Sample solution: 1 mg/mL of Rizatriptan Benzoate in *Solution A*
System suitability solution: 1 mg/mL of USP Rizatriptan Benzoate System Suitability Mixture RS in *Solution A*
Sensitivity solution: 0.5 µg/mL of Rizatriptan Benzoate obtained by suitable dilution of the *Sample solution* with *Solution A*
Chromatographic system: Prepare as directed in the *Assay*.
System suitability
Sample: *System suitability solution* and *Sensitivity solution*
[NOTE—The relative retention times for rizatriptan, rizatriptan impurity C, and benzoic acid are 1.0, about 1.3, and about 2.1, respectively.]
Suitability requirements
Resolution: NLT 2.0 between rizatriptan and rizatriptan impurity C, *System suitability solution*
Signal-to-noise ratio: NLT 10 for the rizatriptain peak, *Sensitivity solution*
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of Rizatriptan Benzoate taken:

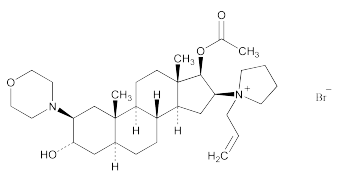
$$\text{Result} = [r_U/(r_T - r_{BA})] \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_T = sum of the areas of all the peaks from the *Sample solution*
r_{BA} = area of the benzoic acid peak from the *Sample solution*
Acceptance criteria
Any individual impurity: NMT 0.10%
Total: NMT 0.3%. [NOTE—Disregard any impurity that is less than 0.05%.]

SPECIFIC TESTS
- **WATER DETERMINATION,** *Method Ia* ⟨**921**⟩**:** NMT 0.5%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Store in well-closed containers at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Rizatriptan Benzoate RS
USP Rizatriptan Benzoate System Suitability Mixture RS. Mixture of rizatriptan benzoate and at least 0.1% of rizatriptan impurity C. Rizatriptan impurity C is 2-{5-[(1*H*-1,2,4-triazol-1-yl)methyl]-1*H*-indol-2-yl}-*N*,*N*-dimethylethanamine.
($C_{15}H_{19}N_5$ 269.34)

Rocuronium Bromide



$C_{32}H_{53}BrN_2O_4$ 609.68
Pyrrolidinium, 1-[(2β,3α,5α,16β,17β)-17-(acetyloxy)-3-hydroxy-2-(4-morpholinyl)androstan-16-yl]-1-(2-propenyl)-, bromide; 1-Allyl-1-(3α,17β-dihydroxy-2β-morpholino-5α-androstan-16β-yl)pyrrolidinium bromide, 17-acetate [119302-91-9].

DEFINITION
Rocuronium Bromide contains NLT 98.0% and NMT 102.0% of $C_{32}H_{53}BrN_2O_4$, calculated on the anhydrous and 2-propanol-free or acetic acid-free basis.

IDENTIFICATION
- **A. INFRARED ABSORPTION** ⟨**197M**⟩
- **B.** The retention time of the rocuronium bromide peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. IDENTIFICATION TESTS—GENERAL,** *Bromide* ⟨**191**⟩**:** Meets the requirements of the silver nitrate test
Sample solution: 10 mg/mL

ASSAY
- **PROCEDURE**
Diluent: Acetonitrile and water (9:1)
Buffer: 4.53 g/L of tetramethylammonium hydroxide pentahydrate. Adjust the solution with phosphoric acid to a pH of 7.4.
Mobile phase: Acetonitrile and *Buffer* (9:1)
Standard solution: 1 mg/mL of USP Rocuronium Bromide RS in *Diluent*
Sample solution: 1 mg/mL of Rocuronium Bromide in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-µm packing L3
Flow rate: 2 mL/min
Temperature: 30°
Injection size: 5 µL
System suitability
[NOTE—The system may need equilibration for 4 h.]
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 $C_{32}H_{53}BrN_2O_4$ in the portion of Rocuronium Bromide 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 Rocuronium Bromide RS in the *Standard solution* (mg/mL)
C_U = concentration of Rocuronium Bromide in the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the anhydrous and 2-propanol-free or acetic acid-free basis

IMPURITIES
Inorganic Impurities
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
Organic Impurities
- **PROCEDURE**
Diluent, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.
Peak identification solution: 1 mg/mL of USP Rocuronium Peak Identification Mixture RS in *Diluent*
Standard solution: 0.01 mg/mL of USP Rocuronium Bromide RS in *Diluent*
Sample solution: 10 mg/mL of Rocuronium Bromide in *Diluent*
Run time: 2.5 times the retention time for rocuronium
System suitability
[NOTE—The system may need equilibration for 4 h.]
Sample: *Peak identification solution*
Suitability requirements
Peak-to-valley ratio: The ratio of the height of the rocuronium related compound H peak to the height of the valley between the rocuronium related compound H peak and the rocuronium peak is NLT 1.5.
Resolution: NLT 3.5 between rocuronium and rocuronium related compound C

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Rocuronium Bromide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

r_S = peak response of rocuronium bromide from the *Standard solution*

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

C_U = concentration of Rocuronium Bromide in the *Sample solution* (mg/mL)

F = relative response factor from *Impurity Table 1*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.5%

[NOTE—Disregard any peak eluting before rocuronium bromide related compound A, and any peak with an area less than 0.5 times that of the principal peak from the *Standard solution.*]

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Rocuronium related compound A[a]	0.20	2.1	0.2
Rocuronium related compound G[b]	0.44	2.3	0.1
Rocuronium related compound F[c]	0.75	0.79	0.1
Rocuronium related compound B[d]	0.80	1.0	0.3
Rocuronium related compound D[e]	0.90	1.0	0.1
Rocuronium related compound H[f]	0.95	2.9	0.1
Rocuronium bromide	1.0	—	—
Rocuronium related compound C[g]	1.20	1.0	0.3
Rocuronium related compound E[h]	1.53	1.0	0.1
Any individual unspecified impurity	—	—	0.10

[a] 3α-Hydroxy-2β-(morpholin-4-yl)-16β-(pyrrolidin-1-yl)-5α-androstan-17β-yl acetate.

[b] 2β-(Morpholin-4-yl)-16β-(pyrrolidin-1-yl)-5α-androstan-3α,17β-diol.

[c] 1-[3α,17β-Bis(acetyloxy)-2β-(pyrrolidin-1-yl)-5α-androstan-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

[d] 1-[3α,17β-Bis(acetyloxy)-2β-(morpholin-4-yl)-5α-androstan-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

[e] 1-[3α-(Acetyloxy)-17β-hydroxy-2β-(morpholin-4-yl)-5α-androstan-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

[f] 1-[17β-(Acetyloxy)-2-(morpholin-4-yl)-3-oxo-5α-androst-1-en-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

[g] 1-[3α,17β-Dihydroxy-2β-(morpholin-4-yl)-5α-androstan-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

[h] 1-[17β-(Acetyloxy)-3α-hydroxy-2β-(pyrrolidin-1-yl)-5α-androstan-16β-yl]-1-(prop-2-enyl)pyrrolidinium.

SPECIFIC TESTS

- **LIMIT OF 2-PROPANOL**

[NOTE—Perform this test only if 2-propanol is a known organic manufacturing process impurity.]

Standard stock solution: Transfer 35.0 µL of ethyl ether, 32.0 µL of 2-propanol, and 19.0 µL of methylene chloride to a 100-mL volumetric flask containing 90 mL of dimethylformamide (DMF), and dilute with DMF to volume.

Standard solution: Transfer 2.5 mL of the *Standard stock solution* to a 25-mL volumetric flask containing 20 mL of DMF, and dilute with DMF to volume.

Dilute standard solution: Transfer 1.0 mL of the *Standard solution* and 4.0 mL of water to a 20-mL headspace vial. Immediately close the vial with a cap, and mix.

Sample solution: Transfer 50 mg of Rocuronium Bromide to a 20-mL headspace vial. Dissolve in 1.0 mL of DMF. Add 4 mL of water, immediately close the vial with a cap, and mix.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 60-cm fused silica column coated with a 1.8-µm layer of liquid phase G43

Temperature: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	50	8
50	20	250	8

Injector: 140°

Detector block: 280°

Carrier gas: Helium with a linear velocity of 55 cm/s or nitrogen with a linear velocity of 25 cm/s

Split ratio: 1:6

Head space autosampler

Sample equilibration temperature: 90°

Sample equilibration time: 15 min

Transfer line temperature: 140°

System suitability

Sample: *Dilute standard solution*

[NOTE—The relative retention times for ethyl ether, 2-propanol, and methylene chloride are 0.87, 1.0, and 1.08, respectively.]

Suitability requirements

Resolution: NLT 1.0 between ethyl ether and 2-propanol; NLT 1.0 between 2-propanol and methylene chloride

Relative standard deviation: NMT 10.0% for the 2-propanol peak

Analysis

Samples: *Dilute standard solution* and *Sample solution*

Calculate the percentage of 2-propanol in the portion of Rocuronium Bromide taken:

$$\text{Result} = [(r_U/r_S) \times (V \times D/W) \times 100]/F$$

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

r_S = peak response of rocuronium bromide from the *Dilute standard solution*

V = volume of 2-propanol taken to prepare the *Standard stock solution* (µL)

D = relative density of 2-propanol (mg/µL), 0.786

W = weight of Rocuronium Bromide taken to prepare the *Sample solution* (mg)

F = dilution factor for the *Standard solution*, 1000

Acceptance criteria: NMT 1.0%

- **LIMIT OF ACETIC ACID**

[NOTE—Perform this test only if acetic acid is a known organic manufacturing process impurity.]

Mobile phase: 6.1 g of sodium perchlorate in 800 mL of water. Adjust with 1 N sulfuric acid to a pH of 2.0. Dilute to 1 L.

Standard solution: 0.2 mg/mL of glacial acetic acid in *Mobile phase*
Sample solution: 6.0 mg/mL of Rocuronium Bromide in *Mobile phase*. [NOTE—Sonication may be necessary to completely dissolve the rocuronium bromide.]
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 205 nm
Column: 4.6-mm × 15-cm; packing L1
Temperature: 30°
Flow rate: 1 mL/min
Injection size: 20 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention time of acetic acid is about 3.8 min.]
Suitability requirements
Column efficiency: NLT 5000 theoretical plates
Tailing factor: NMT 1.8
Relative standard deviation: NMT 5.0% for three injections
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of acetic acid in the portion of Rocuronium Bromide taken:

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

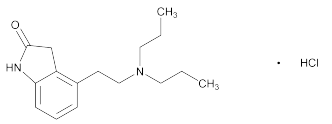
r_U = peak response for acetic acid from the *Sample solution*
r_S = peak response for acetic acid from the *Standard solution*
C_S = concentration of acetic acid in the *Standard solution* (mg/mL)
C_U = concentration of Rocuronium Bromide in the *Sample solution* (mg/mL)
Acceptance criteria: NMT 5.0%

- **WATER DETERMINATION,** *Method Ic* ⟨**921**⟩**:** NMT 4.0%
- **pH** ⟨**791**⟩**:** 7.0–9.5
Sample solution: 10 mg/mL
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781**⟩**:** Between 28.5° and 32.0°, measured on the anhydrous and solvent-free basis at 20°
Sample solution: 10 mg/mL in 0.05 M hydrochloric acid
- **COLOR AND ACHROMICITY** ⟨**631**⟩
Reference solution: Mix 33 mL of *Matching Fluid G* and 67 mL of water.
Sample solution: 10 mg/mL of Rocuronium Bromide in water
Analysis: Proceed as directed for *Color and Achromicity* ⟨631⟩.
Acceptance criteria: The *Sample solution* is not more intensely colored than the *Reference solution.*

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light and moisture. Store at –20° or below. If the article contains acetic acid, store it between 2° and 8°.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Rocuronium Bromide RS
USP Rocuronium Peak Identification Mixture RS
Mixture of approximately 0.2% to 0.4% each of rocuronium related compound A, rocuronium related compound B, rocuronium related compound C, rocuronium related compound D, rocuronium related compound E, rocuronium related compound F, rocuronium related compound G, and rocuronium related compound H in a matrix of rocuronium bromide.

Ropinirole Hydrochloride



$C_{16}H_{24}N_2O \cdot HCl$ 296.84
2*H*-Indol-2-one, 4-[2-(dipropylamino)ethyl]-1,3-dihydro-, monohydrochloride;
4-[2-(Dipropylamino)ethyl]-2-indolinone monohydrochloride [91374-20-8].

DEFINITION
Ropinirole Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{16}H_{24}N_2O \cdot HCl$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B.** The retention time of the ropinirole hydrochloride peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. IDENTIFICATION TEST—GENERAL,** *Chloride* ⟨**191**⟩**:** Meets the requirements
Sample: 20 mg/mL

ASSAY

- **PROCEDURE**
Buffer: 1.88 g of sodium 1-hexanesulfonate and 1 g of phosphoric acid in 1 L of water. Adjust with dilute triethylamine solution (1 mL/10 mL) to a pH of 6.5.
Diluent: Acetonitrile and water (1:4)
Mobile phase: Acetonitrile and *Buffer* (1:4)
Standard solution: 0.1 mg/mL of USP Ropinirole Hydrochloride RS in *Diluent*. Sonication may be used to aid dissolution.
Sample solution: 0.1 mg/mL of Ropinirole Hydrochloride in *Diluent*. Sonication may be used to aid dissolution.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 25-cm; 5-µm packing L7
Column temperature: 30°
Flow rate: 1.0 mL/min
Injection size: 10 µL
Run time: 2.5 times the retention time of ropinirole
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 1.6
Relative standard deviation: NMT 1.5%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{16}H_{24}N_2O \cdot HCl$ in the portion of Ropinirole Hydrochloride 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 the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)