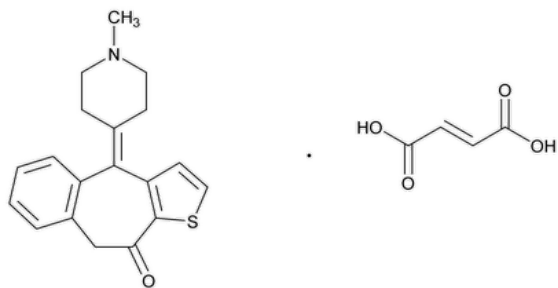


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Add the following:

▲Ketotifen Fumarate



$C_{19}H_{19}NOS \cdot C_4H_4O_4$ 425.50
10*H*-Benzo[4,5]cyclohepta[1,2-*b*]thiophen-10-one, 4,9-dihydro-4-(1-methyl-4-piperidinylidene)-, (*E*)-2-butenedioate (1:1);
4,9-Dihydro-4-(1-methyl-4-piperidylidene)-10*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophen-10-one fumarate (1:1);
4-(1-Methylpiperidin-4-ylidene)-4,9-dihydro-10*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophen-10-one fumarate CAS RN®: 34580-14-8; UNII: HBD503W0RO.

DEFINITION
Ketotifen Fumarate contains NLT 98.0% and NMT 102.0% of ketotifen fumarate ($C_{19}H_{19}NOS \cdot C_4H_4O_4$), 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**

[NOTE—Protect solutions containing ketotifen fumarate from light.]

Solution A: 0.35 mL of [triethylamine](#) in 1 L of [water](#)

Solution B: 0.35 mL of [triethylamine](#) in 1 L of [methanol](#)

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	40	60
12	40	60
20	10	90
25	10	90
26	40	60
31	40	60

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

Standard solution: 0.3 mg/mL of [USP Ketotifen Fumarate RS](#) in *Diluent*

Sample solution: 0.3 mg/mL of Ketotifen Fumarate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 297 nm

Column: 4.0-mm × 15-cm; 3-μm packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ketotifen fumarate ($C_{19}H_{19}NOS \cdot C_4H_4O_4$) in the portion of Ketotifen Fumarate taken:

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

r_U = peak response of ketotifen from the *Sample solution*

r_S = peak response of ketotifen from the *Standard solution*

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

C_U = concentration of Ketotifen 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%

• ORGANIC IMPURITIES

Solution A, Solution B, Mobile phase, Diluent, and Sample solution: Prepare as directed in the Assay.

System suitability solution: 0.3 mg/mL of [USP Ketotifen Fumarate RS](#) and 15 μg/mL of [USP Ketotifen Related Compound G RS](#) in *Diluent*

Sensitivity solution: 0.15 μg/mL of [USP Ketotifen Fumarate RS](#) in *Diluent*

Standard solution: 0.3 μg/mL each of [USP Ketotifen Fumarate RS](#), [USP Ketotifen Related Compound A RS](#), and [USP Ketotifen Related Compound G RS](#) in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 297 nm

Column: 4.0-mm × 15-cm; 3-μm packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 30 μL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between ketotifen and ketotifen related compound G, *System suitability solution*

Relative standard deviation: NMT 5.0% for ketotifen related compound G, ketotifen, and ketotifen related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10 for ketotifen, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of ketotifen related compound A and ketotifen related compound G in the portion of Ketotifen Fumarate taken