Gliclazide Prolonged-release Tablets

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

Gliclazide Prolonged-release Tablets

Gliclazide Sustained-release Tablets; Gliclazide Extended-release Tablets

Gliclazide Prolonged-release Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of gliclazide, $C_{15}H_{21}N_3O_3S$.

Usual strengths. 30 mg; 60 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Dissolution (2.5.2).
NOTE- Protect the solutions from light.
Apparatus No. 2 (Paddle),
Medium. 900 ml of buffer solution prepared by dissolving 6.8 g of *potassium dihydrogen phosphate* in 1000 ml of *water*, adjusted to pH 7.4 with *10 M potassium hydroxide*,
Speed and time. 100 rpm and 1 hour, 4 hours, 12 hours.

Withdraw a suitable volume of the medium and filter.

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. Dissolve 66 mg of *gliclazide IPRS* in 20 ml of *methanol* and dilute to 100.0 ml with the dissolution medium. Dilute 5.0 ml of the solution to 100.0 ml with the dissolution medium.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with end capped octylsilane bonded to porous silica (5 µm),
- sample temperature: 15°,
- mobile phase: a mixture of 0.1 volume of *triethylamine*, 0.1 volume of *trifluoroacetic acid*, 45 volumes of *acetonitrile* and 55 volumes of *water*,
- flow rate: 0.9 ml per minute,
- spectrophotometer set at 235 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injection is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{15}H_{21}N_3O_3S$ in the medium.

At 1 hour, not more than 20 per cent; at 4 hours, not less than 20 per cent and not more than 55 per cent, and at 12 hours, not less than 80 per cent.

The percentages of the labelled amount of Gliclazide, $C_{15}H_{21}N_30_3S$ dissolved at the times specified conforms to 2.5.2 Dissolution test, Acceptance Table 2.

Related substances. Determine by liquid chromatography (2.4.14).

Note- Protect the solutions from light.

Solvent mixture A. 1 volume of *acetonitrile* and 2 volumes of *water.*

Solvent mixture B. 45 volumes of *acetonitrile* and 55 volumes of *water.*

Test solution. Disperse a quantity of powdered tablets containing 0.8 g of Gliclazide in *acetonitrile* with the aid of ultrasound for 20 minutes and dilute to 200.0 ml with *acetonitrile,* filter. Dilute 5.0 ml of the filtrate to 25.0 ml with solvent mixture A, filter.

Reference solution (a). A 0.00016 per cent w/v solution of *gliclazide IPRS* in solvent mixture B.

Reference solution (b). Dissolve 1.0 mg of *gliclazide IPRS* and 3 mg of *1-(3-azabicyclo[3.3.0]oct-3-yl)-3-o-tolylsulphonylurea IPRS* in 5 ml of *acetonitrile,* dilute to 10.0 ml with *water*. Dilute 1.0 ml of the solution to 20.0 ml with solvent mixture B.

Reference solution (c). Dissolve 1.6 mg of *1-(3-azabicyclo[3.3.0]oct-3-yl)-3-o-tolylsulphonylurea IPRS* in 5 ml of *acetonitrile,* dilute to 10.0 ml with *water*. Dilute 1.0 ml of the solution to 100.0 ml with solvent mixture B.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with end capped octylsilane bonded to porous silica (5 µm),
- sample temperature: 10°,
- mobile phase: A mixture of 0.1 volume of *triethylamine*, 0.1 volume of *trifluoroacetic acid*, 40 volumes of *acetonitrile* and 60 volumes of *water*,
- flow rate: 0.9 ml per minute,
- spectrophotometer set at 235 nm,
- injection volume: 20 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to gliclazide and 1-(3-azabicyclo[3.3.0]oct-3-yl)-3-o-tolylsulphonylurea is not less than 1.8.

Inject reference solution (a), (c), and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to 1-(3-azabicyclo[3.3.0]oct-3-yl)-3-o-tolylsulphonylurea is not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.2 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent) and the sum of the areas of all the secondary peaks other than 1-(3-azabicyclo[3.3.0]oct-3-yl)-3-o-tolylsulphonylurea is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.4 per cent). Ignore any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Note- Protect the solutions from light.

Solvent mixture. 40 volumes of *acetonitrile* and 60 volumes of *water*.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 0.4 g of Gliclazide, in *acetonitrile* with the aid of ultrasound for 20 minutes and dilute to 200.0 ml with *acetonitrile,* filter. Dilute 5.0 ml of the filtrate to 50.0 ml with the solvent mixture, filter.

Reference solution. Weigh and transfer 0.1 g of *gliclazide IPRS* to a 200-ml volumetric flask, add 50 ml of *acetonitrile,* shake well and sonicate for 10 minutes and dilute to volume with *acetonitrile.* Dilute 10.0 ml of the solution to 25.0 ml with the solvent mixture.

Use chromatographic system as described under Dissolution.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injection is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{15}H_{21}N_3O_3S$ in tablets.

Storage. Store protected from light and moisture, at a temperature not exceeding 30°.