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

Glibenclamide Tablets

General Notices

Action and use

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

DEFINITION

Glibenclamide Tablets contain Glibenclamide.

PRODUCTION

The dissolution test below is carried out to demonstrate the appropriate release of Glibenclamide subject to approval from the competent authority.

Prepare a mixture containing 0.8134% w/v of *anhydrous disodium hydrogen phosphate* and 0.1350% w/v of *potassium dihydrogen orthophosphate* (solution A).

Carry out the *dissolution test for tablets and capsules*, Appendix XII B1. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

TEST CONDITIONS

(a) Use Apparatus 2 rotating the paddle at 100 revolutions per minute.
(b) Use 900 mL of solution A at a temperature of 37° as the medium.

PROCEDURE

(1) Withdraw 10 mL of the medium, filter (Minisart GS 25mm filters are suitable) and use the filtrate, discarding the first 5 mL of the filtrate.
(2) Dissolve *glibenclamide BPCRS* in the minimum quantity of *methanol* and dilute to an appropriate concentration with solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 225 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

40 volumes of 0.1M *potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 with *orthophosphoric acid* and 60 volumes of *acetonitrile*.

DETERMINATION OF CONTENT

Calculate the total content of glibenclamide, $C_{23}H_{28}ClN_3O_5S$, in the medium from the chromatograms obtained and using the declared content of $C_{23}H_{28}ClN_3O_5S$ in *glibenclamide BPCRS*.

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

Content of glibenclamide, $C_{23}H_{28}ClN_3O_5S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as that of the principal peak in the chromatogram obtained with solution (2).
B. In the test for Related substances, the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (4).

TESTS

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Extract a quantity of the powdered tablets containing 20 mg of Glibenclamide with four 5-mL quantities of a mixture of 10 volumes of *acetone* and 20 volumes of *dichloromethane*, evaporate the combined extracts to dryness at a temperature not exceeding 40° at a pressure of 2 kPa and dissolve the residue in 4 mL of a mixture of equal volumes of *chloroform* and *methanol*.
(2) 0.012% w/v of *4-[2-(5-chloro-2-methoxybenzamido)ethyl]benzenesulfonamide BPCRS* in a mixture of equal volumes of *chloroform* and *methanol*.
(3) 0.0020% w/v of *methyl* N-*4-[2-(5-chloro-2-methoxybenzamido)ethyl]benzenesulfonylcarbamate BPCRS* in a mixture of equal volumes of *chloroform* and *methanol*.
(4) 0.5% w/v of *glibenclamide BPCRS* in a mixture of equal volumes of *chloroform* and *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating substance *silica gel GF_{254}*.
(b) Use the mobile phase described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

5 volumes of *ethanol (96%)*, 5 volumes of *glacial acetic acid*, 45 volumes of *chloroform* and 45 volumes of *cyclohexane*.

LIMITS

In the chromatogram obtained with solution (1);

any spots corresponding to 4-[2-(5-chloro-2-methoxybenzamido)ethyl]benzenesulfonamide and methyl *N*-4-[2-(5-chloro-2-methoxybenzamido)ethyl]benzenesulfonylcarbamate are not more intense than the spots in the chromatograms obtained with solutions (2)(2.4%) and (3)(0.4%) respectively.

Uniformity of content

Tablets containing 5 mg or less of Glibenclamide 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.

(1) Powder one tablet, add a mixture of 2 mL of *water* and 20 mL of *methanol*, mix with the aid of ultrasound until fully dispersed and filter through a 0.2-µm membrane filter (Anatop LC is suitable).

(2) Add 2 mL of *water* to 20 mL of a 0.025% w/v solution of *glibenclamide BPCRS* in *methanol*, mix with the aid of ultrasound until fully dispersed and filter (0.2-µm Anatop LC is suitable).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Assay may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{23}H_{28}ClN_3O_5S$ in each tablet using the declared content of $C_{23}H_{28}ClN_3O_5S$ in *glibenclamide BPCRS*.

ASSAY

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

(1) Mix, with the aid of ultrasound, a quantity of the powdered tablets containing 5 mg of Glibenclamide with a mixture of 2 mL of *water* and 20 mL of *methanol* until fully dispersed and filter through a 0.2-µm membrane filter (Anatop LC is suitable).
(2) Dissolve 50 mg of *glibenclamide BPCRS* in 10 mL of *methanol* with the aid of ultrasound for 20 minutes, add sufficient *methanol* to produce 50 mL and dilute 1 volume of this solution to 4 volumes with *methanol*. To 20 mL of this solution add 2 mL of *water* and mix.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS is suitable).
(b) Use isocratic elution using the mobile phase below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 300 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

47 volumes of *acetonitrile* and 53 volumes of a 1.36% w/v solution of *potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

Calculate the content of $C_{23}H_{28}ClN_3O_5S$ in the tablets using the declared content of $C_{23}H_{28}ClN_3O_5S$ in *glibenclamide BPCRS*.