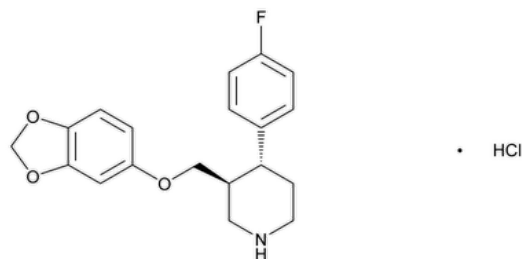


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Paroxetine Hydrochloride

Change to read:



$C_{19}H_{20}FNO_3 \cdot HCl$ 365.83

$C_{19}H_{20}FNO_3 \cdot HCl \cdot \frac{1}{2}H_2O$ 374.83

Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, (3S,trans)-;

(-)-(3S,4R)-4-(p-Fluorophenyl)-3-[(1,3-benzodioxol-5-yloxy)methyl]piperidine hydrochloride;

(3S,4R)-3-[(Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine hydrochloride.

Anhydrous CAS RN®: 78246-49-8; UNII: 3I3T11UD2S.

Hemihydrate CAS RN®: 110429-35-1; UNII: X2ELS050D8.

DEFINITION

Paroxetine Hydrochloride is anhydrous or contains one-half molecule of water of hydration. It contains NLT 98.5% and NMT 102.0% of paroxetine hydrochloride ($C_{19}H_{20}FNO_3 \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197M, 197K, or 197A

Standard: Dissolve [USP Paroxetine Hydrochloride RS](#) in a mixture of [water](#) and [isopropyl alcohol](#) (1 in 10). Heat to 70° to dissolve, recrystallize, and dry the residue under vacuum at 50° for 3 h.

Sample: Dissolve Paroxetine Hydrochloride in a mixture of [water](#) and [isopropyl alcohol](#) (1 in 10). Heat to 70° to dissolve, recrystallize, and dry the residue under vacuum at 50° for 3 h.

Acceptance criteria: Meets the requirements

- B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

Sample solution: 10 mg/mL of Paroxetine Hydrochloride in [methanol](#) and [water](#) (50:50)

Acceptance criteria: Meets the requirements

- C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution* as obtained in the Assay.

ASSAY

PROCEDURE

Buffer: 0.05 M [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.5.

Mobile phase: [Acetonitrile](#), *Buffer*, and [triethylamine](#) (30:70:1). [NOTE—The ratio for acetonitrile, *Buffer*, and triethylamine may be varied between 25:75:1 and 40:70:1 to meet system suitability requirements.] Adjust with [glacial acetic acid](#) to a pH of 5.5.

System suitability solution: 0.5 mg/mL each of [USP Paroxetine Hydrochloride RS](#) and [USP Paroxetine Related Compound B RS](#) in [water](#)

Standard solution: 0.5 mg/mL of [USP Paroxetine Hydrochloride RS](#) in [water](#)

Sample solution: 0.5 mg/mL of Paroxetine Hydrochloride in [water](#)

Chromatographic system

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

Mode: LC

Detector: UV 295 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L13](#)

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 1.5 times the retention time of paroxetine

System suitability

Sample: *System suitability solution*

[NOTE—The approximate relative retention times for paroxetine related compound B and paroxetine are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between paroxetine related compound B and paroxetine

Tailing factor: NMT 2.0 for paroxetine

Relative standard deviation: NMT 0.73% for paroxetine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of paroxetine hydrochloride ($C_{19}H_{20}FNO_3 \cdot HCl$) in the portion of Paroxetine Hydrochloride taken:

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

r_U = peak response of paroxetine from the *Sample solution*

r_S = peak response of paroxetine from the *Standard solution*

C_S = concentration of [USP Paroxetine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Paroxetine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

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

• **LIMIT OF PAROXETINE RELATED COMPOUND C**

Mobile phase: [n-Hexane](#), [absolute alcohol](#), [trifluoroacetic acid](#), and [water](#) (900:100:2:2)

Diluent: [n-Hexane](#) and [absolute alcohol](#) (50:50)

System suitability solution: 0.1 mg/mL each of [USP Paroxetine Hydrochloride RS](#) and [USP Paroxetine Related Compound C RS](#) in *Diluent*

Standard solution: 0.1 mg/mL of [USP Paroxetine Related Compound C RS](#) in *Diluent*

Sample solution: 5 mg/mL of Paroxetine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 295 nm

Column: 4.6-mm × 25-cm; 10-μm packing [L51](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 5 μL

Run time: NLT 2.3 times the retention time of paroxetine

System suitability

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

[NOTE—The relative retention times for paroxetine related compound C and paroxetine are about 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between paroxetine and paroxetine related compound C, *System suitability solution*

Tailing factor: NMT 2.5 for the paroxetine related compound C peak, *System suitability solution*

Relative standard deviation: NMT 10.0% for paroxetine related compound C, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of paroxetine related compound C in the portion of Paroxetine Hydrochloride taken:

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

r_U = peak response of paroxetine related compound C from the *Sample solution*

r_s = peak response of paroxetine related compound C from the *Standard solution*

C_s = concentration of [USP Paroxetine Related Compound C RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of Paroxetine Hydrochloride, on the anhydrous basis, in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.1%

• **LIMIT OF PAROXETINE RELATED COMPOUND E**

[NOTE—Perform this test only if paroxetine related compound E is a known process impurity.]

Solution A: Dissolve 30 g of [sodium perchlorate](#) in 900 mL of [water](#). Add 3.5 mL of [phosphoric acid](#) and 2.4 mL of [triethylamine](#). Dilute with [water](#) to 1000 mL. Adjust with [phosphoric acid](#) or [triethylamine](#) to a pH of 2.0.

Solution B: [Acetonitrile](#)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
2	85	15
20	80	20
20.1	55	45
25	55	45
26	85	15
35	85	15

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

Sensitivity solution: 0.006 µg/mL of [USP Paroxetine Related Compound E RS](#) (equivalent to 0.005 µg/mL of paroxetine related compound E free base) in *Diluent*

Standard solution: 0.012 µg/mL of [USP Paroxetine Related Compound E RS](#) (equivalent to 0.010 µg/mL of paroxetine related compound E free base) in *Diluent*

Sample solution: 10,000 µg/mL of Paroxetine Hydrochloride in *Diluent*. Sonicate as needed to aid dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 242 nm

Column: 3.0-mm × 15-cm; 3-µm packing [L1](#)

Column temperature: 35°

Flow rate: 0.6 mL/min

Injection volume: 100 µL

System suitability

Sample: *Sensitivity solution* and *Standard solution*

[NOTE—The relative retention times for paroxetine related compound E and paroxetine are about 0.6 and 1.0, respectively.]

Suitability requirements

Relative standard deviation: NMT 10.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of paroxetine related compound E in the portion of Paroxetine Hydrochloride taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$



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