larger peak areas at 262 nm than at 240 nm; melengestrol acetate related compound A will generate a larger peak area at 240 nm than at 262 nm]: the relative retention times are about 0.78, 1.0, and 1.05 for melengestrol acetate related compound A, melengestrol acetate, and melengestrol acetate related compound B, respectively; the resolution, *R,* between melengestrol acetate related compound A and melengestrol acetate related compound B is not less than 5.0; the column efficiency for the melengestrol acetate related compound A peak is greater than 1500 theoretical plates; the tailing factor is less than 2.0; and the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, identify the peaks, and determine which detector wavelength generates the larger peak area for each impurity. Using the larger peak area, calculate the percentage of each impurity in the portion of Melengestrol Acetate taken by the formula:

$$100(C_S / C_U)(r_i / r_S)$$

in which C_S is the concentration, in mg per mL, of either melengestrol related compound A or melengestrol related compound B in the *Standard solution* [NOTE—If using the impurity peak area generated at 240 nm, C_S is the concentration of melengestrol related compound A; if using the impurity peak area generated at 262 nm, C_S is the concentration of melengestrol related compound B]; C_U is the concentration, in mg per mL, of melengestrol acetate in the *Test solution;* r_i is the peak area of each impurity obtained from the *Test solution;* and r_S is the peak area of either melengestrol related compound A or melengestrol related compound B obtained from the *Standard solution* [NOTE—If using the impurity peak area generated at 240 nm, r_S is the peak area of melengestrol related compound A; if using the impurity peak area generated at 262 nm, C_S is the peak area of melengestrol related compound B]: not more than 0.5% of any identified impurity is found; not more than 0.2% of any unidentified impurity is found; and not more than 1.0% of total impurities is found.

Assay—

Mobile phase—Prepare a mixture of acetonitrile and water (50:50).

Standard preparation—Dissolve an accurately weighed quantity of USP Melengestrol Acetate RS in methanol to obtain a solution having a known concentration of about 0.5 mg per mL.

Assay preparation—Transfer about 50 mg of Melengestrol Acetate, accurately weighed, to a 100-mL volumetric flask, and dissolve in and dilute with methanol to volume.

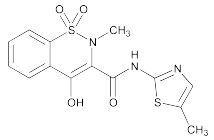
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 287-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation* as directed for *Procedure:* the column efficiency is not less than 1500 theoretical plates; the tailing factor is not more than 2; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* in duplicate into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $C_{25}H_{32}O_4$ in the portion of Melengestrol Acetate taken by the formula:

$$2CW(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of the *Standard preparation; W* is the weight, in mg, of Melengestrol Acetate used to prepare the *Assay preparation;* r_U is the average peak area of the melengestrol acetate peak obtained from the *Assay preparation;* and r_S is the average peak area of the melengestrol acetate peak obtained from the *Standard preparation.*

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 [71125-38-7].

DEFINITION

Meloxicam contains NLT 99.0% and NMT 100.5% of $C_{14}H_{13}N_3O_4S_2$, calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨197K⟩
- **B. ULTRAVIOLET ABSORPTION** ⟨197U⟩

Wavelength range: 240–450 nm
Sample solution: 10 µg/mL in methanol

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: Dissolve 4 mg each of USP Meloxicam RS and USP Meloxicam Related Compound A RS in 25 mL of *Diluent*, and complete the volume to 50 mL with water.
Standard solution: Dissolve 20 mg of USP Meloxicam RS in 50 mL of *Diluent*, and complete the volume to 100 mL with water.
Sample solution: Dissolve 20 mg of Meloxicam in 50 mL of *Diluent*, and complete the volume to 100 mL with water.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 360 nm
Column: 4.6-mm × 15-cm; packing L1
Column temperature: 45°
Flow rate: 1.0 mL/min
Injection size: 10 µL
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 meloxicam peak
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{14}H_{13}N_3O_4S_2$ 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)

Impurity Table 1

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	260/350	—	—
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

[a] 2-Amino-5-methyl-thiazole.
[b] 4-Hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylic acid ethyl ester 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.

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

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm

Organic Impurities

- **PROCEDURE 1**

[NOTE—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: Use the gradient table below.

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: Dissolve 4 mg each of USP Meloxicam RS, USP Meloxicam Related Compound A RS, and USP Meloxicam Related Compound B RS in 5 mL of *Diluent*, and complete the volume to 50 mL with methanol.

Standard solution: Dissolve 12 mg of USP Meloxicam RS in 5 mL of *Diluent*, complete the volume to 20 mL with methanol, and dilute 2 mL to 100 mL with methanol.

Sample solution: Dissolve 80 mg of Meloxicam in 5 mL of *Diluent*, and complete the volume to 20 mL with methanol.

Chromatographic system

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

Mode: LC

Detector: UV 260–350 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 size: 5 µL

System suitability

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

[NOTE—Relative retention times are listed in *Impurity Table 1*.]

Suitability requirements

Resolution: NLT 3.0 between meloxicam related compound A and meloxicam at 350 nm, and 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 Meloxicam in the *Sample solution* (mg/mL)

F = relative response factor (see *Impurity Table 1*)

[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 *Impurity Table 1*. For an unknown impurity, calculate the percentage content, using peak responses recorded at the wavelength that gives the greater response.]

Acceptance criteria

Individual impurity: See *Impurity Table 1*.

Total impurities: NMT 0.3%

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

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

Mobile phase: See the gradient table below.

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: 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, USP Meloxicam Related Compound C RS, and USP Meloxicam Related Compound D 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.
System suitability stock solution: 2 mg/mL of USP Meloxicam RS in *Diluent A*
System suitability solution: Transfer 5 mL of *System suitability stock solution* and 1 mL of *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 size: 20 µL
System suitability
Samples: *Standard solution* and *System suitability solution*
[NOTE—Relative retention times are listed in *Impurity Table 2*.]
Suitability requirements
Resolution: NLT 5.0 between meloxicam related compound D and meloxicam at 350 nm, *System suitability solution*
Relative standard deviation: NMT 5.0% for meloxicam related compound C and for meloxicam related compound D at 350 nm and NMT 5.0% for meloxicam related compound B at 260 nm, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Meloxicam taken:

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

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 the USP Meloxicam RS for unknown impurities.]
C_U = concentration of Meloxicam in 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 *Impurity Table 2*. For an unknown impurity, calculate the percentage content using peak responses recorded at the wavelength that gives the greater response.]
Acceptance criteria
Individual impurities: See *Impurity Table 2*.
Total impurities: NMT 0.3%

Impurity Table 2

Name	Relative Retention Time	Wavelength (nm)	Acceptance Criteria, NMT (%)
Meloxicam	1.0	260/350	—
Meloxicam related compound B[a]	0.8	260	0.1
Meloxicam related compound C[b]	3.2	350	0.1
Meloxicam related compound D[c]	2.4	350	0.1
Individual unknown impurity	—	260/350	0.1

[a] 2-Amino-5-methyl-thiazole.
[b] Isopropyl-4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate-1,1-dioxide.
[c] 4-Methoxy-2-methyl-*N*-(5-methyl-1,3-thiazol-2yl)-2*H*-1,2-benzothiazine-3-carboxamide-1,1-dioxide.

SPECIFIC TESTS
- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample at 105° for 4 h: it loses NMT 0.5% of its weight.

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
4-Hydroxy-2-methyl-2*H*-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-2*H*-1,2-benzothiazine-3-carboxylate-1,1-dioxide.
USP Meloxicam Related Compound D RS
4-Methoxy-2-methyl-*N*-(5-methyl-1,3-thiazole-2yl)-2*H*-1,2-benzothiazine-3-carboxamide-1,1-dioxide.

Meloxicam Oral Suspension

» Meloxicam Oral Suspension contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of meloxicam ($C_{14}H_{13}N_3O_4S_2$).

Packaging and storage—Preserve in well-closed containers. Store at 25°, excursions permitted between 15° and 30°.

USP Reference standards ⟨11⟩**—**
USP Meloxicam RS
USP Meloxicam Related Compound B RS
2-Amino-5-methyl-thiazole.

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Test solution—Transfer a volume of Oral Suspension, equivalent to about 2.5 mg of meloxicam, to a 10-mL volumetric flask. Dilute with acetone to volume, and mix for 10 minutes. If necessary, pass through fluted filter paper.

Standard solution: 0.25 mg per mL, prepared by dissolving USP Meloxicam RS in 1 mL of water and diluting with acetone to volume.

Developing solvent solution: a mixture of chloroform, methanol, and ammonium hydroxide (80:20:1)

Procedure—Proceed as directed in the chapter. After removing the plate from the chamber and drying, examine the chro-