World Health Organization

GLICLAZIDE SUSTAINED-RELEASE TABLETS

(GLICLAZIDUM COMPRESSI PROLONGATI)

Draft proposal for inclusion in *The International Pharmacopoeia*

(30 June 2025)

DRAFT FOR COMMENTS

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For any technical questions, you may contact **Dr Herbert Schmidt**, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (schmidth@who.int), with a copy to **Ms Sinéad Jones** (jonessi@who.int, nsp@who.int).
Comments should be submitted through the online platform on or by **29 August 2025**. Please note that only comments received by this deadline will be considered for the preparation of this document.
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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/25.975

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Description	Date
First draft prepared.	March 2025
Discussion at the informal Consultation on Quality Control and Pharmacopoeial Specifications of Medicines	April 2025
Draft revision sent out for public consultation	August – September 2025
Draft revision presented at the 59th meeting of the Expert Committee on Specifications for Pharmaceutical Preparations	October 2025
Further follow-up action as required.	

*[**Note from the Secretariat**. The monograph on Gliclazide sustained-release tablets is proposed for inclusion in* The International Pharmacopoeia*.*

The monograph is based on information found in other pharmacopoeias, in the scientific literature and on laboratory investigations.

Draft monographs are subject to change.]

GLICLAZIDE SUSTAINED-RELEASE TABLETS

(GLICLAZIDUM COMPRESSI PROLONGATI)

Category. Antidiabetic drug.

Storage. Gliclazide sustained-release tablets should be kept in a well-closed container.

Additional information. Strengths in the current WHO Model List of Essential Medicines (EML): 30 mg, 60 mg and 80 mg sustained -release tablets.

Requirements

Comply with the monograph for *Tablets.*

Definition. Gliclazide sustained-release tablets contain not less than 90.0% and not more than 110.0% of the labelled amount of Gliclazide ($C_{15}H_{21}N_3O_3S$). They are formulated so that the active ingredient is released over a period of several hours.

Production. A suitable dissolution test is carried out to demonstrate the appropriate release of Gliclazide. The dissolution profile reflects the in vivo performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

Identity tests

- Either test A alone, or any two of tests B, C or D may be applied.

A. Shake a quantity of the powdered tablets equivalent to 0.12 g of Gliclazide with 20 mL of dichloromethane R, centrifuge, filter[1] and evaporate the filtrate to dryness. Carry out the examination as described under *1.7 Spectrophotometry in the infrared region*. The infrared absorption spectrum is concordant with the

[1] A 0.45 µm PTFE membrane syringe filter was found suitable.

spectrum obtained from gliclazide RS treated similarly.

B. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using the conditions and solutions given under "Assay". The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to the retention time of the peak due to gliclazide in the chromatogram obtained with solution (2).

C. The absorption spectrum (*1.6 Spectrophotometry in the visible and ultraviolet regions*) of a 0.01 mg per mL solution of the test substance prepared in a mixture of 45 volumes of acetonitrile R and 55 volumes of water R, when observed between 200 nm and 300 nm, exhibits minimum at about 213 nm and a maximum at about 229 nm.

Alternatively, and in combination with identity test B, where a diode-array detector is available, record the UV spectrum of the principal peak in the chromatograms with a diode array detector in the range of 210 nm to 400 nm. The UV spectrum of the principal peak in the chromatogram obtained with solution (1) corresponds to the UV spectrum of the peak due to gliclazide in the chromatogram obtained with solution (2).

D. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R6 as the coating substance and a freshly prepared mixture of toluene R and ethyl acetate R (1:1 *V*/*V*) as the mobile phase.

Apply separately to the plate 2 µL of each of the following 2 solutions. For solution (A), transfer a quantity of the powdered tablets, nominally containing 10 mg of gliclazide, to a 25 mL flask and add 15 mL of dichloromethane R. Stopper the flask and sonicate for 15 minutes. Make up to volume, filter the suspension and use the clear supernatant. For solution (B), use a solution containing 0.4 mg of gliclazide RS per mL.

Develop the plate. After removing the plate from the chromatographic chamber

allow it to dry in air or in a current of air. Allow the plate to cool and examine the chromatogram in daylight and under ultraviolet light (254 and 360 nm).

The principal spot in the chromatogram obtained with solution (A) corresponds in position, appearance and intensity with the spot due to gliclazide in the chromatogram obtained with solution (B).

Related substances. Prepare the solutions immediately before use. Carry out the test as described under *1.14.1 Chromatography*, High-pressure liquid chromatography, using a stainless steel column (4 mm x 25 cm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octylsilyl groups[2] (4 µm).

As the mobile phase, use a mixture of 0.1 volume of triethylamine R, 0.1 volume of trifluoroacetic acid R, 40 volumes of acetonitrile R and 60 volumes of water R.

Operate with a flow rate of 0.9 mL per minute. As a detector, use an ultraviolet spectrophotometer set at a wavelength of 235 nm. Maintain the autosampler temperature at 4 °C.

Prepare the following solutions. Use as a diluent a mixture of 45 volumes of acetonitrile R and 55 volumes of water R.

For solution (1), shake a quantity of the powdered tablets, nominally containing 40.0 mg of gliclazide for about an hour with 90 mL of acetonitrile R. Dilute to 200.0 mL with water R, filter[3] and use the filtrate.

For solution (2), dilute 1.0 mL of solution (1) to 200.0 mL with the diluent.

[2] A Superspher 60 RP-8 LiChroCART column has been found suitable.
[3] A 0.45 µm PTFE membrane syringe filter was found suitable.

For solution (3), dissolve 8 mg of gliclazide impurity F RS in 100.0 mL of the diluent. Dilute 0.5 mL of this solution to 100.0 mL with the diluent.

For solution (4), dissolve 5 mg of the test substance, 5 mg of gliclazide impurity A and 15 mg of gliclazide impurity F RS in 23 mL of acetonitrile R and dilute to 50.0 mL with water R. Dilute 1 mL of the solution to the 100 mL with the diluent.

For solution (5), dilute 10.0 mL of solution (2) to 50.0 mL with the diluent.

Inject 100 µL each of solutions (1), (2) (3), (4) and (5). Record the chromatogram for about 2 times the retention time of gliclazide (retention time about 16 minutes).

Use the chromatogram obtained with solution (4) to identify the peaks due to gliclazide and gliclazide impurities A and F.

The impurities are eluted, if present, at the following relative retentions with reference to gliclazide: impurity A about 0.3; impurity F about 0.9.

The test is not valid unless, in the chromatogram obtained with solution (4), the resolution between gliclazide impurity F and gliclazide is at least 1.5 and the resolution between gliclazide impurity A and the preceding negative system peak is at least 1.5. Also, the test is not valid unless in the chromatogram obtained with solution (5) the peak due to gliclazide is detected with a signal-to-noise ratio of at least 10.

In the chromatogram obtained with solution (1):

- the area of any peak corresponding to impurity A is not greater than the area of the peak due to gliclazide in the chromatogram obtained with solution (2) (0.5 %);
- the area of any peak corresponding to impurity F is not greater than the area of the peak due to gliclazide impurity F in the chromatogram obtained with solution (3) (0.2 %);

- the area of any other impurity peak is not greater than 0.4 times the peak due to gliclazide in the chromatogram obtained with solution (2) (0.2 %).
- The sum of the areas of all impurity peaks is not greater than 1.0 %. Disregard any peaks with an area of less than the area of the peak due to gliclazide in the chromatogram obtained with solution (5) (0.10 %).

Assay. Carry out the test as described under 1.14.1 Chromatography, Liquid chromatography, using the conditions given under "Related substances", with the following modifications.

Prepare the following solutions. Use as a diluent a mixture of 45 volumes of acetonitrile R and 55 volumes of water R.

For solution (1), weigh and powder 20 tablets. Shake a quantity of the powdered tablets, nominally containing 40.0 mg of the test substance, for about an hour with 90 mL of acetonitrile R. Dilute to 200.0 mL with water R, filter[3] and use the filtrate.

For solution (2), dissolve 40.0 mg of gliclazide RS in 200.0 mL of diluent.

Inject 50 µL each of solutions (1) and (2).

Measure the areas of the peaks corresponding to gliclazide obtained in the chromatograms of solutions (1) and (2) and calculate the percentage content of Gliclazide ($C_{15}H_{21}N_3O_3S$) in the tablets, using the declared content of $C_{15}H_{21}N_3O_3S$ in gliclazide RS.

Impurities

The impurities limited by the requirements of this monograph include A, C, D, E, F and G listed in the monograph on Gliclazide.

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