

BRIEFING

Ziprasidone Hydrochloride. A USP Pending Monograph is proposed for a different form of ziprasidone hydrochloride.

This proposal is based on supporting data received for inclusion of this form of the drug substance into the compendia. Currently, there is an official *USP–NF* monograph for Ziprasidone Hydrochloride which differs from this anhydrous form with respect to organic impurities and water content. The proposal therefore includes the tests for *Organic Impurities* and *Water Determination*, which will be considered for adoption into the *USP–NF*, once the product is fully approved by the FDA, via a flexible monograph approach. The liquid chromatographic procedure in the test for *Organic Impurities* is based on analyses performed with the Waters Symmetry C18 brand of L1 column. The typical retention time for ziprasidone is about 19 min.

Description and Solubility: Light pink to pink-colored powder. Soluble in formic acid; insoluble in *n*-hexane and in methanol.

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Add the following:

► **Ziprasidone Hydrochloride**

Draft 1

IMPURITIES

• **ORGANIC IMPURITIES**

Solution A: 2.5 g/L of phosphoric acid in water

Solution B: Acetonitrile and water (95:5)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
20	70	30
25	65	35
30	60	40
45	60	40
46	85	15
55	85	15

Diluent: *Solution A* and acetonitrile (1:1)

Standard solution: 0.5 µg/mL of USP Ziprasidone Hydrochloride RS in *Diluent*

Sample solution: 0.5 mg/mL of Ziprasidone 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 L1

Flow rate: 0.9 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response 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)

F = relative response factor of each individual impurity (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ziprasidone related compound A ^a	0.48	0.70	0.15
Hydroxy ziprasidone ^b	0.86	1.0	0.15
Ziprasidone	1.0	—	—
Isopropylidene ziprasidone ^c	1.4	0.52	0.15
Indolinone ziprasidone ^d	2.0	1.2	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

^a 3-(Piperazin-1-yl)benzo[d]isothiazole monohydrochloride.

^b 5-[2-[4-(Benzo[d]isothiazol-3-yl)piperazin-1-yl]-1-hydroxyethyl]-6-chloroindolin-2-one.

^c 5-[2-[4-(Benzo[d]isothiazol-3-yl)piperazin-1-yl]ethyl]-6-chloro-3-(propan-2-ylidene)indolin-2-one.

^d 6-Chloro-5-(2-chloroethyl)indolin-2-one.

SPECIFIC TESTS

- **WATER DETERMINATION, Method I (921):** NMT 1.5% (1-µL-2012)