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Gliclazide Prolonged-release Tablets

General Notices

Gliclazide Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

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

DEFINITION

Gliclazide Prolonged-release Tablets contain Gliclazide. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Gliclazide. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

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

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of powdered tablets containing 0.12 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

Related substances

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

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

(1) Shake a quantity of the powdered tablets containing 40 mg of Gliclazide for about an hour with 90 mL of *acetonitrile*. Dilute to 200 mL with *water* and filter (0.45 µm PTFE is suitable).
(2) Dilute 1 volume of solution (1) to 200 volumes with solution A.
(3) Dissolve 8 mg of *gliclazide impurity F BPCRS* in 100 mL of solution A. Further dilute 0.5 volumes of this solution to 100 volumes with solution A.
(4) 0.0003% w/v of *gliclazide impurity F BPCRS* and 0.0001% w/v each of *gliclazide BPCRS* and *gliclazide impurity A BPCRS* in solution A.
(5) Dilute 1 volume of solution (2) to 5 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Lichrosorb 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 an autosampler temperature of 4°.
(f) Use a detection wavelength of 235 nm.
(g) Inject 100 µL of each solution.
(h) Allow the chromatography to proceed for twice the retention time of gliclazide.

MOBILE PHASE

0.1 volume of *triethylamine*, 0.1 volume of *trifluoroacetic acid*, 40 volumes of *acetonitrile* and 60 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4):

the *resolution* between the peaks due to impurity F and gliclazide is at least 1.5;

the *resolution* between the peak due to impurity A and the preceding negative system peak is at least 1.5.

CALCULATION OF IMPURITIES

For impurity F, use the concentration of impurity F in solution (3).

For all other impurities, use the concentration of gliclazide in solution (2).

For the reporting threshold, use the concentration of gliclazide in solution (5).

For peak identification, use solution (4).

Gliclazide retention time: about 14 minutes.

Relative retention: impurity A, about 0.3; impurity F, about 0.9.

LIMITS

— impurity A: not more than 0.5%;

— impurity F: not more than 0.2%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in solution A as described under Related substances.

(1) Shake a quantity of the powdered tablets containing 40 mg of Gliclazide for about an hour with 90 mL of *acetonitrile*. Dilute to 200 mL with *water* and filter (a 0.45-µm PTFE filter is suitable).
(2) 0.02% w/v of *gliclazide BPCRS*.
(3) 0.0003% w/v of *gliclazide impurity F BPCRS* and 0.0001% w/v of *gliclazide BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used with the exception of a detection wavelength: use 235 nm for solution (3) and 262 nm for solutions (1) and (2).

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3) at 235 nm, the *resolution* between impurity F and gliclazide is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of gliclazide, $C_{15}H_{21}N_3O_3S$, in the prolonged-release tablets from the chromatograms obtained and 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 A, C, D, E, F and G listed under Gliclazide.