Gliclazide Prolonged-release Tablets

Details for the public consultation of this monograph are as follows:

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<th>EAG/Panel/Working Party</th>
<th>Medicinal Chemicals 2</th>
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<td>Contact Details</td>
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<td>Deadline for Comment</td>
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<td>BP 2025</td>
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<td>Notes</td>
<td>New monograph. If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.</td>
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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.

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_{3}O_{3}S**

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 prepared in solution A.

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 1 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.

3. Dissolve 8 mg of gliclazide impurity F BPCS in 25 mL of acetonitrile, dilute to 50 mL with water and dilute 1 volume of the resulting solution to 10 volumes with solution A.

4. 0.0003% w/v of gliclazide impurity F BPCS and 0.0001% w/v each of gliclazide BPCS and gliclazide impurity A BPCS.

5. Dissolve 10 mg of gliclazide BPCS in 9 mL of acetonitrile. Add 2 mL of 1M hydrochloric acid and allow to stand for 2 hours. Neutralise the solution with 0.9 mL of 2M sodium hydroxide and add 13.5 mL of acetonitrile. Dilute to produce 50 mL with water and filter (generation of impurity A).

6. Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with octylsilyl silica gel for chromatography (5 µm) (Licrosorb 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;

and, in the chromatogram obtained with solution (6):

the signal-to-noise ratio of the principal peak in the chromatogram is at least 40.

CALCULATION OF IMPURITIES

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

For each other impurity, use the concentration of gliclazide in solution (2).

For the reporting threshold, use the concentration of gliclazide in solution (6).
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 1 hour with 90 mL of acetonitrile. Dilute to 200 mL with water and filter (0.45 µm PTFE 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 each of gliclazide BPCRS and gliclazide impurity A BPCRS.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used, with the exception of run time and with a detection wavelength of 235 nm for solution (3) and 262 nm for all other solutions.

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_{3}O_{3}S, in the prolonged release tablets from the chromatograms obtained and using the declared content of C_{15}H_{21}N_{3}O_{3}S, in gliclazide BPCRS.

IMPURITIES

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