cis-1-(*p*-{[2-(2,4-Dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy}phenyl)-4-isopropylpiperazine.
$C_{26}H_{31}Cl_2N_5O_3$ 532.46 ■2S *(USP38)*

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
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**

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 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 methanol
System suitability solution: 0.25 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 *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: UV 254 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 for the ketorolac related compound B and ketorolac peaks are 0.8 and 1.0, respectively.]
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*
Column efficiency: NLT 2700 theoretical plates, *Standard 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 solution: 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**⟩

Procedure for content uniformity
Blank: Methanol
Standard solution: 12 µg/mL of USP Ketorolac Tromethamine RS in methanol
Sample solution: Transfer 1 Tablet to a suitable volumetric flask that will provide a final concentration of about 0.1 mg/mL of ketorolac tromethamine. Add a quantity of water equivalent to about 10% of the volume of the flask, and sonicate until the Tablet is disintegrated. Add a quantity of methanol equivalent to 40% of the volume of the flask, and sonicate for about 10 min to dissolve the ketorolac tromethamine. Cool to ambient temperature, dilute with methanol to volume, and mix. Centrifuge or allow to settle. Transfer 6.0 mL of the clear supernatant to a 50-mL volumetric flask, and dilute with methanol to volume.
Instrumental conditions
Mode: UV absorption spectroscopy
Analytical wavelength: UV 322 nm
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:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*
C_S = concentration of USP Ketorolac Tromethamine RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of ketorolac tromethamine in the *Sample solution* (µg/mL)

Acceptance criteria: Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Mobile phase, Diluent, and **System suitability solution:** 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*.
Chromatographic system and **System suitability:** Proceed as directed in the *Assay*.
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 = peak response of each individual impurity 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● (RB 1-Feb-2015)
Ketorolac related compound D	2.6	0.5
Total unspecified impurity	—	0.5
Total impurities	—	1.0

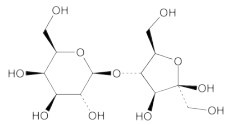
ADDITIONAL REQUIREMENTS

- **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

Lactulose Concentrate

Change to read:



$C_{12}H_{22}O_{11}$ 342.30
D-Fructose, 4-*O*-*β*-D-galactopyranosyl-;■2S (*USP38*)
4-*O*-*β*-D-Galactopyranosyl-D-fructofuranose [4618-18-2].

DEFINITION

Lactulose Concentrate is a solution of sugars prepared from Lactose. It consists principally of lactulose together with minor quantities of lactose and galactose, and traces of other related sugars and water. It contains NLT 95.0% and NMT 105.0% of the labeled amount of lactulose ($C_{12}H_{22}O_{11}$). It contains no added substances.

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.**

Sample solution: Dilute a portion of Concentrate with water (1 in 20).
Analysis: Add a few drops of the *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.
Acceptance criteria: A red precipitate of cuprous oxide is formed.

ASSAY

- **PROCEDURE**

Buffer: 1.15 g/L of monobasic sodium phosphate in water
Mobile phase: Acetonitrile and *Buffer* (82:18). Ensure that the concentration of acetonitrile in the *Mobile phase* is between 78% and 85% to obtain appropriate retention times.
Standard solution: 40 mg/mL of USP Lactulose RS, 4.8 mg/mL of USP Anhydrous Lactose RS, and 3.2 mg/mL of USP Epilactose RS in a mixture of acetonitrile and water (1:1)
Sample solution: Nominally equivalent to 40 mg/mL of lactulose prepared as follows. Transfer a quantity of Concentrate containing 2.0 g of lactulose to a 50-mL volumetric flask, and dissolve in 20 mL of water. Add 25.0 mL of acetonitrile, allow the solution to reach ambient temperature, and dilute with water to volume.