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Ketorolac Tromethamine Tablets

DEFINITION

Ketorolac Tromethamine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of ketorolac tromethamine ($C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV absorption spectra of the ketorolac peak of the *Sample solution* and that of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: Methanol, water, and glacial acetic acid (55:44:1)

Diluent: Methanol and water (1:1). [Note—Protect all volumetric solutions from light.]

Standard stock solution: 0.24 mg/mL of USP Ketorolac Tromethamine RS in methanol

Standard solution: 24 µg/mL of USP Ketorolac Tromethamine RS in *Diluent* from *Standard stock solution*

System suitability stock solution: 25 µg/mL each of USP Ketorolac Related Compound A RS, USP Ketorolac Related Compound B RS, USP Ketorolac Related Compound C RS, and USP Ketorolac Related Compound D RS in methanol

System suitability solution: 0.25 µg/mL each of USP Ketorolac Related Compound A RS, USP Ketorolac Related Compound B RS, USP Ketorolac Related Compound C RS, and USP Ketorolac Related Compound D RS in *Standard solution* from *System suitability stock solution*

Sample stock solution: 0.2 mg/mL of ketorolac tromethamine prepared as follows. Transfer 10 Tablets to a suitable volumetric flask. Add a quantity of water equivalent to about 10% of the volume of the flask, and sonicate until the Tablets are disintegrated. Add a quantity of methanol equivalent to 40% of the volume of the flask, and sonicate for 10 min to dissolve the ketorolac tromethamine. Cool to ambient temperature, dilute with methanol to volume, and mix. Centrifuge, or allow to settle.

Sample solution: 0.02 mg/mL of ketorolac tromethamine in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector

Assay: UV 254 nm

Identification test B: Diode array, UV 200–400 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.2 mL/min

Injection volume: 100 µL

Run time: 3.8 times the retention time of the ketorolac peak

System suitability

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

[Note—The relative retention times are 0.8 for ketorolac related compound B and 1.0 for the ketorolac peaks.]

Suitability requirements

Resolution: NLT 1.5 each between the ketorolac and ketorolac related compound B, and ketorolac and ketorolac related compound C peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

Acceptance criteria: 90.0%–110%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 600 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: USP Ketorolac Tromethamine RS in *Medium*

Sample solutions: Sample per *Dissolution ⟨711⟩*. Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Instrumental conditions

Mode: UV absorption spectroscopy

Analytical wavelength: 322 nm

Tolerances: NLT 75% (*Q*) of the labeled amount of ketorolac tromethamine ($C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Mobile phase, Chromatographic system, and **Diluent:** Proceed as directed in the *Assay*.

Standard solution: Use the *System suitability solution*, prepared as directed in the *Assay*.

Sample solution: Proceed as directed for the *Sample solution* in the *Assay*.

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.5 each between the ketorolac and ketorolac related compound B, and ketorolac and ketorolac related compound C peaks

Relative standard deviation: NMT 5.0% for ketorolac related compound A, ketorolac related compound B, ketorolac related compound C, and ketorolac related compound D

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each known impurity in the portion of Tablets taken:

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

r_U = peak response of each known impurity in the *Sample solution*

r_S = peak response of each known impurity in the *Standard solution*

C_S = concentration of each impurity in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other impurity in the portion of Tablets taken:

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

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

r_T = sum of responses for all the peaks in the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ketorolac related compound A	0.5	0.5
Ketorolac related compound B	0.8	0.5
Ketorolac	1.0	—
Ketorolac related compound C	1.2	0.8
Ketorolac related compound D	2.6	0.5
Total unspecified impurity	—	0.5
Total impurities	—	1.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers at controlled room temperature, protected from light and excessive humidity.
- **USP Reference Standards** ⟨11⟩

USP Ketorolac Tromethamine RS

USP Ketorolac Related Compound A RS
5-Benzoyl-*N*-[1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl]-2,3-dihydro-1*H*-pyrrolizine-1-carboxamide.
$C_{19}H_{22}N_2O_5$ 358.39

USP Ketorolac Related Compound B RS
5-Benzoyl-2,3-dihydro-1*H*-pyrrolizin-1-ol.
$C_{14}H_{13}NO_2$ 227.26

USP Ketorolac Related Compound C RS
5-Benzoyl-2,3-dihydro-1*H*-pyrrolizin-1-one.
$C_{14}H_{11}NO_2$ 225.24

USP Ketorolac Related Compound D RS
5-Benzoyl-2,3-dihydro-1*H*-pyrrolizine.
$C_{14}H_{13}NO$ 211.26

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
KETOROLAC TROMETHAMINE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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