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Glyburide Tablets

DEFINITION
Glyburide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**

  Sample: Grind a number of Tablets, equivalent to 15 mg of glyburide, to a fine powder. Add 30 mL of acetonitrile, and shake. Filter the mixture, evaporate the filtrate to dryness, and dry the residue under vacuum at 60° for 3 h.

  Acceptance criteria: Meet the requirements

- **B.** 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**

  Mobile phase: Dissolve 2.6 g of monobasic ammonium phosphate in 450 mL of water. Add 550 mL of acetonitrile, filter, and degas. Adjust, if necessary, with phosphoric acid or sodium hydroxide to a pH of 5.25 ± 0.30.

  System suitability stock solution: 0.1 mg/mL of USP Glyburide Related Compound A in acetonitrile

  System suitability solution: To 10 mg of USP Glyburide RS add 20 mL of the *System suitability stock solution*, and shake vigorously to dissolve. Add 4.0 mL of water.

  Standard solution: To 10 mg of USP Glyburide RS add 20.0 mL of acetonitrile, and shake vigorously to dissolve. Add 4.0 mL of water.

  Sample solution: Transfer NLT 20 Tablets to a suitable container. Add water equivalent to 0.4 mL of water per mg of glyburide, and swirl to disperse and wet Tablet material. Then add acetonitrile equivalent to 2.0 mL of acetonitrile per mg of glyburide, and shake for 30 min. Centrifuge a portion of the suspension, and use the clear supernatant.

  Chromatographic system

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

  Mode: LC

  Detector: UV 254 nm

  Column: 4.6-mm × 25-cm; packing L7

  Flow rate: 2 mL/min

  Injection volume: 10 µL

  System suitability

  Sample: *System suitability solution*

  [Note—The relative retention times for glyburide related compound A and glyburide are about 0.5 and 1.0, respectively.]

  Suitability requirements

  Resolution: NLT 4.0 between glyburide related compound A and glyburide

  Relative standard deviation: NMT 2.0% for glyburide

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (W_S/V_S)/(W_U/V_U) \times 100$$

  r_U = peak response from the *Sample solution*

  r_S = peak response from the *Standard solution*

  W_S = weight of USP Glyburide RS, used to prepare the *Standard solution* (mg)

V_S = sum of volumes of acetonitrile and water used to prepare the *Standard solution* (mL)

W_U = nominal amount of glyburide used to prepare the *Sample solution* (mg)

V_U = sum of volumes of acetonitrile and water used to prepare the *Sample solution* (mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1 (nonmicronized glyburide)

Medium: 0.05 M borate buffer, pH 9.5 (381.5 g of sodium borate and 19.1 g of sodium hydroxide in 20 L of water, and adjust with phosphoric acid to a pH of 9.5 ± 0.1); 500 mL

Apparatus 2: 75 rpm

Time: 45 min

Mobile phase: Acetonitrile and water (1:1) containing 4.0 mL of phosphoric acid per L of solution

Standard stock solution: 0.15 mg/mL of USP Glyburide RS in *Medium*. Sonicate for about 25 min to dissolve, and dilute with *Medium* to volume.

Standard solutions: Dilute the *Standard stock solution* with *Medium* to obtain 0.003 mg/mL (for Tablets labeled to contain 1.5 mg), 0.006 mg/mL (for Tablets labeled to contain 3.0 mg), 0.009 mg/mL (for Tablets labeled to contain 4.5 mg), and 0.012 mg/mL (for Tablets labeled to contain 6.0 mg).

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) 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*, 500 mL

Tolerances: NLT 70% (*Q*) of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) is dissolved.

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

Medium: 0.05 M phosphate buffer, pH 8.5 (6.8 g of monobasic potassium phosphate and 1.99 g of sodium hydroxide in 1 L of water, and adjust with diluted phosphoric acid or diluted sodium hydroxide to a pH of 8.5 ± 0.05); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Acetonitrile and water containing 5 g/L of monobasic ammonium phosphate (480:520)

Standard stock solution: Transfer 67 mg of USP Glyburide RS to a 500-mL volumetric flask, dissolve in 40 mL of methanol with sonication for 5 min, and dilute with *Medium* to volume.

Standard solutions: Dilute the *Standard stock solution* with *Medium* to obtain solutions having known concentrations of 0.0017 mg/mL (for Tablets labeled to contain 1.5 mg), 0.0034 mg/mL (for Tablets labeled to contain 3 mg), 0.0047 mg/mL (for Tablets labeled to contain 4.5 mg), and 0.0067 mg/mL (for Tablets labeled to contain 6 mg).

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.5-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.0-mm × 25-cm; 10-µm packing L7

Flow rate: 1.5 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 glyburide ($C_{23}H_{28}ClN_3O_5S$) 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 75% (*Q*) of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) is dissolved.

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

Medium: 0.05 M phosphate buffer, pH 7.5 (40.8 g of monobasic potassium phosphate and 9.4 g of sodium hydroxide, in 6 L of water, and adjust with diluted sodium hydroxide to a pH of 7.5 ± 0.1); 900 mL

Apparatus 2: 50 rpm

Time: 45 min

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

Diluent: Acetonitrile and water (5:1)

Standard stock solution: 0.67 mg/mL of USP Glyburide RS in *Diluent*

Standard solution: 6.7 µg/mL of USP Glyburide RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L7

Flow rate: 2 mL/min

Injection volume: 75 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) 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 75% (Q) of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) is dissolved.

Test 4 (nonmicronized glyburide)**:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.05 M borate buffer, pH 8.0, with 0.014 M hexadecyltrimethylammonium bromide (prepared by dissolving about 180.0 g of hexadecyltrimethylammonium bromide, 55.6 g of boric acid, 67.1 g of potassium chloride, and 2.8 g of sodium hydroxide in 1500 mL of water at 50° under vigorous stirring for several hours, cooling to room temperature, diluting with water to 2000 mL, adjusting with diluted hydrochloric acid or diluted sodium hydroxide to a pH of 8.00 ± 0.05, and diluting 50 mL of this solution with water to 900 mL); 900 mL

Apparatus 1: 50 rpm

Time: 45 min

Mobile phase: Acetonitrile and water (11:9) containing 5.2 g of monobasic ammonium phosphate for each 2 L

Standard stock solution: 0.27 mg/mL of USP Glyburide RS in alcohol. Transfer 1.0 mL of this solution to a 100-mL volumetric flask, and dilute with *Medium* to volume.

Standard solution: 2.8 µg/mL of USP Glyburide RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 5-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; packing L7

Flow rate: 2 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 glyburide ($C_{23}H_{28}ClN_3O_5S$) 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 75% (Q) of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) is dissolved.

Test 5 (micronized glyburide): If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Medium: 0.05 M phosphate buffer, pH 7.5 (40.8 g of monobasic potassium phosphate and 9.4 g of sodium hydroxide, in 6 L of water, and adjust with diluted sodium hydroxide to a pH of 7.5 ± 0.1); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: USP Glyburide RS in *Medium* in a concentration similar to the one expected in the *Sample solution*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Mobile phase, Diluent, Chromatographic system, System suitability, and **Analysis:** Proceed as directed for *Test 3*.

Tolerances: NLT 75% (*Q*) of the labeled amount of glyburide ($C_{23}H_{28}ClN_3O_5S$) is dissolved.

IMPURITIES

• **Organic Impurities**

Mobile phase: Dissolve 0.087 g of dibasic potassium phosphate and 0.612 g of monobasic potassium phosphate in 550 mL of water to obtain a solution with a pH of 6.00 ± 0.05. Add 450 mL of methanol.

Diluent: Dissolve 0.871 g of dibasic potassium phosphate in 550 mL of water, and dilute with methanol to 1 L.

Standard stock solution: 0.1 mg/mL each of USP Glyburide RS and USP Glyburide Related Compound A RS in methanol

Standard solution: 0.0004 mg/mL each of USP Glyburide RS and USP Glyburide Related Compound A RS in *Mobile phase* from the *Standard stock solution*. This solution is stable for 48 h when stored at room temperature.

Sample solution: Weigh, and powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to about 20 mg of glyburide, to a 100-mL volumetric flask. Add 80 mL of *Diluent*, and sonicate for 15 min, then shake the flask for 10 min. Dilute with *Diluent* to volume, and mix. Centrifuge a portion of this solution, and use a clear supernatant. This solution is stable for 14 h when stored at room temperature.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 3.9-mm × 15-cm; 4-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for glyburide related compound A and glyburide are about 0.3 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 15 between glyburide related compound A and glyburide

Relative standard deviation: NMT 5% for glyburide related compound A

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of glyburide related compound A in the portion of Tablets taken:

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

r_U = peak response of glyburide related compound A from the *Sample solution*

r_S = peak response of glyburide related compound A from the *Standard solution*

C_S = concentration of USP Glyburide Related Compound A RS in the *Standard solution* (mg/mL)

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

Acceptance criteria

Glyburide related compound A: NMT 5.3%

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.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Glyburide RS

USP Glyburide Related Compound A RS

4-[2-(5-Chloro-2-methoxybenzamido)ethyl]▲benzenesulfonamide.▲ (ERR 1-Oct-2021)

$C_{16}H_{17}ClN_2O_4S$ 368.83

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

Chromatographic Database Information: Chromatographic Database

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