Quetiapine Extended-Release Tablets

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DEFINITION

Quetiapine Extended-Release Tablets contain quetiapine fumarate [$(C_{21}H_{25}N_3O_2S)_2 \cdot C_4H_4O_4$] equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests** ⟨197⟩**,** *Infrared Spectroscopy***:** 197F

  Standard solution: Transfer 10 mg of USP Quetiapine Fumarate RS to a suitable vial. Add 10 mL of acetone and cap the vial. Sonicate for about 10 min. Allow the solution to equilibrate to room temperature. Evaporate the acetone completely. Add 2 mL of chloroform. Gently swirl for several minutes. Pass through a suitable filter of 0.45-µm pore size. Use the filtrate.

  Sample solution: Grind NLT 10 Tablets. Transfer an amount of powder equivalent to NLT 10 mg of quetiapine fumarate to a suitable vial. Add 10 mL of acetone and cap the vial. Sonicate for about 10 min. Allow the solution to equilibrate to room temperature. Evaporate the acetone completely. Add 2 mL of chloroform. Gently swirl for several minutes. Pass through a suitable filter of 0.45-µm pore size. Use the filtrate.

  Acceptance criteria: Meet the requirements
- **B.** The retention time 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: Dissolve 2.6 g/L of dibasic ammonium phosphate in water.

  Mobile phase: Methanol, acetonitrile, and *Buffer* (54:7:39)

  Diluent: Acetonitrile and water (50:50)

  System suitability stock solution: 0.05 mg/mL of USP Quetiapine Related Compound H RS in *Mobile phase*

  System suitability solution: 0.005 mg/mL of USP Quetiapine Related Compound H RS and 0.5 mg/mL of USP Quetiapine System Suitability RS in *Mobile phase* prepared as follows. Transfer 5 mg of USP Quetiapine System Suitability RS to a 10-mL volumetric flask. Add 7 mL of *Mobile phase* and sonicate to dissolve. Transfer 1 mL of *System suitability stock solution* to the volumetric flask. Dilute with *Mobile phase* to volume.

  Standard solution: 0.2 mg/mL of USP Quetiapine Fumarate RS in *Mobile phase*

  Sample stock solution: Transfer NLT 5 Tablets to a homogenizer vessel. Add 50 mL of acetonitrile, swirl to wet, and allow to stand for approximately 10 min. Add an additional 160 mL of *Diluent* and extract for about 10 min. Transfer the contents of the homogenizer to a 500-mL volumetric flask. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size and use the filtrate.

  Sample solution: Nominally 0.16–0.18 mg/mL of quetiapine from the *Sample stock solution* in *Mobile phase*

  Chromatographic system

  (See *Chromatography* ⟨621⟩*, System Suitability*.)

  Mode: LC

  Detector: UV 230 nm

  Column: 4.6-mm × 25-cm; 5-µm packing L7

  Flow rate: 1.3 mL/min

  Injection volume: 30 µL

  Run time: NLT 2.5 times the retention time of quetiapine

  System suitability

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

  [Note—See ▲*Table 10*▲ (RB 1-Dec-2021) for the relative retention times.]

  Suitability requirements

  Resolution: NLT 1.5 between quetiapine related compound G and quetiapine related compound H; NLT 2.0 between the quetiapine desethoxy and quetiapine peaks; *System suitability solution*

  Tailing factor: NMT 1.5, *Standard solution*

  Relative standard deviation: NMT 2.0%, *Standard solution*

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) in the portion of Tablets taken:

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

  r_U = peak response from the *Sample solution*

  r_S = peak response from the *Standard solution*

  C_S = concentration of USP Quetiapine Fumarate RS in the *Standard solution* (mg/mL)

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

  M_{r1} = molecular weight of quetiapine free base, 383.51

  M_{r2} = molecular weight of quetiapine fumarate, 883.09

  N = number of moles of quetiapine free base per mole of quetiapine fumarate, 2

  Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

  Test 1

  Medium 1: Citrate buffer, pH 4.8. Dissolve 9.6 g of anhydrous citric acid in 600 mL of water. Add 90 mL of 1 N sodium hydroxide. Dilute with water to 1 L; 900 mL.

  Medium 2: Dissolve 17.9 g of dibasic sodium phosphate dodecahydrate in 400 mL of water. Add 460 mL of 1 N sodium hydroxide VS and dilute with water to 1 L; 100 mL.

  [Note—It is recommended to check the pH of the mixture of 90 mL of *Medium 1* and 10 mL of *Medium 2*, which should be between 6.4 and 6.8. If the pH of the mixture is less than 6.4, 10 mL/L of 1 N sodium hydroxide VS may be added to *Medium 2*. If the pH of the mixture is greater than 6.8, 10 mL/L of 1 N hydrochloric acid VS may be added to *Medium 2*.]

  Start the test with 900 mL of *Medium 1*. Add 100 mL of *Medium 2* to the vessel after 5 h of the test and continue the test.

  Apparatus 1: 200 rpm

  Times: 1, 6, 12, and 20 h

  Diluent: *Medium 1* and *Medium 2* (90:10)

  Standard solution: (*L*/400) mg/mL of USP Quetiapine Fumarate RS in *Diluent*, where *L* is the label claim in mg/Tablet

  Sample solution: Pass a suitable portion of the solution under test through a suitable filter.

  Instrumental conditions

  Mode: UV

  Analytical wavelength: About 290 nm

  Blank: *Diluent*