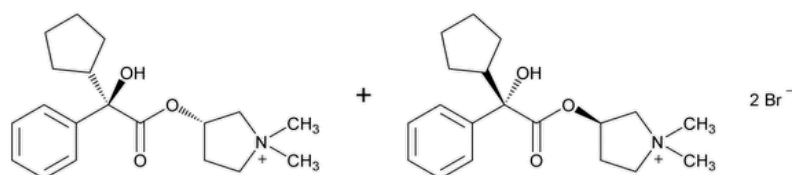


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# Glycopyrrolate

## Change to read:



$C_{19}H_{28}BrNO_3$  ▲398.34▲ (USP 1-Dec-2019)

Pyridinium, 3-[(*SR*)-(cyclopentylhydroxyphenyl)acetyl]oxy]-1,1-dimethyl-, [*RS*-] bromide;

(*RS*)-[3-(*SR*)-Hydroxy-1,1-dimethylpyridinium bromide] α-cyclopentylmandelate CAS RN®: ▲51186-83-5.▲ (USP 1-Dec-2019)

## DEFINITION

Glycopyrrolate contains NLT 98.0% and NMT 102.0% of glycopyrrolate ( $C_{19}H_{28}BrNO_3$ ), calculated on the dried basis.

## IDENTIFICATION

### Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#)▲ (CN 1-MAY-2020) ▲ or [\(197A\)](#): Meets the requirements▲ (USP 1-Dec-2019)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C.** [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Bromide](#)

**Sample solution:** 25 mg/mL

**Acceptance criteria:** Meets the requirements

## ASSAY

### Change to read:

#### • PROCEDURE

**Buffer solution:** Prepare a solution of 1.0 g of [anhydrous sodium sulfate](#) 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:** 0.1 mg/mL of Glycopyrrolate in *Mobile phase*

#### 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:** 1.2 mL/min

**Injection volume:** 50 μL

#### System suitability

**Sample:** *Standard solution*

#### Suitability requirements

**Tailing factor:** NMT 2.0

**Relative standard deviation:** ▲NMT 0.73%▲ (USP 1-Dec-2019)

#### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of glycopyrrolate ( $C_{19}H_{28}BrNO_3$ ) in the portion of Glycopyrrolate 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)

$C_U$  = concentration of Glycopyrrolate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.0%–102.0% on the dried basis

## IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.3%

**Change to read:**

- **ORGANIC IMPURITIES, PROCEDURE 1**

[NOTE—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 1* is recommended when  $\Delta$ glycopyrrolate related compound A $\Delta$  (USP 1-Dec-2019) may be present (see [Table 2](#)); *Procedure 2* is recommended when didehydroglycopyrrolate,

$\Delta$ glycopyrrolate related compound I $\Delta$  (USP 1-Dec-2019) and  $\Delta$ glycopyrrolate related compound L $\Delta$  (USP 1-Dec-2019) may be present (see [Table 4](#)).]

**Buffer solution:** Prepare a solution of 1.0 g of [anhydrous sodium sulfate](#) 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 [anhydrous sodium sulfate](#), 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:** 1.5  $\mu$ g/mL each of [USP Glycopyrrolate RS](#), [USP Glycopyrrolate Related Compound A RS](#), [USP Glycopyrrolate Related Compound B RS](#), and [USP Glycopyrrolate Related Compound C RS](#) in *Diluent*. Sonicate, if necessary, to facilitate dissolution.

**Sample solution:** 1.0 mg/mL of Glycopyrrolate in *Diluent*

## Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

**Mode:** LC

**Detector:** UV 222 nm

**Column:** 4.6-mm  $\times$  15-cm; 5- $\mu$ m 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 each peak

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the glycopyrrolate related compounds A, B, and C in the portion of Glycopyrrolate taken:

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

$r_U$  = peak response of each related compound from the *Sample solution*

$r_S$  = peak response of the corresponding related compound from the *Standard solution*

$C_S$  = concentration of the corresponding Reference Standard in the *Standard solution* (mg/mL)

$C_U$  = concentration of Glycopyrrolate in the *Sample solution* (mg/mL)

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

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

$r_U$  = peak response of each 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)

$C_U$  = concentration of Glycopyrrolate in the *Sample solution* (mg/mL)

**Acceptance criteria:** See [Table 2](#).

**Table 2**

| Name                                                | Relative Retention Time | Acceptance Criteria, NMT (%) |
|-----------------------------------------------------|-------------------------|------------------------------|
| ▲Glycopyrrolate related compound A▲(USP 1-Dec-2019) | 0.45                    | 0.15                         |
| Glycopyrrolate                                      | 1.00                    | —                            |
| ▲Glycopyrrolate related compound B▲(USP 1-Dec-2019) | 1.14                    | 0.15                         |
| ▲Glycopyrrolate related compound C▲(USP 1-Dec-2019) | 2.68                    | 0.15                         |
| Any individual unspecified impurity                 | —                       | 0.10                         |
| Total impurities                                    | —                       | 0.50                         |

▲ ▲ (USP 1-Dec-2019)

**Change to read:**