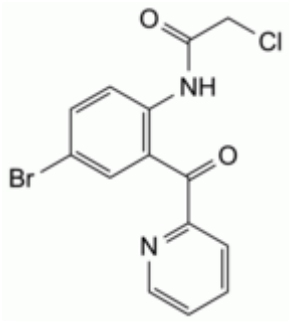
IMPURITIES

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

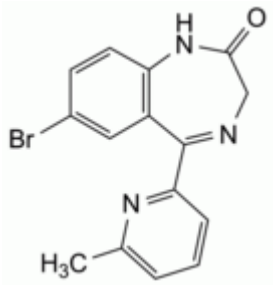
impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, D, E.



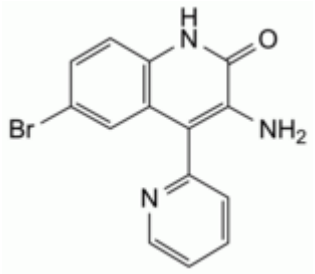
A. (2-amino-5-bromophenyl)(pyridin-2-yl)methanone,



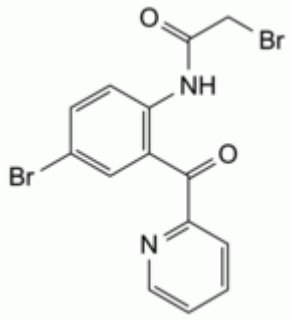
B. *N*-[4-bromo-2-(pyridine-2-carbonyl)phenyl]-2-chloroacetamide,



C. 7-bromo-5-(6-methylpyridin-2-yl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one,



D. 3-amino-6-bromo-4-(pyridin-2-yl)quinolin-2(1*H*)-one,



E. 2-bromo-*N*-[4-bromo-2-(pyridine-2-carbonyl)phenyl]acetamide.

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