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Glycopyrrolate Tablets

DEFINITION

Glycopyrrolate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of glycopyrrolate ($C_{19}H_{28}BrNO_3$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2019)

ASSAY

Change to read:

• **Procedure**

Buffer solution: Prepare a solution of 1.0 g of sodium sulfate anhydrous and 200 mg of sodium 1-hexanesulfonate monohydrate in 650 mL of water. To this solution add 3.0 mL of 1 N sulfuric acid, and mix.

Mobile phase: Acetonitrile, methanol, and *Buffer solution* (20:15:65)

Standard solution: 0.1 mg/mL of USP Glycopyrrolate RS in *Mobile phase*

Sample solution: ▲Nominally▲ (USP 1-Aug-2019) 0.1 mg/mL of glycopyrrolate in *Mobile phase*. Prepare by transferring 10 Tablets to a suitable volumetric flask. Add *Mobile phase* to 50% of the volume of the flask, and sonicate for 10 min or until the Tablets disintegrate completely. Add *Mobile phase* to 75% of the volume of the flask, shake mechanically for 30 min, and dilute with *Mobile phase* to volume. Centrifuge a portion of the solution, and pass the supernatant through a suitable filter, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 222 nm. ▲For *Identification B*, use a diode array detector in the range of 210–400 nm.▲ (USP 1-Aug-2019)

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

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of glycopyrrolate ($C_{19}H_{28}BrNO_3$) in the portion of Tablets taken:

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

r_U = peak response of glycopyrrolate from the *Sample solution*

r_S = peak response of glycopyrrolate from the *Standard solution*

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

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer solution: 1.0 g of sodium sulfate anhydrous and 200 mg of sodium 1-pentanesulfonate in 620 mL of water

Mobile phase: Acetonitrile, methanol, *Buffer solution*, and 1 N sulfuric acid (200:180:620:3)

Standard stock solution: 0.2 mg/mL of USP Glycopyrrolate RS in *Medium*. A small volume of methanol, not exceeding 20% of the final volume, can be used to solubilize glycopyrrolate.

Standard solution: (*L*/500) mg/mL of glycopyrrolate in *Medium* from the *Standard stock solution*, where *L* is the label claim in mg/Tablet. Prepare this solution fresh, and refrigerate immediately at 5°.

Sample solution: Pass a portion of the solution under test through a suitable filter, discarding the first few milliliters of the filtrate. Refrigerate the samples at 5°.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Temperatures

Autosampler: 5°

Column: 40°

Flow rate: 1.2 mL/min

Injection volume: 80 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 ▲▲ (USP 1-Aug-2019) percentage of the labeled amount of glycopyrrolate 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 ▲USP Glycopyrrolate RS▲ (USP 1-Aug-2019) in the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of glycopyrrolate ($C_{19}H_{28}BrNO_3$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer solution: Prepare a solution of 1.0 g of sodium sulfate anhydrous and 200 mg of sodium 1-hexanesulfonate monohydrate in 650 mL of water. To this solution add 3.0 mL of 1 N sulfuric acid, and mix.

Diluent: Prepare a solution of 1.0 g of sodium sulfate anhydrous, 6.8 g of monobasic potassium phosphate, and 200 mg of sodium 1-hexanesulfonate monohydrate in 650 mL of water. To this solution add 3.0 mL of 1 N sulfuric acid, 150 mL of methanol, and 200 mL of acetonitrile, and mix. Adjust with phosphoric acid to a pH of 2.8.

Solution A: Acetonitrile, methanol, and *Buffer solution* (20:15:65)

Solution B: Acetonitrile, methanol, and *Buffer solution* (50:15:35)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
25	10	90
35	10	90
37	100	0
45	100	0

Standard solution: 0.0015 mg/mL each of USP Glycopyrrolate RS, USP Glycopyrrolate Related Compound B RS, and USP Glycopyrrolate Related Compound C RS in *Diluent*. Sonicate, if necessary, to facilitate dissolution.

Sample solution: ▲Nominally▲ (USP 1-Aug-2019) 0.5 mg/mL of glycopyrrolate in *Diluent*. Prepare by transferring the equivalent of 25 mg of glycopyrrolate from a portion of NLT 20 powdered Tablets to a 50-mL volumetric flask. Add 30 mL of *Diluent*, sonicate for 10 min, shake mechanically for 30 min, and dilute with *Diluent* to volume. Centrifuge a portion of the solution, and pass the supernatant through a suitable filter, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between glycopyrrolate and glycopyrrolate related compound B

Tailing factor: NMT 2.0 for the glycopyrrolate peak

Relative standard deviation: NMT 6.0% for the glycopyrrolate and glycopyrrolate related compound C peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of glycopyrrolate related compound C in the portion of Tablets taken:

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

r_U = peak response of glycopyrrolate related compound C from the *Sample solution*

r_S = peak response of glycopyrrolate related compound C from the *Standard solution*

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

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

Calculate the percentage of any other individual impurity in the portion of Tablets taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

r_S = peak response of glycopyrrolate from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
5-Nitroisophthalic acid[a]	0.45	—[b]
Glycopyrrolate	1.00	—
Glycopyrrolate base[c]	1.14	—[b]
Cyclopentylmandelic acid[d]	2.68	0.5
Any other individual impurity	—	0.2
Total impurities	—	1.2

[a] Glycopyrrolate related compound A.

[b] Disregard the peaks due to 5-nitroisophthalic acid and glycopyrrolate base, because these are process impurities and are controlled in the drug substance monograph.

[c] Glycopyrrolate related compound B.

[d] Glycopyrrolate related compound C.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Glycopyrrolate RS

USP Glycopyrrolate Related Compound B RS

▲[Note—May be available as a free base or a hydrochloride salt.]▲ (USP 1-Aug-2019)

1-Methylpyrrolidin-3-yl-2-cyclopentyl-2-hydroxy-2-phenylacetate.

$C_{18}H_{25}NO_3$ 303.40

▲1-Methylpyrrolidin-3-yl 2-cyclopentyl-2-hydroxy-2-phenylacetate hydrochloride. $C_{18}H_{25}NO_3 \cdot HCl$ 339.86▲ (USP 1-Aug-2019)

USP Glycopyrrolate Related Compound C RS

2-Cyclopentyl-2-hydroxy-2-phenylacetic acid.

$C_{13}H_{16}O_3$ 220.26

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

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

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