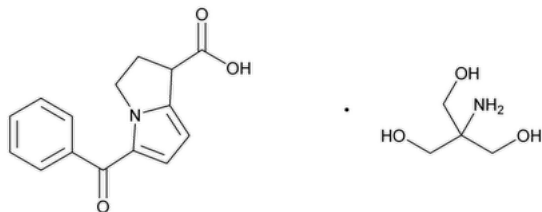


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Ketorolac Tromethamine



$C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$ 376.40

1*H*-Pyrrolizine-1-carboxylic acid, 5-benzoyl-2,3-dihydro, (±)-, compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1); (±)-5-Benzoyl-2,3-dihydro-1*H*-pyrrolizine-1-carboxylic acid, compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) CAS RN®: 74103-07-4; UNII: 4EVE5946BQ.

DEFINITION

Ketorolac Tromethamine contains NLT 98.5% and NMT 101.5% of ketorolac tromethamine ($C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$), 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.
- **C. THIN-LAYER CHROMATOGRAPHY, Tromethamine Test**

Diluent: [Dichloromethane](#) and methanol (2:1)

Standard solution: 5 mg/mL of [USP Ketorolac Tromethamine RS](#) in *Diluent*

Sample solution: 5 mg/mL of Ketorolac Tromethamine in *Diluent*

Chromatographic system

(See [Chromatography \(621\), Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 40 µL

Developing solvent system: [Dichloromethane](#), [acetone](#), and [glacial acetic acid](#) (95:5:2)

Spray reagent: Freshly prepared alcoholic solution containing 30 mg/mL of [ninhydrin](#)

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, and allow the solvent to evaporate. Spray the plate with *Spray reagent*, and heat the plate at about 150° for 2–5 min.

Acceptance criteria: Yellow spots with pink to purple borders develop on the plate in the areas where the *Standard solution* and the *Sample solution* were applied.

ASSAY

PROCEDURE

Protect all the solutions from light.

Buffer: 5.75 g/L of [monobasic ammonium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Tetrahydrofuran](#) and *Buffer* (30:70)

Diluent: [Tetrahydrofuran](#) and water (30:70)

System suitability solution: In a 250-mL separator, mix 100 mL of water, 100 mL of [dichloromethane](#), 30 mg of [USP Ketorolac Tromethamine RS](#), and 1 mL of 1 N hydrochloric acid. Insert the stopper, shake, and allow the layers to separate. Transfer the lower [dichloromethane](#) layer to a stoppered borosilicate glass flask, and discard the upper layer. Expose the [dichloromethane](#) solution to direct sunlight for 10–15 min. Transfer 1.0 mL of the solution to a vial, evaporate in a current of air or in a stream of nitrogen to dryness, add 1.0 mL of *Diluent*, and swirl to dissolve. [NOTE—This solution may be stored under refrigeration and used as long as the chromatogram obtained as directed for *Analysis* is suitable for identifying the peaks due to the ketorolac 1-keto analog and ketorolac 1-hydroxy analog, and for the measurement of the resolution between the ketorolac 1-keto analog and ketorolac.]

Standard solution: 0.4 mg/mL of [USP Ketorolac Tromethamine RS](#) in *Diluent*

Sample solution: 0.4 mg/mL of Ketorolac Tromethamine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 313 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 μL

System suitability

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

[NOTE—The relative retention times for the ketorolac 1-hydroxy analog, the ketorolac 1-keto analog, and ketorolac are about 0.63, 0.89, and 1.0, respectively. Make adjustments, if necessary, to achieve a retention time for ketorolac of about 8–12 min.]

Suitability requirements

Resolution: NLT 1.5 between ketorolac 1-keto analog and ketorolac, *System suitability solution*

Column efficiency: NLT 5500 theoretical plates, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ketorolac tromethamine ($C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$) in the portion of Ketorolac Tromethamine taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

C_U = concentration of Ketorolac Tromethamine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–101.5% on the dried basis

IMPURITIES

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

Change to read:

- **ORGANIC IMPURITIES**

Mobile phase, Diluent, System suitability solution, Standard solution, ▲ (ERR 1-Jul-2021) **Sample solution, ▲ and System suitability: ▲** (ERR 1-Jul-2021) Proceed as directed in the Assay.

Chromatographic system

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

Mode: LC

Detector: UV 313 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 μL

Run time: 3 times the retention time of ketorolac

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Ketorolac Tromethamine taken:

$$\text{Result} = (r_U/r_T) \times F \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Impurity having a 0.54 relative retention time	0.54	2.2	0.5
Ketorolac 1-hydroxy analog	0.63	0.67	0.1
Impurity having a 0.66 relative retention time	0.66	0.91	0.5
Ketorolac 1-keto analog	0.89	0.52	0.1
Individual unspecified impurity	—	1.0	0.5
Ketorolac tromethamine	1.0	1.0	—
Total impurities	—	—	1.0

SPECIFIC TESTS

- [pH \(791\)](#)

Sample solution: 10 mg/mL

Acceptance criteria: 5.7–6.7

- [Loss on Drying \(731\)](#)

Analysis: Dry under vacuum at 60° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°.

- [USP REFERENCE STANDARDS \(11\)](#)

[USP Ketorolac Tromethamine RS](#)

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

Topic/Question	Contact	Expert Committee
KETOROLAC TROMETHAMINE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)

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