Meloxicam

Molecular formula: \( C_{14}H_{13}N_3O_4S_2 \)
Molecular weight: 351.40

**DEFINITION**
Meloxicam contains NLT 99.0% and NMT 100.5% of Meloxicam (\( C_{14}H_{13}N_3O_4S_2 \)), calculated on the dried basis.

**ASSAY**

**PROCEDURE**

Solution A: Mixture of a 0.1% (w/v) solution of ammonium acetate with 10% ammonia solution to a pH of 9.1

Mobile phase: Methanol and Solution A (21:29)

System suitability solution: 0.08 mg/mL each of USP Meloxicam RS and USP Meloxicam Related Compound A RS. Prepared by dissolving in 50% of the flask volume of Diluent and diluting with water to volume.

Standard solution: 0.2 mg/mL of USP Meloxicam RS. Prepared by dissolving in 50% of the flask volume of Diluent and diluting with water to volume.

Sample solution: 0.2 mg/mL of Meloxicam. Prepared by dissolving in 50% of the flask volume of Diluent and diluting with water to volume.

Chromatographic system

(System Suitability)

Mode: LC

Detector: UV 360 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 10 \( \mu \)L

System suitability

Sample: System suitability solution

[NOTE—The relative retention times for meloxicam related compound A and meloxicam are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between meloxicam related compound A and meloxicam

Tailing factor: NMT 2.0 for the meloxicam peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of meloxicam (\( C_{14}H_{13}N_3O_4S_2 \)) in the portion of Meloxicam taken:

\[
\text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_u}{C_s} \right) \times 100
\]

\( r_u \) = peak response of meloxicam from the Sample solution

\( r_s \) = peak response of meloxicam from the Standard solution

\( C_u \) = concentration of USP Meloxicam RS in the Standard solution (mg/mL)

Acceptance criteria: 99.0%–100.5% on the dried basis

**IMPURITIES**

- **Residue on Ignition (281):** NMT 0.1%
- **Heavy Metals, Method II (231):** NMT 10 ppm
- **Organic Impurities, Procedure 1**
  Perform either Procedure 1 or Procedure 2, depending on the manufacturing process used.

Solution A: 0.1% (w/v) solution of monobasic potassium phosphate adjusted with 1 N sodium hydroxide to a pH of 6.0

Solution B: Methanol

Diluent: Methanol and 1 N sodium hydroxide (50:3)

Mobile phase: See Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>15</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>15.1</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>18</td>
<td>60</td>
<td>40</td>
</tr>
</tbody>
</table>

System suitability solution: 0.08 mg/mL each of USP Meloxicam RS, USP Meloxicam Related Compound A RS, and USP Meloxicam Related Compound B RS. Prepared by dissolving in 10% of the flask volume of Diluent and diluting with water to volume.

Standard stock solution: 0.6 mg/mL of USP Meloxicam RS. Prepared by dissolving in 25% of the flask volume of Diluent and diluting with methanol to volume.

Standard solution: 0.012 mg/mL of USP Meloxicam RS in methanol from the Standard stock solution

Sample solution: 4 mg/mL of Meloxicam. Prepared by dissolving in 25% of the flask volume of Diluent and diluting with methanol to volume.

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 260 and 350 nm (variable wavelength or multi-wavelength detector)

Column: 4.6-mm × 15-cm; 5-\( \mu \)m packing L1

Flow rate: 1 mL/min

Injection volume: 5 \( \mu \)L

System suitability

Samples: System suitability solution and Standard solution

[NOTE—The relative retention times are listed in Table 2.]

Suitability requirements

Resolution: NLT 3.0 between meloxicam related compound A and meloxicam at 350 nm; NLT 3.0 between meloxicam related compound B and meloxicam at 260 nm, System suitability solution

Relative standard deviation: NMT 10%, Standard solution

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of each impurity in the portion of Meloxicam taken:

\[
\text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_u}{C_s} \right) \times (1/F) \times 100
\]

\( r_u \) = peak response of each impurity from the Sample solution

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**Meloxicam**

\( r_S \) = peak response of meloxicam at 350 nm from the Standard solution

\( C_S \) = concentration of USP Meloxicam RS in the Standard solution (mg/mL)

\( C_U \) = concentration of the Sample solution (mg/mL)

\( F \) = relative response factor (see Table 2)

[NOTE—For the specified impurities, calculate the percentage content of each impurity, using the peak responses from the Sample solution recorded at the detection wavelength given in Table 2. For an unknown impurity, calculate the percentage content, using peak responses recorded at the wavelength that gives the greater response.]

**Acceptance criteria:** See Table 2.

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**Change to read:**

- **Organic Impurities, Procedure 2**

  If an article complies with this test, the labeling indicates that it meets the requirements under Organic Impurities, Procedure 2.

**Solution A and Solution B:** Proceed as directed in Procedure 1.

**Mobile phase:** See Table 3.

### Table 3

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>25</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>30</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>40</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>45</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>50</td>
<td>45</td>
<td>55</td>
</tr>
</tbody>
</table>

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**Diluent B:** Methanol and water (2:3)

**Diluent A:** Diluent B and 0.4 N sodium hydroxide (50:3)

**Standard stock solution A:** 50 µg/mL of USP Meloxicam RS in Diluent A. Dilute 2 mL of this solution with Diluent B to 10 mL.

**Standard stock solution B:** Transfer 5 mg each of USP Meloxicam Related Compound B RS and USP Meloxicam Related Compound C RS into a 100-mL volumetric flask. Add 6 mL of 0.4 N sodium hydroxide, and sonicate for 2 min. Add 40 mL of methanol to the resulting solution, sonicate for 2 min, and dilute with water to volume.

**Standard solution:** Transfer 1 mL each of Standard stock solution A and Standard stock solution B into a 10-mL volumetric flask, dilute with Diluent B to volume, and mix.

**Sample solution:** Dissolve 20 mg of Meloxicam in 10 mL of Diluent A, and dilute with Diluent B to 20 mL.

**Chromatographic system**

(See Chromatography 〈621〉, System Suitability.)

**Mode:** LC

**Detector:** UV variable wavelength or multi-wavelength detector at 260 nm and 350 nm

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

**Column temperature:** 45°

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**Suitability requirements**

[NOTE—The relative retention times are listed in Table 2.]

**Relative standard deviation:** NMT 5.0% for meloxicam related compound C at 350 nm and NMT 5.0% for meloxicam related compound B at 260 nm

**Analysis**

**Samples:** Standard solution and Sample solution

### Table 2

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Wavelength (nm)</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meloxicam related compound B&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.4</td>
<td>260</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>1.0</td>
<td>260/350</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Meloxicam related compound A&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.4</td>
<td>350</td>
<td>1.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Methyl-meloxicam&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.7</td>
<td>350</td>
<td>1.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Ethyl-meloxicam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.9</td>
<td>350</td>
<td>1.0</td>
<td>0.05</td>
</tr>
<tr>
<td>Individual unknown impurity</td>
<td>—</td>
<td>260/350</td>
<td>—</td>
<td>0.1</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.3</td>
</tr>
</tbody>
</table>

<sup>a</sup> 2-Amino-5-methyl-thiazole.

<sup>b</sup> 4-Hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylic acid ethyl ester 1,1-dioxide.

<sup>c</sup> N-(3,5-Dimethylthiazol-2(3H)-ylidene)-4-hydroxy-2-methyl-2H-benz[e][1,2]thiazine-3-carboxamide 1,1-dioxide.

<sup>d</sup> N-(3-Ethyl-5-methylthiazol-2(3H)-ylidene)-4-hydroxy-2-methyl-2H-benz[e][1,2]thiazine-3-carboxamide 1,1-dioxide.
Calculate the percentage of each impurity in the portion of Meloxicam 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 impurity from the Sample solution
- \( r_S \) = peak response of the corresponding related compound from the Standard solution
- \( C_S \) = concentration of the corresponding USP Related Compound RS in the Standard solution (mg/mL). \([\text{NOTE}—\text{Use the concentration of the USP Meloxicam RS for unknown impurities.}]\)
- \( C_U \) = concentration of the Sample solution (mg/mL)

**Acceptance criteria:** See Table 4.

**Table 4**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Wavelength (nm)</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meloxicam</td>
<td>1.0</td>
<td>260/350</td>
<td>—</td>
</tr>
<tr>
<td>Meloxicam related compound B(^a)</td>
<td>0.8</td>
<td>260</td>
<td>0.1</td>
</tr>
<tr>
<td>Meloxicam related compound C(^b)</td>
<td>3.2</td>
<td>350</td>
<td>0.1</td>
</tr>
<tr>
<td>Individual unknown impurity</td>
<td>—</td>
<td>260/350</td>
<td>0.1</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>0.3</td>
</tr>
</tbody>
</table>

\(^a\) 2-Amino-5-methyl-thiazole.

\(^b\) Isopropyl-4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylate-1,1-dioxide.

**SPECIFIC TESTS**

- **Loss on Drying** (731)
  
  **Analysis:** Dry a sample at 105° for 4 h.
  
  **Acceptance criteria:** NMT 0.5%

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

- **Labeling:** The labeling states with which Procedure under Organic Impurities the article complies if a test other than Procedure 1 is used.

**Change to read:**

- **USP Reference Standards** (11)
  
  USP Meloxicam RS
  USP Meloxicam Related Compound A RS
  4-Hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylic acid ethylester 1,1-dioxide.
  USP Meloxicam Related Compound B RS
  2-Amino-5-methyl-thiazole.
  USP Meloxicam Related Compound C RS
  Isopropyl-4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylate-1,1-dioxide.

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