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Ziprasidone Capsules

DEFINITION

Ziprasidone Capsules contain an amount of ziprasidone hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of ziprasidone ($C_{21}H_{21}ClN_4OS$).

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.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

PROCEDURE

Buffer: 0.3% (v/v) of [triethylamine](#) in [water](#)

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65). Adjust with [glacial acetic acid](#) to a pH of 6.0.

Diluent: [Acetonitrile](#), [water](#), and [glacial acetic acid](#) (70:30:5)

Standard stock solution: 1.0 mg/mL of [USP Ziprasidone Hydrochloride RS](#) in *Diluent*

Standard solution: 0.2 mg/mL of [USP Ziprasidone Hydrochloride RS](#) from the *Standard stock solution* in *Mobile phase*

Sample stock solution: Nominally 1 mg/mL of ziprasidone prepared as follows. Empty the contents of NLT 20 Capsules into a container.

Blend the contents. Transfer an amount of the contents, equivalent to NLT 50 mg of ziprasidone, to a suitable volumetric flask. Dissolve the contents in 60% of the flask volume of *Diluent*. Sonicate for NLT 5 min. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45- μ m pore size and use the filtrate to prepare the *Sample solution*.

Sample solution: Nominally 0.2 mg/mL of ziprasidone prepared from the filtered *Sample stock solution* and *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, a diode array detector may be used in the wavelength range of 200–300 nm.

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Flow rate: 2.0 mL/min

Injection volume: 20 μ L

Run time: 1.5 times the retention time of ziprasidone

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 ziprasidone ($C_{21}H_{21}ClN_4OS$) in the portion of Capsules taken:

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

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

M_{r1} = molecular weight of ziprasidone free base, 412.94

M_{r2} = molecular weight of ziprasidone hydrochloride; 467.41 for the monohydrate, $\blacktriangle$ 449.39 $\blacktriangle$ (ERR 1-Sep-2023) for the anhydrous form

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#)

Test 1

Tier 1

Phosphate buffer, pH 7.5: Dissolve 7.8 g of [monobasic sodium phosphate dihydrate](#) and 20 g of [sodium dodecyl sulfate](#) in 1 L [water](#).

Sonicate to dissolve and adjust with [phosphoric acid](#) or $\blacktriangle$ [sodium hydroxide solution](#) $\blacktriangle$ (ERR 1-Sep-2023) to a pH of 7.5.

Medium: *Phosphate buffer, pH 7.5*; 900 mL

Apparatus 2: 75 rpm. Use a suitable sinker, if necessary.

Time: 45 min

Buffer: 0.3% (v/v) of [triethylamine](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 6.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (45:55)

Diluent: [Acetonitrile](#), [water](#), and [glacial acetic acid](#) (70:30:5)

Standard stock solution: 0.24 mg/mL of [USP Ziprasidone Hydrochloride RS](#) prepared as follows. Dissolve a suitable amount of [USP Ziprasidone Hydrochloride RS](#) in a suitable volumetric flask first in 60% of the flask volume of *Diluent*, and then dilute with *Diluent* to volume.

Standard solution: 0.024 mg/mL of [USP Ziprasidone Hydrochloride RS](#) in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution through a suitable filter of 0.45- μ m pore size. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: 1.5 times the retention time of ziprasidone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ziprasidone ($C_{21}H_{21}ClN_4OS$) dissolved:

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

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)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

M_r = molecular weight of ziprasidone free base, 412.94

M_r = molecular weight of ziprasidone hydrochloride; 467.41 for the monohydrate, ▲449.39▲ (ERR 1-Sep-2023) for the anhydrous form

Tolerances: NLT 75% (Q) of the labeled amount of ziprasidone ($C_{21}H_{21}ClN_4OS$) is dissolved.

If the above tolerance cannot be met, proceed to *Tier 2*.

Tier 2

Solution A: Dissolve 7.8 g of [monobasic sodium phosphate dihydrate](#) in 1 L of [water](#). Sonicate to dissolve and adjust with [phosphoric acid](#) or ▲[sodium hydroxide solution](#)▲ (ERR 1-Sep-2023) to a pH of 7.5. Dissolve 10 g of [pancreatin](#) in the resulting solution.

Solution B: Dissolve 7.8 g of [monobasic sodium phosphate dihydrate](#) in 1 L of [water](#). Adjust with [phosphoric acid](#) or ▲[sodium hydroxide solution](#)▲ (ERR 1-Sep-2023) to a pH of 7.5. Dissolve 90 g of [sodium dodecyl sulfate](#) in the resulting solution. Sonicate to dissolve.

Medium: Transfer 700 mL of *Solution A* to the dissolution vessel and equilibrate at 37° for 15 min. Add 200 mL of *Solution B*; 900 mL.

Apparatus 2: 75 rpm. Use a suitable sinker, if necessary.

Time: 45 min

Analyze the *Sample solution* using the liquid chromatographic procedure described in *Tier 1*.

Tolerances: NLT 75% (Q) of the labeled amount of ziprasidone ($C_{21}H_{21}ClN_4OS$) is dissolved.

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

Tier 1

Medium: 2% [sodium lauryl sulfate](#) in pH 7.5 phosphate buffer (dissolve 6.9 g of [monobasic sodium phosphate monohydrate](#) and 1.6 g of [sodium hydroxide](#) in 900 mL of [water](#), adjust with [1 N sodium hydroxide](#) to a pH of 7.5 and dilute with [water](#) to 1000 mL); 900 mL

Apparatus 2: 75 rpm. Use a suitable sinker, if necessary.

Time: 60 min

Tier 2

Medium A: pH 7.5 phosphate buffer (dissolve 6.9 g of [monobasic sodium phosphate monohydrate](#) and 1.6 g of [sodium hydroxide](#) in 900 mL of [water](#), adjust with [1 N sodium hydroxide](#) to a pH of 7.5 and dilute with [water](#) to 1000 mL) with 1% pancreatin; 700 mL

Medium B: pH 7.5 phosphate buffer with 9% of [sodium lauryl sulfate](#); 200 mL

Apparatus 2: 75 rpm. Use a suitable sinker, if necessary.

Time: 15 min for *Medium A*; 45 min for *Medium A* with the addition of *Medium B*

Solution A: Dissolve 2.7 g of [monobasic sodium phosphate monohydrate](#) in 1 L of [water](#). Adjust with [1 N sodium hydroxide](#) to a pH of 6.0.

Mobile phase: [Acetonitrile](#) and *Solution A* (50:50)

Diluent: [Acetonitrile](#) and [water](#) (50:50)

Standard stock solution: 0.48 mg/mL of [USP Ziprasidone Hydrochloride RS](#) in *Diluent*

Standard solution: ($L/900$) mg/mL of [USP Ziprasidone Hydrochloride RS](#) in *Medium* from *Standard stock solution*, where L is the label claim of ziprasidone in mg/Capsules

Sample solution: Pass a portion of the solution through a suitable filter of 0.45- μ m pore size.

Procedure: Perform the test using the conditions in *Tier 1*. In the presence of cross-linking repeat the test with new Capsules using the conditions in *Tier 2* as follows. After 15 min with 700 mL of *Medium A*, stop the dissolution bath and timer and add 200 mL of *Medium B* pre-equilibrated at $37 \pm 0.5^\circ$. Restart the bath and timer, and continue the dissolution for an additional 45 min.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

Run time: 1.8 times the retention time of ziprasidone

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 ziprasidone ($C_{21}H_{21}ClN_4OS$) dissolved:



Documents

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