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Quetiapine Tablets

DEFINITION

Quetiapine Tablets contain an amount of quetiapine fumarate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$).

IDENTIFICATION

Change to read:

- A. **▲ Spectroscopic Identification Tests (197), Infrared Spectroscopy: 197F▲** (CN 1-MAY-2020)

Standard solution: Dissolve 10 mg of quetiapine fumarate in 10 mL of acetone. Sonicate for 10 min. Filter and evaporate the solvent. Dissolve the residue in 2 mL of chloroform. Filter and use 20 μ L of the filtrate for analysis.

Sample solution: Finely powder 10 Tablets. Dissolve an amount of the powder equivalent to 10 mg of quetiapine fumarate in 10 mL of acetone, avoiding large pieces of Tablet coating, if any. Sonicate for 10 min. Filter and evaporate the solvent. Dissolve the residue in 2 mL of chloroform. Filter and use the filtrate for analysis.

Blank: Filter 10 mL of acetone and evaporate the solvent. Dissolve the residue using 2 mL of chloroform and filter.

Analysis

Samples: Standard solution, Sample solution, and Blank

Add drop-wise approximately 20 μ L of each of the samples separately onto a clean IR transmission window, allowing each drop to dry before adding the next. Record the spectra.

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

• PROCEDURE

Buffer: 1.4 g/L of monobasic potassium phosphate in water. To 1 L of this solution, add 1 mL of triethylamine and adjust with dilute phosphoric acid to a pH of 6.5 (1 in 10, v/v).

Mobile phase: Acetonitrile and Buffer (35:65)

Standard solution: 0.1 mg/mL of [USP Quetiapine Fumarate RS](#) in Mobile phase

Sample stock solution: Nominally 2.0 mg/mL of quetiapine prepared as follows. Transfer NLT 5 Tablets to a suitable volumetric flask. Add water to fill 5% of the final volume, and sonicate to disperse the Tablets. Add Mobile phase to fill 60% of the final volume, and sonicate for 30 min with intermittent shaking. Dilute with Mobile phase to volume. Centrifuge for 5 min. Pass a portion of the solution through a suitable filter of 0.45- μ m pore size.

Sample solution: Nominally 0.1 mg/mL of quetiapine prepared by diluting an aliquot of the Sample stock solution with Mobile phase

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm \times 15-cm; 5- μ m packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

Run time: 2 times the retention time of quetiapine

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

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

r_U = peak response of quetiapine from the Sample solution

r_S = peak response of quetiapine 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)

N = number of moles of quetiapine/mole of quetiapine fumarate, 2

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

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

Test 1

Medium: Water; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 1.4 g/L of monobasic potassium phosphate in water. To 1 L of this solution, add 1 mL of triethylamine and adjust with dilute phosphoric acid to a pH of 6.0 (1 in 10).

Mobile phase: Acetonitrile and Buffer (35:65)

Standard stock solution: 3.3 mg/mL of [USP Quetiapine Fumarate RS](#) prepared as follows. Dissolve the Standard first in methanol using 10% of the final volume, and dilute with Medium to volume.

Standard solution: 0.03 mg/mL of [USP Quetiapine Fumarate RS](#) in Medium from the Standard stock solution

Sample solution: Pass a portion of the solution through a suitable filter of 0.45-μm 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 225 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 2 mL/min

Injection volume: 50 μL

Run time: 1.5 times the retention time of quetiapine

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 quetiapine ($C_{21}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times N \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of quetiapine from the Sample solution

r_S = peak response of quetiapine from the Standard solution

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

V = volume of *Medium*, 900 mL

N = number of moles of quetiapine/mole of quetiapine fumarate, 2

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

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

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) is dissolved.

Test 2

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

Medium: 1 g/L of sodium chloride in water; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 20 min

Standard stock solution: 1.3 mg/mL of [USP Quetiapine Fumarate RS](#) prepared as follows. Transfer a suitable quantity of [USP Quetiapine Fumarate RS](#) to a suitable volumetric flask. Dissolve in about 25% of the flask volume of methanol. Dilute with *Medium* to volume.

Standard solution: ($L/900$) mg/mL of [USP Quetiapine Fumarate RS](#) from a suitable volume of the *Standard stock solution* in *Medium*, where L is the label claim in mg/Tablet.

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

Blank: *Medium*

Instrumental conditions

Mode: UV

Analytical wavelength: 290 nm with background correction at 490 nm

Cell: See [Table 1](#).

Table 1

| Label claim, L (mg/Tablet) | Cell (cm) |
|---------------------------------|--------------|
| 25 | 1.0 |
| 50 | 1.0 |
| 100 | 0.5 |
| 150 | 0.2 |
| 200 | 0.2 |
| 300 | 0.1 |
| 400 | 0.1 |

Analysis

Samples: *Medium*, *Standard solution*, and *Sample solution*

Calculate the percentage of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times N \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

N = number of moles of quetiapine/mole of quetiapine fumarate, 2

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

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

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) is dissolved.

Test 3

If the product complies with this procedure, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times

For Tablets labeled to contain 25 mg: 30 min

For Tablets labeled to contain 50, 100, 200, 300, or 400 mg: 45 min

Standard solution: 0.34 mg/mL of [USP Quetiapine Fumarate RS](#) in 0.1 N hydrochloric acid

Dilute standard solution: 0.06 mg/mL of [USP Quetiapine Fumarate RS](#) from the *Standard solution* in 0.1 N hydrochloric acid

Sample solution: Withdraw a suitable portion of the solution under test. Transfer 9 mL of the portion to a 10-mL volumetric flask and dilute with 1 N hydrochloric acid to volume. Pass a portion of the resulting solution through a suitable filter of 0.45- μ m pore size and discard the first 2 mL.

Instrumental conditions

Mode: UV

Analytical wavelength: 282 nm

Cells

For Tablets labeled to contain 25 or 50 mg: 0.5 cm

For Tablets labeled to contain 100, 200, 300, or 400 mg: 0.1 cm

Blank: 0.1 N hydrochloric acid

Analysis

Samples: *Standard solution, Dilute standard solution, Sample solution, and Blank*

For Tablets labeled to contain 25 or 50 mg

Calculate the percentage of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (A_u/A_s) \times C_s \times D \times N \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

A_u = absorbance of the *Sample solution*

A_s = absorbance of the *Dilute standard solution*

C_s = concentration of [USP Quetiapine Fumarate RS](#) in the *Dilute standard solution* (mg/mL)

D = dilution factor, 1.1

N = number of moles of quetiapine/mole of quetiapine fumarate, 2

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

For Tablets labeled to contain 100, 200, 300, or 400 mg

Calculate the percentage of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) dissolved:

$$\text{Result} = (A_u/A_s) \times C_s \times D \times N \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

A_u = absorbance of the *Sample solution*

A_s = absorbance of the *Standard solution*

C_s = concentration of [USP Quetiapine Fumarate RS](#) in the *Standard solution* (mg/mL)

D = dilution factor, 1.1
 N = number of moles of quetiapine/mole of quetiapine fumarate, 2
 M_{r1} = molecular weight of quetiapine free base, 383.51
 M_{r2} = molecular weight of quetiapine fumarate, 883.09
 V = volume of *Medium*, 900 mL
 L = label claim (mg/Tablet)

Tolerances

For Tablets labeled to contain 25 mg: NLT 75% (Q) of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) is dissolved.

For Tablets labeled to contain 50, 100, 200, 300, or 400 mg: NLT 70% (Q) of the labeled amount of quetiapine ($C_{21}H_{25}N_3O_2S$) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

Buffer: Dissolve 0.8 g of anhydrous dibasic sodium phosphate and 0.6 g of potassium dihydrogen orthophosphate in 1 L of water.

Solution A: Acetonitrile and *Buffer* (10:90). Adjust with dilute phosphoric acid (1 in 10, v/v) to a pH of 6.7.

Solution B: Acetonitrile

Diluent: Acetonitrile and *Solution A* (65:35)

Mobile phase: See *Table 2*.

Table 2

| Time (min) | Solution A (%) | Solution B (%) |
|---------------|-------------------|-------------------|
| 0 | 80 | 20 |
| 20 | 75 | 25 |
| 30 | 65 | 35 |
| 35 | 35 | 65 |
| 55 | 25 | 75 |
| 56 | 80 | 20 |
| 65 | 80 | 20 |

System suitability solution: 0.5 mg/mL of [USP Quetiapine System Suitability RS](#) in *Diluent* prepared as follows. Transfer the required quantity of [USP Quetiapine System Suitability RS](#) to a suitable volumetric flask. Add 70% of the flask volume and sonicate to dissolve. Dilute with *Diluent* to volume.

Standard solution: 1.2 μ g/mL of [USP Quetiapine Fumarate RS](#) in *Diluent*. Sonication may be used to aid in dissolution.

Sample solution: Nominally 0.5 mg/mL of quetiapine in *Diluent* from a portion of weighed and crushed Tablets (NLT 10). Sonicate for 10 min with intermittent shaking.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm \times 15-cm; 5- μ m packing L7

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

System suitability

Samples: System suitability solution and Standard solution

Suitability requirements**Resolution:** NLT 2.0 between quetiapine desethoxy and quetiapine peaks, *System suitability solution***Tailing factor:** NMT 1.5 for the quetiapine peak, *System suitability solution***Relative standard deviation:** NMT 5.0%, *Standard solution***Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of any individual degradation product in the portion of Tablets taken:

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

 r_U = peak response of each individual impurity from the *Sample solution* r_S = peak response of quetiapine 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) N = number of moles of quetiapine/mole of quetiapine fumarate, 2 M_{r1} = molecular weight of quetiapine free base, 383.51 M_{r2} = molecular weight of quetiapine fumarate, 883.09**Acceptance criteria:** See [Table 3](#). Disregard any peak with an area below 0.05% in the *Sample solution*.**Table 3**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|-------------------------|------------------------------|
| Quetiapine N-oxide ^a | 0.28 | 0.2 |
| Quetiapine related compound B | 0.39 | 0.2 |
| Quetiapine related compound G | 0.69 | 0.2 |
| Quetiapine desethoxy ^{b,c} | 0.88 | — |
| Quetiapine | 1.0 | — |
| Bis(dibenzothiazepinyl) piperazine ^{b,d} | 2.0 | — |
| Any individual unspecified degradation product | — | 0.2 |
| Total impurities | — | 0.5 |

^a 4-(Dibenzo[b,f][1,4]thiazepin-11-yl)-1-[2-(2-hydroxyethoxy)ethyl]piperazine 1-oxide.^b Process impurities controlled in the drug substance. Included for identification purposes only. Not reported for the drug product and not included in the total impurities.^c 2-[4-(Dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethanol.^d 1,4-Bis(dibenzo[b,f][1,4]thiazepin-11-yl)piperazine.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS (11):**
 - [USP Quetiapine Fumarate RS](#)
 - [USP Quetiapine System Suitability RS](#)

It contains quetiapine fumarate and at least 0.1% of each of the following impurities: Quetiapine related compound B: 11-(Piperazin-1-yl)dibenzo[*b,f*][1,4]thiazepine; Quetiapine related compound G: Dibenzo[*b,f*][1,4]thiazepin-11(10H)-one; and Quetiapine desethoxy: 2-[4-(Dibenzo[*b,f*][1,4]thiazepin-11-yl)piperazin-1-yl]ethanol.

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

| Topic/Question | Contact | Expert Committee |
|----------------------------|---|---------------------------|
| QUETIAPINE TABLETS | Documentary Standards Support | SM42020 Small Molecules 4 |
| REFERENCE STANDARD SUPPORT | RS Technical Services RSTECH@usp.org | SM42020 Small Molecules 4 |

Chromatographic Database Information: [Chromatographic Database](#)

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