Ketorolac Tromethamine Tablets

DEFINITION
Ketorolac Tromethamine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of ketorolac tromethamine (C15H13NO3·C4H11NO3).

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 methanol 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
    - **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 (C15H13NO3·C4H11NO3) in the portion of Tablets taken:
  \[
  \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
  \]
  \(r_U\) = 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 (C15H13NO3·C4H11NO3) 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 for 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 (C15H13NO3·C4H11NO3) in the portion of Tablets taken:
  \[
  \text{Result} = \left( \frac{A_U}{A_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
  \]
  \(A_U\) = 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:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

\(r_U\) = 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:

\[
\text{Result} = \left( \frac{r_U}{r_T} \right) \times 100
\]

\(r_U\) = 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>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketorolac related compound A</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Ketorolac related compound B</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Ketorolac related compound C</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Ketorolac related compound D</td>
<td>2.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Total unspecified impurity</td>
<td>—</td>
<td>0.5</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**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-1H-pyrrolizine-1-carboxamide.
    - \(C_{19}H_{22}N_2O_5\) 358.39
  - USP Ketorolac Related Compound B RS
    - 5-Benzoyl-2,3-dihydro-1H-pyrrolizin-1-ol.
    - \(C_{14}H_{13}NO_2\) 227.26
  - USP Ketorolac Related Compound C RS
    - 5-Benzoyl-2,3-dihydro-1H-pyrrolizin-1-one.
    - \(C_{14}H_{11}NO_2\) 225.24
  - USP Ketorolac Related Compound D RS
    - 5-Benzoyl-2,3-dihydro-1H-pyrrolizine.
    - \(C_{14}H_{13}NO\) 211.26

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