Glipizide

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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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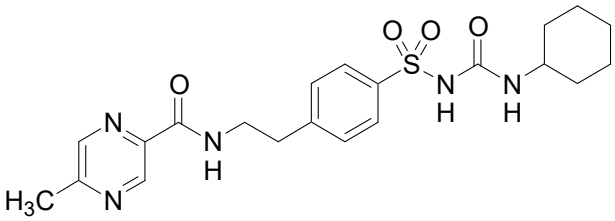
Further follow-up action as required.	

Glipizide. Page 2479
Change **to**: **Glipizide**



$C_{21}H_{27}N_5O_4S$ Mol. Wt. 445.5

Glipizide is 1-cyclohexyl-3-[[*p*-[2-(5-methylpyrazinecarboxamido)ethyl]phenyl]sulphonyl]urea.

Glipizide contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{21}H_{27}N_5O_4S$, calculated on the dried basis.

Category. Hypoglycaemic.

Description. A white to off-white powder.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *glipizide IPRS* or with the reference spectrum of glipizide.

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

Tests

Related substances

A. *Limit of methyl-N-4-[2-(5-methylpyrazine-2-carboxamido)ethyl] benzenesulphonyl carbamate.* Determine by liquid chromatography (2.4.14).

NOTE - Use low-actinic glassware for solutions containing glipizide and glipizide related compounds.

Solvent mixture. 20 volumes of *acetonitrile*, 20 volumes of *methanol* and 60 volumes of *water*.

Test solution. Dissolve 25 mg of the substance under examination in *methanol* and dilute to 25.0 ml with *methanol*. Dilute 4.0 ml of the solution to 10.0 ml with the solvent mixture and mix.

Reference solution (a). A 0.01 per cent w/v solution of *glipizide IPRS* in *methanol*.

Reference solution (b). A 0.01 per cent w/v solution of *glipizide related compound A IPRS* in *methanol*. To 2.0 ml of the solution, add 2.0 ml of reference solution (a) and dilute to 100.0 ml with the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as YMC 18 ODS-A),
- column temperature: 30°,
- mobile phase: a mixture of 60 volumes of 0.4 per cent v/v solution of *n-butylamine* in *water*, adjusted to pH 3.0 with *orthophosphoric acid*, 20 volumes of *acetonitrile* and 20 volumes of *methanol*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 35 µl.

Name	Relative retention time
Glipizide related compound A[1]	0.12
Glipizide related compound B[2]	0.12
Methyl-*N*-4-[2-(5-methylpyrazine-2-carboxamido)ethyl] benzenesulphonyl carbamate	0.18
Glipizide (Retention time: about 45 minutes)	1.0
Glipizide related compound C[3]	1.1

NOTE - Glipizide related compound B, if present, elutes immediately after Glipizide related compound A, and these two peaks are not resolved by this method.

[1]*N*-{2-[(4-Aminosulphonyl)phenyl]ethyl}-5-methyl-pyrazinecarboxamide,

[2]6-Methyl-*N*-[2-(4-sulphamoylphenyl)ethyl]pyrazine-2-carboxamide,

[3]1-Cyclohexyl-3-[[4-[2-[[(6-methylpyrazin-2-yl)carbonyl]amino]ethyl]phenyl]sulfonyl]urea.

Inject reference solution (b). The test is not valid unless the relative standard deviation for replicate injections is not more than 5.0 per cent for both the peaks.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to methyl-*N*-4-[2-(5-methylpyrazine-2-carboxamido)ethyl] benzenesulphonyl carbamate impurity is not more than the area of the glipizide peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any other secondary peak is not more than the area of the glipizide peak in the chromatogram obtained with reference solution (b) (0.5 per cent). Ignore any peak due to glipizide related compound A, glipizide related compound B and glipizide related compound C and any peak with an area less than 0.1 times the area of the glipizide peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

B. *Limit of Glipizide related compound A, B and C.* Determine by liquid chromatography (2.4.14).

NOTE - Use low-actinic glassware for solutions containing glipizide and glipizide related compounds.

Buffer solution. Dissolve 2.84 g of *anhydrous disodium hydrogen phosphate* in 1000 ml of *water*, adjusted to pH 6.0 with *orthophosphoric acid*.

Test solution. Dissolve 100 mg of the substance under examination in *methanol* with the aid of ultrasound for 5 minutes and dilute to 100.0 ml with *methanol*. Transfer 10.0 ml of the solution to a 100-ml volumetric flask containing 20 ml of *acetonitrile* and 60 ml of the buffer solution, sonicate for 5 minutes and dilute to volume with the buffer solution.

Reference solution (a). A 0.1 per cent w/v solution of *glipizide IPRS* in *methanol*. Transfer 10.0 ml of the solution to a 100-ml volumetric flask containing 20 ml of *acetonitrile* and 60 ml of the buffer solution, sonicate for 5 minutes and dilute to volume with the buffer solution.

Reference solution (b). A solution containing 0.01 per cent w/v, each of, *glipizide related compound A IPRS, glipizide related compound B IPRS* and *glipizide related compound C IPRS* in *methanol*.

Reference solution (c). Dilute 1.0 ml of reference solution (b) to 20.0 ml with *methanol*. Transfer 10.0 ml of the solution in 100-ml volumetric flask containing 20 ml of *acetonitrile* and 60 ml of the buffer solution, sonicate for 5 minutes and dilute to volume with the buffer solution.

Reference solution (d). Dilute 1.0 ml of reference solution (b) to 20.0 ml with *methanol*. Dilute 1.0 ml of the solution to 10.0 ml with reference solution (a).

Reference solution (e). Dilute 5.0 ml of reference solution (d) to 25.0 ml with the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with pentafluorophenyl groups bonded to porous silica (5 µm) (Such as Kinetex PFP),
- column temperature: 40°,
- mobile phase: a mixture of 70 volumes of the buffer solution, 20 volumes of *acetonitrile* and 10 volumes of *methanol*,

– flow rate: 1 ml per minute,
– spectrophotometer set at 225 nm,
– injection volume: 10 µl.

The elution order is glipizide related compound A, glipizide related compound B and glipizide related compound C.

Inject reference solution (d) and (e). The test is not valid unless the resolution between the peaks due to glipizide related compound A and glipizide related compound B is not less than 1.8 and between the peaks due to glipizide and glipizide related compound C is not less than 1.8, the tailing factor is not more than 2.0 for glipizide peak, the relative standard deviation for replicate injections is not more than 1.5 per cent for glipizide peak and not more than 5.0 per cent, each of, glipizide related compound A, B and C peak in the chromatogram obtained with reference solution (d) and the signal-to-noise ratio is not less than 15 for, each of, glipizide related compound A, B and C peaks in the chromatogram obtained with reference solution (e).

Inject reference solution (c) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to glipizide related compound A, glipizide related compound B and glipizide related compound C, each of, is not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.5 per cent).

The sum of all the impurities (determined in Related substances A and Related substances B) is not more than 1.5 per cent.

Sulphated ash (2.3.18). Not more than 0.4 per cent.

Loss on drying (2.4.19). Not more than 1.0 per cent, determined on 1.0 g by drying in vacuum at 100° for 3 hours.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances B (Limit of Glipizide related compounds A, B and C) with the following modifications.

Inject reference solution (d) and (e). The test is not valid unless the resolution between the peaks due to glipizide related compound A and glipizide related compound B is not less than 1.8 and between the peaks due to glipizide and glipizide related compound C is not less than 1.8, the tailing factor is not more than 2.0 for glipizide peak, the relative standard deviation for replicate injections is not more than 1.5 per cent for glipizide peak and not more than 5.0 per cent, each of, glipizide related compound A, B and C peak in the chromatogram obtained with reference solution (d) and the signal-to-noise ratio is not less than 15 for, each of, glipizide related compound A, B and C peaks in the chromatogram obtained with reference solution (e).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{21}H_{27}N_5O_4S$.

Storage. Store protected from light and moisture.

2.4.26. Solubility
Glipizide. Page 279
Change **to: Glipizide**. Freely soluble in *dimethylformamide*; soluble in *0.1 M sodium hydroxide* and slightly soluble in *methylene chloride*.