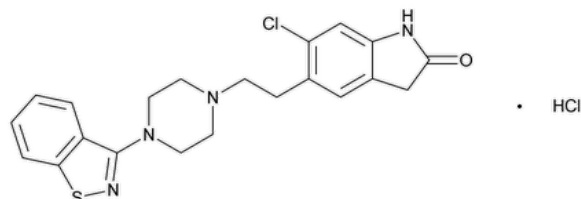


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Ziprasidone Hydrochloride



$C_{21}H_{21}ClN_4OS \cdot HCl$ 449.39

$C_{21}H_{21}ClN_4OS \cdot HCl \cdot H_2O$ 467.41

2H-Indol-2-one, 5-{2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]ethyl}-6-chloro-1,3-dihydro-, monohydrochloride;

5-{2-[4-(1,2-Benzisothiazol-3-yl)-1-piperazinyl]ethyl}-6-chloro-2-indolinone monohydrochloride.

Monohydrate CAS RN®: 138982-67-9; UNII: 216X081ORU.

Anhydrous CAS RN®: 122883-93-6; UNII: JAL53626GG.

DEFINITION

Ziprasidone Hydrochloride contains NLT 97.5% and NMT 102.0% of ziprasidone hydrochloride ($C_{21}H_{21}ClN_4OS \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

• **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K. If a difference appears in the spectra of the analyte and the Reference Standard, dissolve equal portions of the analyte and the Reference Standard in equal volumes of [methanol](#) separately, evaporate to dryness, and record new spectra using the residues.

• **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, Chloride**

Sample solution: Suspend 30 mg of the analyte in 2 mL of [water](#), acidify with 0.15 mL of [2 N nitric acid TS](#), and filter. Use the filtrate.

Acceptance criteria: Meets the requirements

ASSAY

• PROCEDURE

Buffer: 6.8 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Methanol](#) and *Buffer* (40:60)

Diluent: [Methanol](#) and [water](#) (60:40)

Standard solution: 0.23 mg/mL of [USP Ziprasidone Hydrochloride RS](#) in *Diluent*

Sample solution: 0.23 mg/mL of Ziprasidone Hydrochloride in *Diluent*. [NOTE—Because of its hygroscopic nature, the anhydrous form may be dried at 70° under vacuum for 2 h prior to the preparation of the *Sample solution*.]

Chromatographic system

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

Mode: LC

Detector: UV 229 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L7](#)

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

Run time: NLT 2 times the retention time of ziprasidone

System suitability

Sample: *Standard solution*

Suitability requirements**Tailing factor:** NMT 2.0**Relative standard deviation:** NMT 0.73%**Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of ziprasidone hydrochloride ($C_{21}H_{21}ClN_4OS \cdot HCl$) in the portion of Ziprasidone Hydrochloride taken:

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

 r_U = peak response of ziprasidone from the *Sample solution* r_S = peak response of ziprasidone from the *Standard solution* C_S = concentration of [USP Ziprasidone Hydrochloride RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Ziprasidone Hydrochloride in the *Sample solution* (mg/mL)**Acceptance criteria:** 97.5%–102.0% on the anhydrous and solvent-free basis**IMPURITIES**• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%• **LIMIT OF TETRAHYDROFURAN**

[NOTE—Perform this test only if tetrahydrofuran is likely to be present as the result of the manufacturing process.]

Standard solution: 0.05 mg/mL of [tetrahydrofuran](#) in [dimethyl sulfoxide](#). Transfer 4 mL of this solution to a 20-mL headspace vial, and seal.**Sample solution:** Transfer 40 mg of Ziprasidone Hydrochloride and 4.0 mL of [dimethyl sulfoxide](#) to a 20-mL headspace vial, seal, and mix.**Chromatographic system**(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** GC with headspace injector**Detector:** Flame ionization**Column:** 30-m × 0.32-mm fused silica; coated with a 1.8-μm film of phase [G43](#)**Temperatures****Injection port:** 180°**Detector:** 260°**Column:** See [Table 1](#).**Table 1**

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	5
40	2	90	0
90	30	225	2

Carrier gas: Helium**Flow rate:** 1.6 mL/min**Injection volume:** 2 mL**Injection type:** Headspace; split ratio, 30:1**Vial treatment:** Maintain at 105° for 60 min prior to injection**System suitability****Sample:** *Standard solution***Suitability requirements****Relative standard deviation:** NMT 5%**Analysis****Samples:** *Standard solution* and *Sample solution*