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

Gliclazide Tablets

General Notices

Action and use

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

DEFINITION

Gliclazide Tablets contain Gliclazide.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of gliclazide, $C_{15}H_{21}N_3O_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.16 g of Gliclazide with 20 mL of *dichloromethane*, centrifuge and evaporate the supernatant liquid to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of gliclazide *(RS 168)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.
(b) Use 900 mL of *phosphate buffer pH 7.4*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a 10-mL sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, expected to contain 0.00125% w/v of Gliclazide at 226 nm and 290 nm, Appendix II B using *phosphate buffer pH 7.4* in the reference cell. Correct the absorbance obtained at 226 nm by subtracting the absorbance obtained at 290 nm.
(2) Measure the *absorbance* of a 0.00124% w/v solution of *gliclazide BPCRS* using *phosphate buffer pH 7.4* in the reference cell. Correct the absorbance obtained at 226 nm by subtracting the absorbance obtained at 290 nm.

DETERMINATION OF CONTENT

Calculate the total content of $C_{15}H_{21}N_3O_3S$ in the medium from the absorbances obtained and using the declared content of $C_{15}H_{21}N_3O_3S$ in *gliclazide BPCRS*.

LIMITS

The amount of gliclazide released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Prepare the solutions immediately before use.

Solution A: 45 volumes of *acetonitrile* and 55 volumes of *water*.

(1) Shake a quantity of the powdered tablets containing 0.8 g of Gliclazide with 160 mL of *acetonitrile* and dilute to 200 mL with *acetonitrile*. Filter and dilute 1 volume of the filtrate to 5 volumes with a mixture of 1 volume of *acetonitrile* and 2 volumes of *water*.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A. Further dilute 1 volume to 5 volumes with solution A.
(3) Dissolve 5 mg of *gliclazide BPCRS* and 15 mg of *gliclazide impurity F BPCRS* in 25 mL of *acetonitrile*, dilute to 50 mL with *water* and dilute 1 volume of the resulting solution to 20 volumes with solution A.
(4) Dissolve 8 mg of *gliclazide impurity F BPCRS* in 25 mL of *acetonitrile*, dilute to 50 mL with *water* and dilute 1 volume of the resulting solution to 100 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *octylsilyl silica gel for chromatography* (4 µm) (Superspher 60 RP-8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.9 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 235 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for twice the retention time of the principal peak.

MOBILE PHASE

0.1 volumes of *triethylamine*, 0.1 volumes of *trifluoroacetic acid*, 45 volumes of *acetonitrile* and 55 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the relative retention with reference to gliclazide (retention time about 16 minutes) is: impurity F, about 0.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gliclazide and impurity F is at least 1.8.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity F is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the area of any other *secondary peak* is not greater than the area of the principal in the chromatogram obtained with solution (2) (0.2%).

The total impurity content is not greater than 0.4%.

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 0.8 g of Gliclazide with 160 mL of *acetonitrile* and dilute to 200 mL with *acetonitrile*. Filter and dilute 1 volume of the filtrate to 20 volumes with a mixture of 2 volumes of *acetonitrile* and 3 volumes of *water*.
(2) Dissolve 40 mg of *gliclazide BPCRS* in 10 mL of *acetonitrile* and dilute to 200 mL with a mixture of 2 volumes of *acetonitrile* and 3 volumes of *water*.
(3) Dissolve 5 mg of *gliclazide BPCRS* and 15 mg of *gliclazide impurity F BPCRS* in 25 mL of *acetonitrile*, dilute to 50 mL with *water* and dilute 1 volume of the resulting solution to 20 volumes with a mixture of 45 volumes of *acetonitrile* and 55 volumes of *water*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gliclazide and impurity F is at least 1.8.

DETERMINATION OF CONTENT

Calculate the content of $C_{15}H_{21}N_3O_3S$ in the tablets using the declared content of $C_{15}H_{21}N_3O_3S$ in *gliclazide BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, C, D, E, F and G listed under Gliclazide.