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Ketorolac Tromethamine Injection

DEFINITION

Ketorolac Tromethamine Injection is a sterile solution of Ketorolac Tromethamine. It contains 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 spectrum of the ketorolac peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

[Note—Protect all solutions from light.]

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

Diluent: Methanol and water (1:1)

Standard solution: 0.05 mg/mL of USP Ketorolac Tromethamine RS in *Diluent*

Sample solution: Nominally equivalent to 0.05 mg/mL of ketorolac tromethamine in *Diluent* from Injection

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification* test *B*, use a diode array detector in the range of 200–600 nm.

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

Flow rate: 1.2 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5 for the ketorolac peak

Relative standard deviation: NMT 1.0%

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 each mL of Injection taken:

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

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

r_S = peak response of ketorolac 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%–110.0%

IMPURITIES

- **Organic Impurities**

[Note—Protect all solutions from light.]

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

Standard stock solution: 0.10 mg/mL each of USP Ketorolac Tromethamine RS, 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 *Diluent* prepared as follows. Transfer USP Ketorolac Tromethamine RS, 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 to a suitable volumetric flask. Add 4% of the volume of the flask with methanol. Sonicate and dilute with *Diluent* to volume.

Standard solution: 0.2 µg/mL each of USP Ketorolac Tromethamine RS, 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 *Diluent* from the *Standard stock solution*

Sample solution: Prepare nominally equivalent to 0.2 mg/mL of ketorolac tromethamine in *Diluent*.

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2 between ketorolac related compound C and ketorolac

Relative standard deviation: NMT 2.8% for all the peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of ketorolac related compound A, ketorolac related compound B, ketorolac related compound C, and ketorolac related compound D in the portion of Injection taken:

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

r_U = peak response of ketorolac related compound A, ketorolac related compound B, ketorolac related compound C, or ketorolac related compound D from the *Sample solution*

r_S = peak response of ketorolac related compound A, ketorolac related compound B, ketorolac related compound C, or ketorolac related compound D from the *Standard solution*

C_S = concentration of the corresponding related compound in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Injection taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of ketorolac 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: See *Table 1*. Disregard any impurity peak less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ketorolac related compound A	0.4	0.20
Ketorolac related compound B	0.6	0.5
Ketorolac related compound C	0.8	0.5
Ketorolac	1.0	—
Ketorolac related compound D	2.1	0.20

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any unspecified impurity	—	0.20
Total impurities	—	1.50

SPECIFIC TESTS

- **pH ⟨791⟩:** 6.9–7.9
- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 5.8 USP Endotoxin Units/mg of ketorolac tromethamine.
- **Sterility Tests ⟨71⟩:** Meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, protected from light, and store at controlled room temperature.
- **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.

$C_{14}H_{13}NO$ 211.3

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

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

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