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Ropinirole Tablets

DEFINITION

Ropinirole Tablets contain ropinirole hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of ropinirole free base ($C_{16}H_{24}N_2O$).

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-Dec-2019)

ASSAY

Change to read:

• **Procedure**

Buffer: 3.85 g/L of ammonium acetate. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile, methanol, and *Buffer* (7:3:40)

System suitability solution: 0.1 mg/mL of USP Ropinirole Hydrochloride RS and 0.5 µg/mL of USP Ropinirole Related Compound B RS in *Buffer*

Standard solution: 0.1 mg/mL of USP Ropinirole Hydrochloride RS in *Buffer*

Sample solution: Nominally 0.1 mg/mL of ropinirole in *Buffer*▲ (USP 1-Dec-2019) prepared as follows. ▲Transfer NLT 5 Tablets into a suitable volumetric flask and▲ (USP 1-Dec-2019) add 50% of the flask volume with *Buffer*. Shake mechanically for 30 min. Dilute with *Buffer* to volume. Pass a portion of the supernatant through a suitable membrane filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Dec-2019)

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: ▲NLT▲ (USP 1-Dec-2019) 2 times the retention time of ropinirole

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between ropinirole and ropinirole related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ropinirole ($C_{16}H_{24}N_2O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

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

M_{r1} = molecular weight of ropinirole, 260.37

M_{r2} = molecular weight of ropinirole hydrochloride, 296.84

Acceptance criteria: 90.0%–110.0% of ropinirole free base

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 2.9 g/L of sodium citrate dihydrate and 3.3 g/L of anhydrous citric acid in water, pH 4.0; 500 mL

Apparatus 1: 50 rpm

Time: 15 min

Mobile phase: Acetonitrile and *Medium* (1:4)

Standard solution: ▲0.0045 mg/mL▲ (USP 1-Dec-2019) of USP Ropinirole Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first few milliliters. Dilute with *Medium* to a concentration similar to the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 3.0-mm × 7-cm; 5-µm packing L1

Flow rate: 0.6 mL/min

Injection volume: 50 µL

Run time: ▲NLT▲ (USP 1-Dec-2019) 3 times the retention time of ropinirole

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 percentage of the labeled amount of ropinirole ($C_{16}H_{24}N_2O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times D \times (M_{r1}/M_{r2}) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Tablet)

D = dilution factor for the *Sample solution*

M_{r1} = molecular weight of ropinirole, 260.37

M_{r2} = molecular weight of ropinirole hydrochloride, 296.84

V = volume of *Medium*, 500 mL

Tolerances: NLT 85% (Q) of the labeled amount of ropinirole is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 2.1 g/L of citric acid in water. Adjust with a solution containing 121.2 g/L of tris (hydroxymethyl)methylamine in water to a pH of 4.0 ▲▲ (USP 1-Dec-2019) ; 500 mL, deaerated.

Apparatus 1: 50 rpm

Time: 15 min

Standard solution: (*L*/500) ▲mg/mL▲ (USP 1-Dec-2019) of USP Ropinirole Hydrochloride RS in *Medium*, in which *L* is the label claim in mg/Tablet

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Sample solution: Pass a portion of the solution through a ▲suitable▲ (USP 1-Dec-2019) filter of 15- to 20-µm pore size, discarding the first few milliliters. ▲[NOTE—A polyethylene filter may be suitable.]▲ (USP 1-Dec-2019)

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: ▲1 mL/min▲ (USP 1-Dec-2019)

Injection volume: 200 µL for Tablets with a label claim of 0.25, 0.5, 1.0, and 2.0 mg/Tablet; 100 µL for all other strengths

▲**Run time:** NLT 1.3 times the retention time of ropinirole▲ (USP 1-Dec-2019)

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ropinirole ($C_{16}H_{24}N_2O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times V \times 100$$

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

L = label claim (mg/Tablet)

M_{r1} = molecular weight of ropinirole, 260.37

M_{r2} = molecular weight of ropinirole hydrochloride, 296.84

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of ropinirole is dissolved.

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

Buffer: 1.8 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 7.4.

Solution A: Methanol and *Buffer* (20:80)

Solution B: Methanol and *Buffer* (80:20)

Diluent: Dissolve 5 g of sodium dodecyl sulfate in 800 mL of water. Adjust with phosphoric acid or sodium hydroxide to a pH of 6.8. Add 200 mL of methanol, and mix.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
8	85	15
30	30	70
40	10	90
60	10	90
60.1	85	15
70	85	15

System suitability solution: 0.3 µg/mL of USP Ropinirole Hydrochloride RS in *Diluent* and 0.5 µg/mL of USP Ropinirole Related Compound B RS in *Diluent*

Standard solution: 0.2 µg/mL of ropinirole prepared from USP Ropinirole Hydrochloride RS in *Diluent*

Sample solution: Nominally 100 µg/mL of ropinirole from ▲NLT 20 Tablets▲ (USP 1-Dec-2019) prepared as follows. ▲Finely powder the Tablets and▲ (USP 1-Dec-2019) transfer a portion to a suitable volumetric flask. Add 70% of the flask volume with *Diluent*. Shake mechanically for 30 min. Dilute with *Diluent* to volume. Pass a portion of the supernatant through a suitable membrane filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between ropinirole and ropinirole related compound B, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak area of each individual impurity from the *Sample solution*

r_S = peak area from the *Standard solution*

C_S = concentration of ropinirole in the *Standard solution* (µg/mL)

C_U = nominal concentration of ropinirole in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Monopropyl ropinirole[a]	0.24	1.1	0.6
Ropinirole *N*-oxide[b]	0.27	1.0	0.5
Cyclopentanylindolinone[c]	0.55	1.0	0.5
Hydroxy ropinirole[d]	0.64	0.33	0.5
Ropinirole related compound B	0.95	1.4	0.6
Ropinirole	1.00	—	—
Ethyl ropinirole[e]	1.20	—	—
Propylidene ropinirole[f]	1.35	1.6	0.4
Any unspecified degradation product	—	1.0	0.3
Total impurities	—	—	2.0

[a] 4-[2-(Propylamino)ethyl]indolin-2-one.

[b] *N*-[2-(2-Oxoindolin-4-yl)ethyl]-*N*-propylpropan-1-amine oxide.

[c] 1,2a,3,4-Tetrahydro-2*H*-cyclopenta(cd)indol-2-one.

[d] 4-[2-(Dipropylamino)ethyl]-1-hydroxy-1,3-dihydro-2*H*-indol-2-one.

[e] 4-[2-(Dipropylamino)ethyl]-1-ethyl-1,3-dihydro-2*H*-indol-2-one; process impurity included for identification only.

[f] (*Z*)-4-[2-(Dipropylamino)ethyl]-3-propylideneindolin-2-one.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Ropinirole Hydrochloride RS

USP Ropinirole Related Compound B RS

4-[2-(Dipropylamino)ethyl]indoline-2,3-dione hydrochloride.

$C_{16}H_{22}N_2O_2 \cdot HCl$ 310.82

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

Topic/Question	Contact	Expert Committee
ROPINIROLE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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