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Glimepiride Tablets

DEFINITION
Glimepiride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
• **B.** The UV absorption spectra of the major peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**
[Note—Store the solutions containing glimepiride for NMT 24 h.]

Mobile phase: Dissolve 0.5 g of monobasic sodium phosphate in 500 mL of water. Adjust with 10% phosphoric acid to a pH of 2.1–2.7, and add 500 mL of acetonitrile.

Diluent: Acetonitrile and water (9:1)

System suitability solution: 0.1 mg/mL of USP Glimepiride RS and 0.02 mg/mL each of USP Glimepiride Related Compound B RS and USP Glimepiride Related Compound C RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Glimepiride RS in *Diluent*

Sample solution: Transfer 5 whole Tablets into a suitable volumetric flask to prepare a solution of approximately 0.1 mg/mL of glimepiride, based on the label claim. Add water to 10% of the volume of the flask. Shake the flask to completely dissolve the Tablets. Add acetonitrile to about 70% of the volume of the flask, and swirl. Sonicate the samples in a water bath not to exceed 20° for NLT 5 min and NMT 10 min, with occasional shaking. Allow the solutions to come to room temperature, dilute with acetonitrile to volume, mix, and filter.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 228 nm. For *Identification B*, use a diode array detector in the range of 200–340 nm.

Column: 4-mm × 12.5-cm or 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for glimepiride related compound B, glimepiride related compound C, and glimepiride are 0.25, 0.35, and 1.0, respectively. Identify the glimepiride peak and the peaks due to the related compounds based on their relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between glimepiride related compound B and glimepiride related compound C, *System suitability solution*

Tailing factor: NMT 2.0 for the glimepiride peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Glimepiride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of glimepiride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: pH 7.8 phosphate buffer (0.58 g of monobasic potassium phosphate and 8.86 g of dibasic sodium phosphate, anhydrous, in 1000 mL of water, adjusted with 10% phosphoric acid or 1 N sodium hydroxide to a pH of 7.8); 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Mobile phase: Prepare as directed in the *Assay*.

Diluting solution: Methanol and water (1:1)

Standard solution: Prepare a solution of USP Glimepiride RS in a mixture of acetonitrile and water (90:10) having a known concentration of about 0.125 mg/mL of glimepiride. Transfer 4.0 mL of this solution into a 200-mL volumetric flask, dilute with *Medium* to volume, and mix. Transfer 15.0 mL of this solution into a 50-mL volumetric flask, dilute with *Diluting solution* to volume, and mix. The final solution contains about 0.75 µg/mL of glimepiride.

Sample solution: Withdraw approximately 10 mL of the solution under test, and transfer to a centrifuge tube. Centrifuge for 5 min at 2500 rpm. Pipet 3.0 mL of the supernatant into a 10-mL volumetric flask, dilute with *Diluting solution* to volume, and mix.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 228 nm

Column: 4.0-mm × 12.5-cm or 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

Tolerances: NLT 80% (Q) of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: pH 7.8 phosphate buffer (add 250 mL of 0.2 M monobasic potassium phosphate to 223 mL of 0.2 M sodium hydroxide, dilute with water to 1 L, and adjust with 0.2 M sodium hydroxide or phosphoric acid to a pH of 7.8); 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Buffer solution: 4.0 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 5.3.

Mobile phase: Acetonitrile and *Buffer solution* (1:1)

Diluent: Methanol and acetonitrile (1:1)

Standard stock solution: 0.22 mg/mL of USP Glimepiride RS in *Diluent*

Standard solution: (*L*/1000) mg/mL of USP Glimepiride RS in *Medium*, from the *Standard stock solution*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Flow rate: 1.3 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 7.8 phosphate buffer (prepared as indicated for *Test 1*); 900 mL

Apparatus 2: 75 rpm

Time: 20 min

Buffer solution: 1.36 g/L of monobasic potassium phosphate in water. Adjust with 10% sodium hydroxide to a pH of 7.0 ± 0.05.

Mobile phase: *Buffer solution* and acetonitrile (675:325)

Standard stock solution: 0.22 mg/mL of USP Glimepiride RS in methanol

Standard solution: (*L*/1000) mg/mL of USP Glimepiride RS in *Medium*, from the *Standard stock solution*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 228 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of glimepiride ($C_{24}H_{34}N_4O_5S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

[Note—Store the solutions containing glimepiride for NMT 24 h.]

Mobile phase and **Diluent:** Prepare as directed in the *Assay*.

System suitability solution: 4 µg/mL of USP Glimepiride RS and 2 µg/mL each of USP Glimepiride Related Compound B RS and USP Glimepiride Related Compound C RS in *Diluent*

Sensitivity solution: Transfer 5.0 mL of the *System suitability solution* into a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Sample solution: Finely powder NLT 10 Tablets, and transfer a portion of the powder to a 50-mL centrifuge tube. Add *Diluent* to prepare a solution containing 0.1 mg/mL of glimepiride, based on the label claim. Sonicate in a water bath at a temperature not to exceed 20° for NLT 5 min and NMT 10 min, with occasional mixing. Centrifuge the samples, and use the clear supernatant.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 228 nm

Column: 4-mm × 25-cm or 4.6-mm × 25-cm; 4- or 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of the glimepiride peak

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 4 between glimepiride related compound B and glimepiride related compound C, *System suitability solution*

Relative standard deviation: NMT 2.0% of the glimepiride peak, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Reporting threshold for impurities is 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Glimepiride related compound B	0.2	1.3	2.5
Glimepiride related compound C	0.3	1.0	0.5
Glimepiride	1.0	1.0	—
Any other individual impurity	—	1.0	0.5
Total impurities, excluding glimepiride related compound B	—	—	1.0
Total impurities, including glimepiride related compound B	—	—	3.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Glimepiride RS

USP Glimepiride Related Compound B RS

Glimepiride sulfonamide;
3-Ethyl-4-methyl-2-oxo-*N*-(4-sulfamoylphenethyl)-2,5-dihydro-1*H*-pyrrole-1-carboxamide.
$C_{16}H_{21}N_3O_4S$ 351.42

USP Glimepiride Related Compound C RS

Glimepiride urethane;
Methyl ({4-[2-(3-ethyl-4-methyl-2-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxamido)ethyl]phenyl}sulfonyl)carbamate.
$C_{18}H_{23}N_3O_6S$ 409.46

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GLIMEPIRIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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