Calculate the concentration, in mg/mL, of ketoprofen in the sample withdrawn at each time point:

$$\text{Result} = (A_U - A_{CB}) \times (C_S/A_S)$$

A_U = absorbance of the *Sample solution*
A_{CB} = absorbance of the *Capsule blank*
C_S = concentration of USP Ketoprofen RS in the *Standard solution* (mg/mL)
A_S = absorbance of the *Standard solution*

Calculate the percentage of ketoprofen dissolved at each time point:

$$\text{Result} = (D + \Sigma R) \times 100/L$$

D = [amount dissolved (mg)] = volume (mL) remaining before draw × concentration (mg/mL) of sample withdrawn at the sampling time point
R = [amount removed (mg)] = volume (mL) of sample withdrawn × concentration (mg/mL) of sample withdrawn at each time point
100 = conversion factor for percentage
L = Capsule label claim (mg)

Tolerances: The percentage of the labeled amount of ketoprofen released at the times specified conforms to *Acceptance Table 2.*

Time (h)	Amount Dissolved
1	10%–25%
4	55%–80%
8	NLT 80%

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

Procedure for content uniformity: [Note—Protect the *Standard solution* and *Sample solution* from light.]
Mobile phase, Standard solution, System suitability solution, and Chromatographic system: Proceed as directed in the *Assay*.
Sample solution: Transfer the contents of 10 Capsules, 1 Capsule each, to each of 10 250-mL volumetric flasks, add about 150 mL of *Mobile phase* to each flask, and stir for 2 h. Dilute with *Mobile phase* to volume, and mix. Centrifuge, and pipet a volume of clear supernatant that contains about 2.4 mg of ketoprofen into a 100-mL volumetric flask. Dilute with *Mobile phase* to volume.
System suitability
Samples: *Standard solution* and *System suitability solution*
Suitability requirements
Resolution: NLT 3.0 between ketoprofen and ketoprofen related compound A, *System suitability solution*
Tailing factor: NLT 1.5 for the ketoprofen peak, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{16}H_{14}O_3$ in each Capsule:

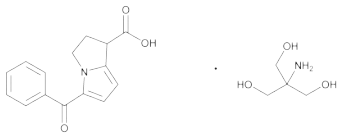
$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Ketoprofen RS in the *Standard solution* (mg/mL)
C_U = concentration of ketoprofen in the *Sample solution* (mg/mL)

SPECIFIC TESTS
- **Water Determination,** *Method I* ⟨**921**⟩**:** NMT 3.0%

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨**11**⟩
USP Ketoprofen RS
USP Ketoprofen Related Compound A RS
α-Methyl-3-(4-methylbenzoyl) benzeneacetic acid.

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) [74103-07-4].

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. Infrared Absorption** ⟨**197K**⟩
- **B. Ultraviolet Absorption** ⟨**197U**⟩
Sample solution: 10 µg/mL
Medium: Methanol
Acceptance criteria: Meets the requirements
- **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 of ninhydrin/mL
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.

USP Monographs

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 keterolac tromethamine ($C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$) in the portion of Keterolac 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%

Delete the following:

- **HEAVY METALS,** *Method II* ⟨231⟩: 20 ppm (Official 1-Dec-2015)
- **ORGANIC IMPURITIES**
Mobile phase, Diluent, System suitability solution, Standard solution, and **Sample solution:** Prepare 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
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

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.**
Sample: *Standard solution* and *Sample solution* (1:1), prepared as directed in the *Assay*
Analysis: Chromatograph the *Sample* as directed in the *Assay*