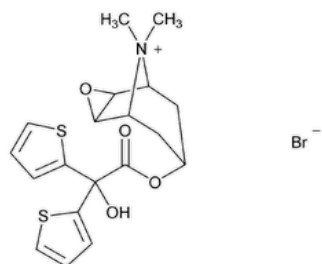


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Add the following:

▲Tiotropium Bromide



$C_{19}H_{22}BrNO_4S_2$ 472.41

3-Oxa-9-azoniatricyclo[3.3.1.0^{2,4}]nonane, 7-[(hydroxydi-2-thienyl)oxy]-9,9-dimethyl-, bromide, (1 α ,2 β ,4 β ,5 α ,7 β)-;

(1*R*,2*R*,4*S*,5*S*,7*S*)-7-(2-Hydroxy-2-di(thiophen-2-yl)acetoxy)-9,9-dimethyl-3-oxa-9-azatricyclo[3.3.1.0^{2,4}]nonan-9-ium bromide CAS RN[®]: 136310-93-5; UNII: XX112XZP0J.

Tiotropium bromide monohydrate

$C_{19}H_{22}BrNO_4S_2 \cdot H_2O$ 490.43 CAS RN[®]: 411207-31-3; UNII: L64SX0195N.

DEFINITION

Tiotropium Bromide contains NLT 98.0% and NMT 102.0% of tiotropium bromide ($C_{19}H_{22}BrNO_4S_2$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** 197A, 197K, or 197M
- **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: 10 mg/mL of Tiotropium Bromide in [water](#)
Acceptance criteria: Meets the requirements of test *B* (silver nitrate precipitate test)

ASSAY

• PROCEDURE

Protect solutions containing tiotropium bromide from light.

Buffer: 5 g/L of [monobasic potassium phosphate](#) and 1 g/L of [sodium methanesulfonate](#) in [water](#). Adjust with 1 M [phosphoric acid](#) to a pH of 3.0.

Solution A: [Acetonitrile](#), [methanol](#), and *Buffer* (40:10:50)

Mobile phase: *Buffer* and *Solution A* (78:22)

System suitability solution: 0.1 mg/mL each of [USP Tiotropium Bromide RS](#) and [USP Tiotropium Related Compound C RS](#) in *Solution A*

Standard solution: 0.1 mg/mL of [USP Tiotropium Bromide RS](#) in *Solution A*

Sample solution: 0.1 mg/mL of Tiotropium Bromide in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 3.0-mm $\times$ 15-cm; 3.5- μ m packing [L56](#)

Column temperature: 50°

Flow rate: 1.2 mL/min

Injection volume: 5 μ L

Run time: NLT 1.6 times the retention time of tiotropium

System suitability**Samples:** *System suitability solution* and *Standard solution***Suitability requirements****Resolution:** NLT 1.5 between tiotropium and tiotropium related compound C, *System suitability solution***Tailing factor:** NMT 1.8, *Standard solution***Relative standard deviation:** NMT 0.73%, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of tiotropium bromide ($C_{19}H_{22}BrNO_4S_2$) in the portion of Tiotropium Bromide taken:

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

 r_U = peak response of tiotropium from the *Sample solution* r_S = peak response of tiotropium from the *Standard solution* C_S = concentration of [USP Tiotropium Bromide RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Tiotropium Bromide in the *Sample solution* (mg/mL)**Acceptance criteria:** 98.0%–102.0% on the anhydrous basis**IMPURITIES**• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%• **ORGANIC IMPURITIES**

Protect solutions containing tiotropium bromide from light.

Solution A: 5 g/L of [monobasic potassium phosphate](#) and 1 g/L of [sodium methanesulfonate](#) in [water](#). Adjust with 1 M [phosphoric acid](#) to a pH of 3.0.**Solution B:** [Acetonitrile](#), [methanol](#), and *Solution A* (40:10:50)**Mobile phase:** See [Table 1](#).**Table 1**

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3	90	10
17	80	20
28	25	75
30	25	75

Standard solution: 20 µg/mL of [USP Tiotropium Bromide RS](#) in *Solution B***Sample solution:** 2000 µg/mL of Tiotropium Bromide in *Solution B***System suitability solution:** 2 µg/mL of [USP Tiotropium Related Compound C RS](#) in the *Sample solution***Sensitivity solution:** 1 µg/mL of [USP Tiotropium Bromide RS](#) in *Solution B***Chromatographic system**(See [Chromatography \(621\)](#), *System Suitability*.)**Mode:** LC**Detector:** UV 240 nm**Column:** 3.0-mm × 15-cm; 3.5-µm packing [L56](#)**Column temperature:** 50°**Flow rate:** 1.2 mL/min**Injection volume:** 5 µL**System suitability**