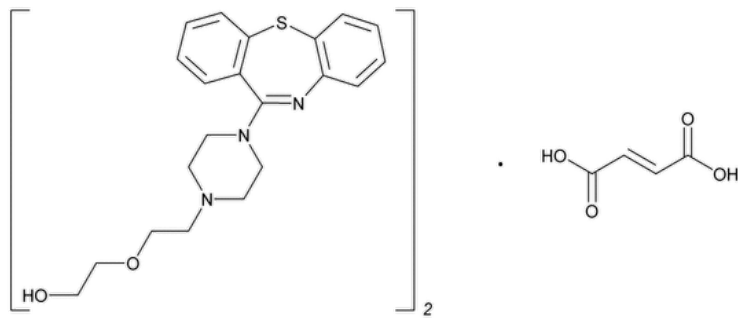


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Quetiapine Fumarate



$(C_{21}H_{25}N_3O_2S)_2 \cdot C_4H_4O_4$ 883.09

Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (E)-2-butenedioate (2:1) (salt);

2-[2-(4-Dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]ethanol fumarate (2:1) (salt) CAS RN[®]: 111974-72-2; UNII: 2S3PL1B6UJ.

DEFINITION

Quetiapine Fumarate contains NLT 98.0% and NMT 102.0% of quetiapine fumarate $[(C_{21}H_{25}N_3O_2S)_2 \cdot C_4H_4O_4]$, calculated on the dried basis.

IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#)
- **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: 2.6 g/L of dibasic ammonium phosphate. Adjust with phosphoric acid to a pH of 6.5.

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

System suitability solution: 1.0 mg/mL of [USP Quetiapine System Suitability RS](#) in *Mobile phase*

Standard stock solution: 0.16 mg/mL of [USP Quetiapine Fumarate RS](#) in *Mobile phase*

Standard solution: 0.08 mg/mL of [USP Quetiapine Fumarate RS](#) from *Standard stock solution* in *Mobile phase*

Sample stock solution: 0.16 mg/mL of Quetiapine Fumarate in *Mobile phase*

Sample solution: 0.08 mg/mL of Quetiapine Fumarate from *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: 50 μL

System suitability

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

[NOTE—The relative retention times for quetiapine desethoxy and quetiapine are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the quetiapine desethoxy and quetiapine peaks, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of quetiapine fumarate $[(C_{21}H_{25}N_3O_2S)_2 \cdot C_4H_4O_4]$ in the portion of Quetiapine Fumarate taken:

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

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 = concentration of Quetiapine Fumarate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

• **ORGANIC IMPURITIES**

Buffer: 3.1 g/L of ammonium acetate in water. Add 2 mL of 25% ammonium hydroxide to each 1 L of solution. The pH of the resulting solution is NLT 9.2.

Solution A: Acetonitrile and *Buffer* (25:75)

Solution B: Acetonitrile

Diluent: *Solution A* and *Solution B* (86:14)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
25	100	0
60	29.3	70.7
60.1	100	0
68	100	0

Peak identification solution: 1 µg/mL of [USP Quetiapine Fumarate RS](#), 10 µg/mL of [USP Quetiapine Related Compound B RS](#), and 2 µg/mL of [USP Quetiapine Related Compound G RS](#) in *Diluent*

System suitability solution: 1 mg/mL of [USP Quetiapine System Suitability RS](#) in *Diluent*

Standard solution: 0.001 mg/mL of [USP Quetiapine Fumarate RS](#) in *Diluent*

Sample solution: 1.0 mg/mL of Quetiapine Fumarate in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *Peak identification solution*, *System suitability solution*, and *Standard solution*

[NOTE—See [Table 2](#) for relative retention times. Quetiapine related compound B will be the largest peak in the *Peak identification solution* chromatogram.]

Suitability requirements

Resolution: NLT 4.0 between the quetiapine desethoxy and quetiapine peaks, *System suitability solution*; NLT 3.0 between quetiapine related compound B and quetiapine related compound G, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Quetiapine Fumarate taken:

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

r_U = peak response of each 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 = concentration of Quetiapine Fumarate in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#). Disregard peaks below 0.05% or with retention times less than 2 min.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fumaric acid ^a	0.08	—	—
Quetiapine quaternary salt ^{b,c}	0.27	0.62	0.15
Quetiapine related compound G	0.55	1.2	0.15
Quetiapine related compound B	0.67	1.2	0.15
Quetiapine desethoxy ^d	0.83	1.0	0.15
Quetiapine	1.0	—	—
Quetiapine tetraethylene glycol analog ^{b,e}	1.2	1.0	0.10
N-Ethyl quetiapine ^{b,f}	1.51	1.1	0.15
Bis(dibenzothiazepinyl) piperazine ^{b,g}	2.22	1.0	0.10
Any other unknown individual impurity	—	—	0.10
Total impurities	—	—	0.50

^a Peak due to counter ion, included for peak identification purposes. Not to be included in total impurities.

^b Process impurity specific to manufacturing process.

^c 4-(Dibenzo[b,f][1,4]thiazepin-11-yl)-1,1-bis[2-(2-hydroxyethoxy)ethyl]piperazin-1-ium.

^d 2-[4-(Dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethanol.

- e ▲ 2-[2-(2-[4-(Dibenzo[*b,f*][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy)ethoxy]ethan-1-ol. ▲ (CN 1-Dec-2024)
- f 11-(4-Ethylpiperazin-1-yl)dibenzo[*b,f*][1,4]thiazepine.
- g 1,4-Bis(dibenzo[*b,f*][1,4]thiazepin-11-yl)piperazine.

SPECIFIC TESTS

- [Loss on Drying \(731\)](#).
Analysis: Dry at 105° to constant weight.
Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, protected from light.

Change to read:

- [USP REFERENCE STANDARDS \(11\)](#).
[USP Quetiapine Fumarate RS](#)
[USP Quetiapine Related Compound B RS](#)
▲ 11-(Piperazin-1-yl)dibenzo[*b,f*][1,4]thiazepine dihydrochloride.
C₁₇H₁₇N₃S · 2HCl 368.32▲ (CN 1-Dec-2024)
[USP Quetiapine Related Compound G RS](#)
Dibenzo[*b,f*][1,4]thiazepin-11(10*H*)-one.
C₁₃H₉NOS 227.28
[USP Quetiapine System Suitability RS](#)

It contains quetiapine fumarate and NLT 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(10*H*)-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 FUMARATE	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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