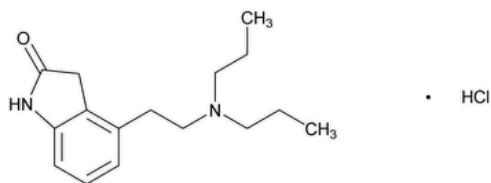


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## Ropinirole Hydrochloride



$C_{16}H_{24}N_2O \cdot HCl$  296.84

2*H*-Indol-2-one, 4-[2-(dipropylamino)ethyl]-1,3-dihydro-, monohydrochloride;

4-[2-(Dipropylamino)ethyl]-2-indolinone monohydrochloride CAS RN<sup>®</sup>: 91374-20-8; UNII: D7ZD41RZI9.

### DEFINITION

Ropinirole Hydrochloride contains NLT 98.0% and NMT 102.0% of ropinirole hydrochloride ( $C_{16}H_{24}N_2O \cdot HCl$ ), calculated on the anhydrous and solvent-free basis.

### IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy*: 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

**Change to read:**

- **C.** [IDENTIFICATION TESTS—GENERAL \(191\)](#), *Chemical Identification Tests, Chloride*

**Sample:** 20 mg/mL ▲ of Ropinirole Hydrochloride in [water](#)▲ (USP 1-May-2021)

**Acceptance criteria:** Meets the requirements ▲▲ (USP 1-May-2021)

### ASSAY

**Change to read:**

#### • 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 (1:10) to a pH of 6.5.

**Diluent:** [Acetonitrile](#) and [water](#) (20:80)

**Mobile phase:** [Acetonitrile](#) and *Buffer* (20:80)

**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 volume:** 10 μL

**Run time:** ▲NLT▲ (USP 1-May-2021) 2.5 times the retention time of ropinirole

#### System suitability

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 1.6

**Relative standard deviation:** ▲NMT 1.0%▲ (USP 1-May-2021)

### Analysis

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

Calculate the percentage of ropinirole hydrochloride ( $C_{16}H_{24}N_2O \cdot HCl$ ) 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)

**Acceptance criteria:** 98.0%–102.0% on the anhydrous and solvent-free basis

### IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

**Change to read:**

- **LIMIT OF PALLADIUM**

[NOTE—Perform this test if Palladium is a known inorganic impurity.]

**Solution A:** Dissolve 2.4 g of [sodium hydroxide](#) in 20 mL of [water](#), and dilute with ▲[glycerin](#)▲ (USP 1-May-2021) to 100 mL.

**Solution B:** 40 mg/mL of [thioacetamide](#) in [water](#). [NOTE—The solution may be filtered if necessary.]

**Buffer:** Carefully add 27 mL of [hydrochloric acid](#) to 25 g of [ammonium acetate](#), and dilute with [water](#) to 100 mL.

**Palladium standard solution:** 10 ppm of Palladium from commercially available ICP grade 1000 ppm Palladium stock solution

**Standard solution:** Pipet 1.0 mL of *Palladium standard solution* into a platinum crucible, and gently evaporate to dryness. Moisten the residue with 0.5 mL of [sulfuric acid](#), and heat over a Bunsen burner until fumes are no longer emitted. Place the crucible in a muffle furnace at 700°, and heat for 5 additional min. Cool, add 5 mL of [hydrochloric acid](#) to the residue, and evaporate to dryness. Add 1 mL of ▲[2 N hydrochloric acid TS](#)▲ (USP 1-May-2021) and, if necessary, dissolve the residue with gentle heating. When cool, transfer the contents to a 50-mL beaker. Wash the crucible twice with 1-mL aliquots of [water](#), and add the washings to the beaker. Pass the solution through a membrane filter of 2-μm pore size into a centrifuge tube.

**Sample solution:** Transfer 1 g of Ropinirole Hydrochloride to a platinum crucible, and heat over a Bunsen burner until the material is completely carbonized. Moisten the contents with 0.5 mL of [sulfuric acid](#), and heat over a Bunsen burner until fumes are no longer emitted. Place the crucible in a muffle furnace at 700°, and heat until all the organic material has been destroyed. When cool, add 5 mL of [hydrochloric acid](#) to the residue, and evaporate to dryness. Add 1 mL of ▲[2 N hydrochloric acid TS](#)▲ (USP 1-May-2021) and, if necessary, dissolve the residue with gentle heating. When cool, transfer the contents to a 50-mL beaker. Wash the crucible twice with 1-mL aliquots of [water](#), and add the washings to the beaker. Pass the solution through a membrane filter of 2-μm pore size into a centrifuge tube.

### Analysis

▲**Samples:** *Standard solution* and *Sample solution*▲ (USP 1-May-2021)

To the filtered *Standard solution* and *Sample solution* add 1 mL of *Solution A*, 0.2 mL of *Solution B*, and 2 mL of *Buffer*. Cap the centrifuge tubes securely, and incubate at 37° for 2 h. Pass the *Sample solution* and *Standard solution* through a membrane filter of 2-μm pore size, wash the membrane with 2-mL aliquots of [water](#), and allow the membrane to dry.

**Acceptance criteria:** The intensity of the spot due to the sample is not more intense than the spot due to the standard (10 ppm).

- **ORGANIC IMPURITIES, PROCEDURE 1**

If methylene ropinirole and propylidene ropinirole are known process impurities, *Organic Impurities, Procedure 2* is recommended. If ropinirole indole derivative and ropinirole oxime are known process impurities, *Organic Impurities, Procedure 3* is recommended.

**Buffer and Diluent:** Prepare as directed in the Assay.

**Solution A:** [Acetonitrile](#) and *Buffer* (15:85)

**Solution B:** [Acetonitrile](#) and [water](#) (60:40)

**Mobile phase:** See [Table 1](#).

Table 1

| Time<br>(min) | Solution A<br>(%) | Solution B<br>(%) |
|---------------|-------------------|-------------------|
| 0             | 100               | 0                 |
| 5             | 100               | 0                 |
| 30            | 60                | 40                |
| 50            | 60                | 40                |
| 55            | 100               | 0                 |
| 65            | 100               | 0                 |

**System suitability solution:** 1 mg/mL of [USP Ropinirole Hydrochloride RS](#) and 1.5 µg/mL of [USP Ropinirole Related Compound B RS](#) in *Diluent*

**Sample solution:** 1 mg/mL of Ropinirole Hydrochloride in *Diluent*

**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 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 1.5 between ropinirole and ropinirole related compound B

**Tailing factor:** NMT 2.0 for the ropinirole peak

**Relative standard deviation:** NMT 2.0% for the ropinirole peak

**Analysis**

**Sample:** *Sample solution*

Calculate the percentage of any individual impurity in the portion of Ropinirole Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

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

$r_T$  = sum of the responses of all the peaks from the *Sample solution*

$F$  = relative response factor (see [Table 2](#))

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

**Table 2**

| Name                                    | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|-----------------------------------------|-------------------------|--------------------------|------------------------------|
| Open ring nitro derivative <sup>a</sup> | 0.39                    | 0.72                     | 0.15                         |
| Monopropyl ropinirole <sup>b</sup>      | 0.58                    | 1.1                      | 0.15                         |
| N-Hydroxyropinirole <sup>c</sup>        | 0.84                    | 0.65                     | 0.15                         |

