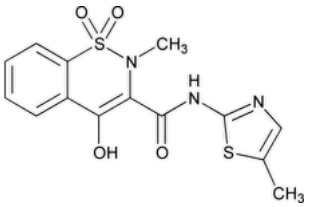
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-1A58A07F-EF8F-48F7-A672-FCD33F0E4E27_5_en-US
DOI: https://doi.org/10.31003/USPNF_M48120_05_01
DOI Ref: ekcmc

Meloxicam



$C_{14}H_{13}N_3O_4S_2$ 351.40

4-Hydroxy-2-methyl-*N*-(5-methyl-2-thiazolyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide CAS RN®: 71125-38-7; UNII: VG2QF83CGL.

DEFINITION

Meloxicam contains NLT 98.0% and NMT 102.0% of meloxicam ($C_{14}H_{13}N_3O_4S_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the meloxicam peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

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

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

Diluent: Methanol and 1 N sodium hydroxide (250:1)

System suitability solution: 0.08 mg/mL each of USP Meloxicam RS and USP Meloxicam Related Compound A RS prepared as follows. Dissolve USP Meloxicam RS and USP Meloxicam Related Compound A RS in 50% of the flask volume of *Diluent*, and dilute with water to volume.

Standard solution: 0.2 mg/mL of USP Meloxicam RS prepared as follows. Dissolve USP Meloxicam RS in 50% of the flask volume of *Diluent*, and dilute with water to volume.

Sample solution: 0.2 mg/mL of Meloxicam prepared as follows. Dissolve Meloxicam in 50% of the flask volume of *Diluent*, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 360 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard 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, *System suitability solution*

Tailing factor: NMT 2.0 for the meloxicam peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

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:

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

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

r_S = peak response of meloxicam 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)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **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

Time (min)	Solution A (%)	Solution B (%)
0	60	40
2	60	40
10	30	70
15	30	70
15.1	60	40
18	60	40

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 as follows. Dissolve USP Meloxicam RS, USP Meloxicam Related Compound A RS, and USP Meloxicam Related Compound B RS in 10% of the flask volume of *Diluent*, and dilute with water to volume.

Standard stock solution: 0.6 mg/mL of USP Meloxicam RS prepared as follows. Dissolve USP Meloxicam RS in 25% of the flask volume of *Diluent*, and dilute 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 as follows. Dissolve Meloxicam in 25% of the flask volume of *Diluent*, and dilute 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-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 5 µL

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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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*.

Table 2

Name	Relative Retention Time	Wavelength (nm)	Relative Response Factor	Acceptance Criteria, NMT (%)
Meloxicam related compound B[a]	0.4	260	1.0	0.1
Meloxicam	1.0	—	—	—
Meloxicam related compound A[b]	1.4	350	0.5	0.1
Methyl-meloxicam[c]	1.7	350	1.0	0.05
Ethyl-meloxicam[d]	1.9	350	1.0	0.05
Individual unknown impurity	—	260/350	1.0	0.1
Total impurities	—	—	—	0.3

[a] 5-Methylthiazol-2-amine.

[b] Ethyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide.

[c] *N*-[3,5-Dimethylthiazol-2(3*H*]-ylidene)-4-hydroxy-2-methyl-2*H*-benzo[*e*][1,2]thiazine-3-carboxamide 1,1-dioxide.

[d] *N*-[3-Ethyl-5-methylthiazol-2(3*H*)-ylidene]-4-hydroxy-2-methyl-2*H*-benzo[*e*][1,2]thiazine-3-carboxamide 1,1-dioxide.

• **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

Time (min)	Solution A (%)	Solution B (%)
0	45	55
25	45	55
30	30	70
40	30	70
45	45	55
50	45	55

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

Diluent B: Methanol and water (2:3)

Standard stock solution A: 0.01 mg/mL of USP Meloxicam RS prepared as follows. Dilute a solution of 0.05 mg/mL of USP Meloxicam RS in *Diluent A* with *Diluent B*.

Standard stock solution B: 0.05 mg/mL each of USP Meloxicam Related Compound B RS and USP Meloxicam Related Compound C RS prepared as follows. Transfer suitable amounts of USP Meloxicam Related Compound B RS and USP Meloxicam Related Compound C RS to an adequate volumetric flask. Add 0.4 N sodium hydroxide to 6% of the flask volume, and sonicate for 2 min. Add an additional 40% of the flask volume of methanol, sonicate for 2 min, and dilute with water to volume.

Standard solution: 0.001 mg/mL of USP Meloxicam RS and 0.0015 mg/mL each of USP Meloxicam Related Compound B RS and USP Meloxicam Related Compound C RS prepared as follows. Transfer suitable volumes of *Standard stock solution A* and *Standard stock solution B* to an adequate volumetric flask, and dilute with *Diluent B* to volume.

Sample solution: 1 mg/mL of Meloxicam prepared as follows. Dissolve a suitable amount of Meloxicam with 50% of the flask volume of *Diluent A*, and dilute with *Diluent B* to volume.

Chromatographic system

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

Mode: LC

Detector: UV variable wavelength or multi-wavelength detector at 260 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

System suitability

Sample: *Standard solution*

[Note—The relative retention times are listed in *Table 4*.]

Suitability requirements

Relative standard deviation: NMT 5.0% for meloxicam, meloxicam related compound B, and meloxicam related compound C

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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). [Note—Use the concentration of USP Meloxicam RS for unknown impurities.]

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

[Note—Use the peak response and concentration of USP Meloxicam RS for unknown impurities; for the specified impurities, calculate the percentage content of each impurity using the *Sample solution* peak responses recorded at the detection wavelength given in *Table 4*. For an unknown impurity, calculate the percentage content using peak responses recorded at the wavelength that gives the greater response.]

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Wavelength (nm)	Acceptance Criteria, NMT (%)
Meloxicam	1.0	350	—
Meloxicam related compound B[a]	0.8	260	0.1
Meloxicam related compound C[b]	3.2	350	0.1
Individual unknown impurity	—	260/350	0.1

Name	Relative Retention Time	Wavelength (nm)	Acceptance Criteria, NMT (%)
Total impurities	—	—	0.3

[a] 5-Methylthiazol-2-amine.

[b] Isopropyl-4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate-1,1-dioxide.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry 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.

• **USP Reference Standards** ⟨11⟩

USP Meloxicam RS

USP Meloxicam Related Compound A RS

Ethyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide.

$C_{12}H_{13}NO_5S$ 283.30

USP Meloxicam Related Compound B RS

5-Methylthiazol-2-amine.

$C_4H_6N_2S$ 114.175

USP Meloxicam Related Compound C RS

Isopropyl-4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate-1,1-dioxide.

$C_{13}H_{15}NO_5S$ 297.33

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

Topic/Question	Contact	Expert Committee
MELOXICAM	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(6)

Current DocID: GUID-1A58A07F-EF8F-48F7-A672-FCD33F0E4E27_5_en-US

Previous DocID: GUID-1A58A07F-EF8F-48F7-A672-FCD33F0E4E27_4_en-US

DOI: https://doi.org/10.31003/USPNF_M48120_05_01

DOI ref: ekcmc