Reference solution (c). Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase. Dilute 1.0 ml of this solution to 20.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.15 m, Ø = 3.9 mm,

– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: dissolve 0.50 g of *sodium edetate R* in 350 ml of *water R*, add 4.0 ml of *hexylamine R* and mix. Adjust to pH 3.0 with *phosphoric acid R*. Add 600 ml of *methanol R* and dilute to 1000 ml with *water R*.

Flow rate: 1.3 ml/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 µl.

Run time: 4 times the retention time of clioquinol.

Relative retention with reference to clioquinol (retention time = about 10 min): impurity A = about 0.4; impurity B = about 0.7; impurity C = about 1.3.

System suitability: reference solution (a):

– *resolution*: minimum 3.0 between the peaks due to clioquinol and impurity C.

Limits:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (2.0 per cent),

– *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (1.0 per cent),

– *impurity C*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (1.0 per cent),

– *any other impurity*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent),

– *total of the nominal contents of impurities A, B, C and any other impurities*: maximum 3.0 per cent,

– *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Halides: maximum 140 ppm, expressed as chlorides.

Shake 0.5 g with 25 ml of *water R* for 1 min and filter. To the filtrate add 0.5 ml of *dilute nitric acid R* and 0.5 ml of *silver nitrate solution R2*. Allow to stand for 5 min. Any opalescence is not more intense than that in a standard prepared at the same time by adding 0.5 ml of *silver nitrate solution R2* to 25 ml of *water R* containing 0.2 ml of *0.01 M hydrochloric acid* and 0.5 ml of *dilute nitric acid R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying over *diphosphorus pentoxide R* at a pressure not exceeding 0.7 kPa for 24 h.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 20 ml of *acetic anhydride R* and add 30 ml of *glacial acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

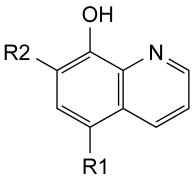
1 ml of *0.1 M perchloric acid* is equivalent to 30.55 mg of total quinolines, calculated as clioquinol.

STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C.



A. R1 = Cl, R2 = H: 5-chloroquinolin-8-ol,

B. R1 = R2 = Cl: 5,7-dichloroquinolin-8-ol,

C. R1 = R2 = I: 5,7-diiodoquinolin-8-ol.

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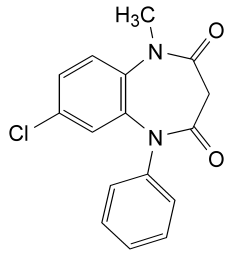
corrected 6.0

CLOBAZAM

Clobazamum



$C_{16}H_{13}ClN_2O_2$ M_r 300.7
[22316-47-8]

DEFINITION

7-Chloro-1-methyl-5-phenyl-1,5-dihydro-3*H*-1,5-benzodiazepine-2,4-dione.

Content: 97.0 per cent to 103.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: slightly soluble in water, freely soluble in methylene chloride, sparingly soluble in alcohol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of clobazam.*

TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 10.0 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 5.0 mg of *clobazam impurity A CRS* in the mobile phase and dilute to 50.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 100.0 ml with the mobile phase.

Reference solution (b). Dissolve 5 mg of *chlordiazepoxide CRS* and 5 mg of *clonazepam CRS* in the mobile phase and dilute to 50 ml with the mobile phase. Dilute 1 ml of the solution to 100 ml with the mobile phase.

Reference solution (c). Dilute 1.0 ml of the test solution to 200.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

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

Mobile phase: *acetonitrile R, water R* (40:60 *V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 230 nm.

Injection: 20 µl.

Run time: 5 times the retention time of clobazam.

Retention time: clobazam = about 15 min.

System suitability: reference solution (b):

– *resolution*: minimum 1.3 between the peaks due to chlordiazepoxide and clonazepam.

Limits:

– *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent),

– *any other impurity*: not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.2 per cent),

– *total of other impurities*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent),

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (c) (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.

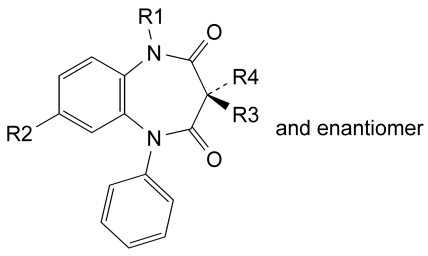
Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on the residue obtained in the test for loss on drying.

ASSAY

Dissolve 50.0 mg in *alcohol R* and dilute to 100.0 ml with the same solvent. Dilute 2.0 ml of the solution to 250.0 ml with *alcohol R*. Measure the absorbance (*2.2.25*) at the maximum at 232 nm.

Calculate the content of $C_{16}H_{13}ClN_2O_2$ taking the specific absorbance to be 1380.

IMPURITIES

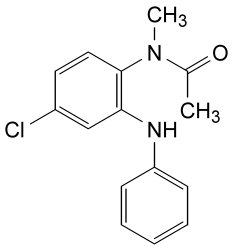


A. R1 = R3 = R4 = H, R2 = Cl: 7-chloro-5-phenyl-1,5-dihydro-3*H*-1,5-benzodiazepine-2,4-dione,

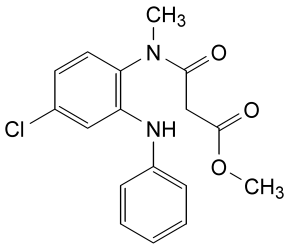
B. R1 = CH_3, R2 = R3 = R4 = H: 1-methyl-5-phenyl-1,5-dihydro-3*H*-1,5-benzodiazepine-2,4-dione,

C. R1 = R3 = CH_3, R2 = Cl, R4 = H: (3*RS*)-7-chloro-1,3-dimethyl-5-phenyl-1,5-dihydro-3*H*-1,5-benzodiazepine-2,4-dione,

D. R1 = R3 = R4 = CH_3, R2 = Cl: 7-chloro-1,3,3-trimethyl-5-phenyl-1,5-dihydro-3*H*-1,5-benzodiazepine-2,4-dione,



E. *N*-[4-chloro-2-(phenylamino)phenyl]-*N*-methylacetamide,



F. methyl 3-[[4-chloro-2-(phenylamino)phenyl]methylamino]-3-oxopropanoate.

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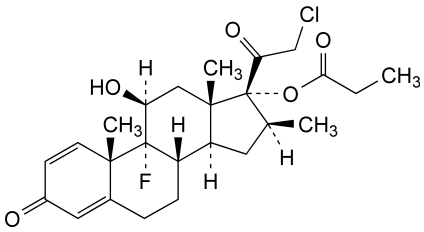
corrected 6.0

CLOBETASOL PROPIONATE

Clobetasoli propionas



$C_{25}H_{32}ClFO_5$ M_r 467.0
[25122-46-7]

DEFINITION

21-Chloro-9-fluoro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-17-yl propanoate.

Content: 97.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: practically insoluble in water, freely soluble in acetone, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *clobetasol propionate CRS*.

TESTS

Specific optical rotation (*2.2.7*): + 112 to + 118 (dried substance).

Dissolve 0.500 g in *acetone R* and dilute to 50.0 ml with the same solvent.