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

Glimepiride Tablets

General Notices

Action and use

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

DEFINITION

Glimepiride Tablets contain Glimepiride.

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

Content of glimepiride, $C_{24}H_{34}N_4O_5S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the powdered tablets containing 10 mg of Glimepiride with 20 mL of *acetonitrile*, centrifuge and filter the supernatant liquid, evaporate to dryness at a temperature not exceeding 30°. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of glimepiride (*RS 463*).
B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of a pH 7.8 buffer solution prepared by mixing 14.5 g of *potassium dihydrogen phosphate* and 277.76 g of *sodium dihydrogen orthophosphate* with sufficient water to make 25 litres, adjusted to pH 7.8 with 10% v/v *orthophosphoric acid* or 1M *sodium hydroxide*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. *Store the solutions at a temperature not exceeding 12° and use within 15 hours*.

(1) After 45 minutes withdraw a sample of the medium and filter. Use the filtrate, diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.0001% w/v of Glimepiride.

(2) Dilute 1 volume of a 0.001% w/v solution of *glimepiride BPCRS* in *acetonitrile* to 10 volumes with the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Phenomenex Lichrospher RP 18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use an auto-sampler temperature of 12°.
(f) Use a detection wavelength of 228 nm.
(g) Inject 50 µL of each solution.

MOBILE PHASE

Equal volumes of a 0.1% w/v solution of *sodium dihydrogen phosphate dihydrate* and *acetonitrile R1*, the pH adjusted to 2.5 with *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the retention time of glimepiride is about 8 minutes.

DETERMINATION OF CONTENT

Calculate the total content of glimepiride, $C_{24}H_{34}N_4O_5S$, in the medium from the chromatograms obtained and using the declared content of $C_{24}H_{34}N_4O_5S$ in *glimepiride BPCRS*.

LIMITS

The amount of glimepiride 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 in a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*. *Store the solutions at a temperature not exceeding 12° and use within 15 hours*.

(1) Shake a quantity of the powdered tablets containing 2 mg of Glimepiride with 8 mL of a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*. Dilute to 10 mL with the same solvent, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.04% w/v of *glimepiride for system suitability BPCRS*.
(4) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (4 µm) (Supelco Superspher RP 18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use an auto-sampler temperature of 12°.
(f) Use a detection wavelength of 228 nm.
(g) Inject 10 µL of each solution.
(h) Allow the chromatography to proceed for 3.5 times the retention time of the peak due to glimepiride.

MOBILE PHASE

Equal volumes of a 0.1% w/v solution of *sodium dihydrogen phosphate dihydrate* and *acetonitrile R1*, the pH adjusted to 2.5 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to glimepiride (retention time about 17 minutes) are: impurity B, about 0.24 and impurity C, about 0.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and impurity C is at least 4.0.

LIMITS

Identify the peak due to impurity B in solution (1) using solution (3) and multiply the peak area by the correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

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

the sum of the areas of any other *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the peak due to glimepiride in the chromatogram obtained with solution (4) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or 2% w/w of Glimepiride comply with the requirements stated under Tablets using the following method of analysis.

Carry out the method for liquid chromatography, Appendix III D, using the following solutions. *Store the solutions at a temperature not exceeding 12° and use within 15 hours*.

(1) To one tablet add 1 mL of *water* and allow to disintegrate. Add 8 mL of a solution containing 1 volume of *water* and 9 volumes of *acetonitrile*, mix with the aid of ultrasound for 15 minutes. Dilute to 10 mL with the same solvent, centrifuge and use the supernatant liquid, diluted if necessary with mobile phase to produce a solution expected to contain 0.01% w/v of Glimepiride.
(2) 0.01% w/v of *glimepiride BPCRS* in a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*.
(3) 0.04% w/v of *glimepiride for system suitability BPCRS* in a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Phenomenex Lichrospher RP 18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use an auto-sampler temperature of 12°.
(f) Use a detection wavelength of 228 nm.
(g) Inject 10 µL of each solution.

MOBILE PHASE

Equal volumes of a 0.1% w/v solution of *sodium dihydrogen phosphate dihydrate* and *acetonitrile R1*, the pH adjusted to 2.5 with *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and impurity C is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{24}H_{34}N_4O_5S$ in each tablet using the declared content of $C_{24}H_{34}N_4O_5S$ in *glimepiride BPCRS*.

ASSAY

For tablets containing less than 2 mg, or 2% w/w of glimepiride

Use the average of the individual results determined in the test for Uniformity of content.

For tablets containing 2 mg or more, or 2% w/w or more of glimepiride

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

(1) To a quantity of powdered tablets containing 10 mg of Glimepiride, add 80 mL of a solution containing 1 volume of *water* and 9 volumes of *acetonitrile*, mix with the aid of ultrasound. Add sufficient of a mixture containing 1 volume of *water* and 9 volumes of *acetonitrile* to produce 100 mL, centrifuge and use the supernatant liquid.
(2) 0.01% w/v of *glimepiride BPCRS* in a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*.
(3) 0.04% w/v of *glimepiride for system suitability BPCRS* in a mixture of 1 volume of *water* and 4 volumes of *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of content 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 impurity B and impurity C is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{24}H_{34}N_4O_5S$ in the tablets using the declared content of $C_{24}H_{34}N_4O_5S$ in *glimepiride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Glimepiride.