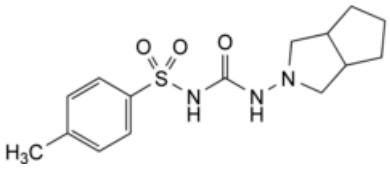
Edition: BP 2025 (Ph. Eur. 11.6 update)

Gliclazide

General Notices

(Ph. Eur. monograph 1524)



$C_{15}H_{21}N_3O_3S$ 323.4 *21187-98-4*

Action and use

Inhibition of ATP-dependent potassium channels (sulfonylurea); treatment of diabetes mellitus.

Preparations

Gliclazide Prolonged-release Tablets

Gliclazide Tablets

Ph Eur

DEFINITION

N-[(Hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)carbamoyl]-4-methylbenzene-1-sulfonamide.

Content

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

CHARACTERS

Appearance

White or almost white powder.

Solubility

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

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison gliclazide CRS.

TESTS

Related substances

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

Solvent mixture acetonitrile R, water R (45:55 *V/V*).

Test solution Dissolve 50.0 mg of the substance to be examined in 23 mL of acetonitrile R and dilute to 50.0 mL with water R.

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

Reference solution (b) Dissolve 5 mg of the substance to be examined and 15 mg of gliclazide impurity F CRS in 23 mL of acetonitrile R and dilute to 50 mL with water R. Dilute 1 mL of the solution to 20 mL with the solvent mixture.

Reference solution (c) Dissolve 15.0 mg of gliclazide impurity F CRS in 45 mL of acetonitrile R and dilute to 100.0 mL with water R. Dilute 1.0 mL of the solution to 100.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.25 m, Ø = 4 mm;

— *stationary phase*: octylsilyl silica gel for chromatography R (4 µm).

Mobile phase triethylamine R, trifluoroacetic acid R, acetonitrile for chromatography R, water for chromatography R (0.1:0.1:45:55 *V/V/V/V*).

Flow rate 0.9 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 20 µL.

Run time Twice the retention time of gliclazide.

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

Relative retention With reference to gliclazide (retention time = about 16 min): impurity F = about 0.9.

System suitability Reference solution (b):

— resolution: minimum 1.8 between the peaks due to impurity F and gliclazide.

Limits:

— *impurity F*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.15 per cent);

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

— *sum of impurities other than F*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Impurity B

Liquid chromatography (2.2.29) as described in the test for related substances with the following modifications.

Test solution Dissolve 0.400 g of the substance to be examined in 2.5 mL of *dimethyl sulfoxide R* and dilute to 10.0 mL with *water R*. Stir for 10 min, store at 4 °C for 30 min and filter.

Reference solution Dissolve 20.0 mg of *gliclazide impurity B CRS* in *dimethyl sulfoxide R* and dilute to 100.0 mL with the same solvent. To 1.0 mL of the solution, add 12 mL of *dimethyl sulfoxide R* and dilute to 50.0 mL with *water R*. To 1.0 mL of this solution, add 12 mL of *dimethyl sulfoxide R* and dilute to 50.0 mL with *water R*.

Injection 50 µL.

Identification of impurities Use the chromatogram obtained with the reference solution to identify the peak due to impurity B.

Retention time Impurity B = about 7 min.

Limit:

— *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (2 ppm).

Loss on drying (2.2.32)

Maximum 0.25 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

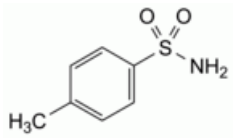
Dissolve 0.250 g in 50 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.2.20).

1 mL of *0.1 M perchloric acid* is equivalent to 32.34 mg of $C_{15}H_{21}N_3O_3S$.

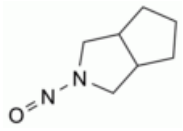
IMPURITIES

Specified impurities *B, F.*

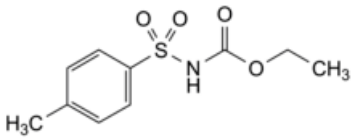
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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, C, D, E, G.*



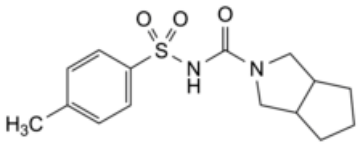
A. 4-methylbenzene-1-sulfonamide,



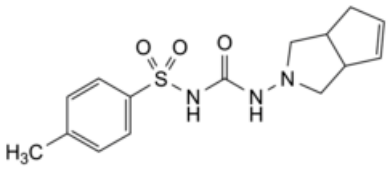
B. 2-nitrosooctahydrocyclopenta[*c*]pyrrole,



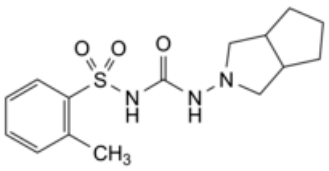
C. ethyl (4-methylbenzene-1-sulfonyl)carbamate,



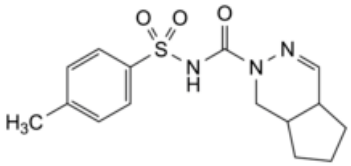
D. *N*-(4-methylbenzene-1-sulfonyl)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-carboxamide,



E. 4-methyl-*N*-[(3,3a,4,6a-tetrahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)carbamoyl]benzene-sulfonamide,



F. 2-methyl-*N*-[(hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)carbamoyl]benzene-1-sulfonamide,



G. *N*-[(4-methylbenzene-1-sulfonyl)-1,4a,5,6,7,7a-hexahydro-2*H*-cyclopenta[*d*]pyridazine-2-carboxamide.

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