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Glipizide and Metformin Hydrochloride Tablets

DEFINITION
Glipizide and Metformin Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of glipizide ($C_{21}H_{27}N_5O_4S$) and metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$).

IDENTIFICATION
Change to read:

- A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197A▲](#) (CN 1-MAY-2020)
Sample: Transfer NLT 10 Tablets to a suitable container, add 10 mL of methanol, and shake to remove any Tablet coating. Drain the methanol, add 20 mL of water, and stir until the Tablets dissolve (1 h). Transfer the solution to a separatory funnel, and extract twice with 10-mL portions of chloroform, shaking for approximately 5 min. Transfer the lower organic layer into a beaker containing 3 to 4 g of anhydrous magnesium sulfate. Repeat the extraction of the solution in the separatory funnel two more times, each time using 20-mL portions of chloroform. Swirl the mixture in the beaker for 1 min. Filter, and collect the filtrate. Evaporate the solvent under vacuum, and dry the residue under vacuum for 4 h at 105°. Mound the residue onto a diamond cell.
Acceptance criteria: The IR spectrum exhibits maxima only at the same wavelengths as a similarly obtained spectrum of [USP Glipizide RS](#).
- B.** The retention time of the major peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay for *Glipizide*.
- C.** The retention time of the major peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay for *Metformin Hydrochloride*.

ASSAY

- GLIPIZIDE**
Solution A: 2.6 g/L of dibasic ammonium phosphate in water. Adjust with ammonium hydroxide to a pH of 8.0.
Solution B: Acetonitrile, water, and *Solution A* (1:14:5)
Solution C: Acetonitrile, water, and *Solution A* (2:1:1)
Diluent: Acetonitrile and water (60:40)
Standard stock solution: Transfer a weighed quantity of [USP Glipizide RS](#) to a suitable low-actinic volumetric flask. Dissolve first in acetonitrile, using 60% of the final volume, by sonicating for 20 min, then dilute with water to volume to obtain a solution having a concentration of 0.1 mg/mL of glipizide. [NOTE—The solution is stable for 2 weeks when stored at 5° and protected from light.]
Standard solution: Transfer 25.0 mL of *Standard stock solution* to a 200-mL low-actinic volumetric flask. Add 75 mL of *Diluent*, and dilute with water to volume to obtain a solution having a known glipizide concentration of 0.0125 mg/mL. [NOTE—The solution is stable for 2 weeks when stored at 5° and protected from light.]
System suitability solution: Transfer approximately 5 mg of [USP Glipizide Related Compound A RS](#) to a 500-mL volumetric flask, and fill halfway with acetonitrile. Sonicate for 30 min to dissolve, and dilute with acetonitrile to volume. Transfer 1 mL of this solution to a 50-mL low-actinic volumetric flask, and dilute with *Standard solution* to volume.
Sample solution: Transfer NLT 5 Tablets to a suitable volumetric flask, and fill halfway with *Diluent*. Sonicate for 30 min, and shake vigorously for another 30 min to dissolve. Dilute with water to volume, and mix to obtain a solution with a final glipizide concentration of 0.0125 mg/mL. Pass a portion of this solution through a nylon or PVDF filter of 0.2-µm pore size, and use the filtrate. [NOTE—The solution is stable for 2 weeks when stored at 5° and protected from light.]
Mobile phase: See the gradient table below.

Time (min)	Solution B (%)	Solution C (%)
0	100	

Time (min)	Solution B (%)	Solution C (%)
3	100	0
18	0	100
20	0	100
22	100	0
30	100	0

Chromatographic system(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 223 nm**Column:** 4.6-mm × 15-cm; 5-μm packing L7**Flow rate:** 1 mL/min**Injection size:** 50 μL**System suitability****Samples:** *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for glipizide related compound A and glipizide are 0.92 and 1.0, respectively.]

Suitability requirements**Resolution:** Greater than 1.2 between glipizide related compound A and glipizide, *System suitability solution***Relative standard deviation:** Less than 2.0%, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of $C_{21}H_{27}N_5O_4S$ 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 Glipizide RS](#) in the *Standard solution* (mg/mL) C_U = nominal concentration of glipizide in the *Sample solution* (mg/mL)**Acceptance criteria:** 90.0%–110.0%**• METFORMIN HYDROCHLORIDE****Solution A:** 9.41 g/L of sodium 1-hexanesulfonate in water, and adjust with trifluoroacetic acid to a pH of 2.0 (50 mM hexanesulfonic acid solution)**Solution B:** Acetonitrile and water (40:60)**Mobile phase:** *Solution A*, *Solution B*, and water (3:2:5)**Diluent pH 2.0:** Acetonitrile, *Solution A*, and water (7:30:63)**Standard solution:** 0.1 mg/mL of [USP Metformin Hydrochloride RS](#) in *Diluent pH 2.0***System suitability solution:** 5 μg/mL of [USP Metformin Related Compound A RS](#) in water. Pipet 0.5 mL of this solution into a 50-mL volumetric flask, and dilute with *Standard solution* to volume.**Sample solution:** Dilute a portion of the *Sample solution*, obtained as directed in the Assay for Glipizide, with *Diluent pH 2.0*, to obtain a solution having a concentration of 0.1 mg/mL of metformin hydrochloride.**Chromatographic system**(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 218 nm**Column:** 4.6-mm × 15-cm; 3.5-μm packing L11**Flow rate:** 1 mL/min