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
- The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **PROCEDURE**

[NOTE—Store the solutions containing glimepiride 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
Column: 4-mm × 12.5-cm; packing L1
Flow rate: 1 mL/min
Injection size: 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 glimepiride 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

Change to read:

- **DISSOLUTION** ⟨**711**⟩

Test 1 (RB 1-Dec-2010)
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, adjust 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 0.00075 mg/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; packing L1
Flow rate: 1.0 mL/min
Injection size: 50 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis: 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 = Tablet label claim (mg)
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 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
pH 5.3 buffer: 4.0 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 5.3.

Mobile phase: Acetonitrile and *pH 5.3 buffer* (1:1)
Diluent: Methanol and acetonitrile (1:1)
Standard stock solution: 0.22 mg/mL of USP Glimepridie RS in *Diluent*
Standard solution: (*L*/1000) mg/mL of USP Glimepiride RS in *Medium*, from the *Standard stock solution*, where *L* is the Tablet label claim in mg
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 size: 100 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis: 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 = Tablet label claim (mg)
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 glimepiride in *Medium*, from the *Standard stock solution*, where *L* is the Tablet label claim in mg
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 size: 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: 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 = Tablet label claim (mg)
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. ● (RB 1-Dec-2010)

• **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; packing L1
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Sensitivity solution*
[Note—The relative retention times for glimepiride related compound B, glimepiride related compound C, and glimepiride are 0.2, 0.3, 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 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*
Calculate the signal-to-noise ratio, *S/N*, for the peaks of glimepiride related compounds B and C:

$$\text{Result} = (2H)/h$$

H = measured height of the respective related compound peak
h = amplitude of the average measured baseline noise

Analysis
Samples: *Standard solution* and *Sample solution*
[Note—Continue the elution for at least two times the retention time of the glimepiride peak.]
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 the responses of all the peaks in the *Sample solution*

F = relative response factor, equal to 1.3 for glimepiride related compound B and 1.0 for any other impurity

Acceptance criteria: NMT 2.5% of glimepiride related compound B, NMT 0.5% of any other individual impurity, NMT 1.0% of total impurities excluding glimepiride related compound B, and NMT 3.5% of total impurities including glimepiride related compound B

[NOTE—Disregard any peak less than 0.1%.]

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

●**Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.● (RB 1-Dec-2010)

- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Glimepiride RS
  USP Glimepiride Related Compound B RS
  Glimepiride sulfonamide.
  USP Glimepiride Related Compound C RS
  Glimepiride urethane.