Gliclazide Tablets

グリクラジド錠

Gliclazide Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of gliclazide ($C_{15}H_{21}N_3O_3S$: 323.41).

Method of preparation Prepare as directed under Tablets, with Gliclazide.

Identification **(1)** To a quantity of powdered Gliclazide Tablets, equivalent to 50 mg of Gliclazide, add 20 mL of methanol, shake thoroughly, filter, and evaporate the filtrate on a water bath to dryness. To the residue add 0.1 g of sodium hydroxide, and heat gradually to melt. After cooling, add 1 mL of water, shake thoroughly, add 1 mL of hydrochloric acid, immediately cover with a nickel (II) hydroxide paper, and warm on a water bath. The gas evolved darkens the nickel (II) hydroxide paper.

(2) To a quantity of powdered Gliclazide Tablets, equivalent to 40 mg of Gliclazide, add 70 mL of methanol, shake thoroughly for 15 minutes, add methanol to make 100 mL, and centrifuge. To 2 mL of the supernatant liquid add methanol to make 100 mL, and use this solution as the sample solution. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits a maximum between 226 nm and 230 nm.

Uniformity of dosage units *<6.02>* Perform the Mass variation test, or the Content uniformity test according to the following method: it meets the requirement.

To 1 tablet of Gliclazide Tablets add 30 mL of methanol, sonicate for 10 minutes, shake thoroughly for 15 minutes, add methanol to make exactly 50 mL, and centrifuge. Pipet V mL of the supernatant liquid, equivalent to about 1.2 mg of gliclazide ($C_{15}H_{21}N_3O_3S$), add methanol to make exactly 20 mL, and use this solution as the sample solution. Then, proceed as directed in the Assay.

Amount (mg) of gliclazide ($C_{15}H_{21}N_3O_3S$)
$= M_S \times A_T / A_S \times 1 / V \times 6 / 5$

M_S: Amount (mg) of Gliclazide RS taken

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 0.05 mol/L disodium hydrogen phosphate-citric acid buffer solution (pH 6.0) as the dissolution medium, the dissolution rates in 5 minutes and in 45 minutes of Gliclazide Tablets are not more than 55% and not less than 75%, respectively.

Start the test with 1 tablet of Gliclazide Tablets, withdraw exactly 20 mL of the medium at the specified minutes after starting the test and supply exactly 20 mL of the dissolution medium warmed to 37±0.5℃ immediately after withdrawing of the medium every time. Filter the media through a membrane filter with a pore size not exceeding 0.45 μm. Discard not less than 10 mL of the first filtrate, pipet V mL of the subsequent filtrate, add the dissolution medium to make exactly V' mL so that each mL contains about 8.9 μg of gliclazide ($C_{15}H_{21}N_3O_3S$), and use these solutions as the sample solutions. Separately, weigh accurately about 22 mg of Gliclazide RS, previously dried at 105℃ for 2 hours, dissolve in 25 mL of methanol, and add the dissolution medium to make exactly 100 mL. Pipet 4 mL of this solution, add the dissolution medium to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances of the sample solution and standard solution, $A_{T1(n)}$ and A_{S1} at 227 nm and $A_{T2(n)}$ and A_{S2} at 300 nm, respectively, as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, using the dissolution medium as the blank.

Dissolution rate (%) with respect to the labeled amount of gliclazide ($C_{15}H_{21}N_3O_3S$) on the nth medium withdrawing (n=1, 2)

$$= M_S \times \left\{ \frac{A_{T1(n)} - A_{T2(n)}}{A_{S1} - A_{S2}} + \sum_{i=1}^{n-1} \left(\frac{A_{T1(i)} - A_{T2(i)}}{A_{S1} - A_{S2}} \times \frac{1}{45} \right) \right\} \times \frac{V'}{V} \times \frac{1}{C} \times 36$$

M_S: Amount (mg) of Gliclazide RS taken
C: Labeled amount (mg) of gliclazide ($C_{15}H_{21}N_3O_3S$) in 1 tablet

Assay Weigh accurately the mass of not less than 20 Gliclazide Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 50 mg of gliclazide ($C_{15}H_{21}N_3O_3S$), add 40 mL of methanol, shake for 10 minutes, add methanol to make exactly 50 mL and centrifuge. Pipet 3 mL of the supernatant liquid, add methanol to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Gliclazide RS, previously dried at 105℃ for 2 hours, dissolve in methanol to make exactly 50 mL. Pipet 3 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the operating conditions described below, and determine the peak areas, At and As, of gliclazide in each solution.

Amount (mg) of gliclazide ($C_{15}H_{21}N_3O_3S$)
$= M_S \times A_T / A_S$

M_S: Amount (mg) of Gliclazide RS taken

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 228 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: A mixture of water and acetonitrile for liquid chromatography (11 : 9)

Flow rate: Adjust so that the retention time of gliclazide is about 6 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of gliclazide are not less than 3500 and 0.7 to 1.2, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of gliclazide is not more than 1.0%.

Containers and storage Containers—Tight containers.

Add the following to 9.01 Reference Standards (1):

Gliclazide RS

Add the following to 9.43 Filters Papers, Filters for filtration, Test Papers, Crucibles, etc.:

Nickel (II) hydroxide paper Immerse a filter paper in a solution of nickel (II) sulfate hexahydrate in ammonia solution (28) (3 in 10), remove the excess liquid, and dry. Immerse this paper in sodium hydroxide TS for 5 to 6 minutes, wash with water, and use in the moist state.