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-

matograms under UV light at 254-nm: the R_F value (approximately 0.45) of the principal dark spot obtained from the *Test solution* corresponds to that obtained from the *Standard solution.*

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

pH ⟨791⟩**:** between 3.5 and 4.5.

Viscosity ⟨911⟩**—**Determine using a shear rate programmable rotational viscometer: between 40 and 100 centipoises, determined at 20°.

Dissolution ⟨711⟩**—**

Medium: pH 7.5 phosphate buffer; 900 mL.

Apparatus 2: 25 rpm.

Time: 15 minutes.

Determine the amount of $C_{14}H_{13}N_3O_4S_2$ dissolved by employing the following method.

Standard solution—Transfer about 20.83 mg of USP Meloxicam RS, accurately weighed, into a 100-mL volumetric flask. Dissolve in 5 mL of methanol and 1 mL of 0.1 M sodium hydroxide, and dilute with *Medium* to volume. Dilute with *Medium* to a final concentration of about 8.3 µg per mL of meloxicam.

Test solution—Shake each sample for 15 minutes. Weigh six portions, equivalent to 7.5 mg of the Oral Suspension, into separate tared 10-mL beakers, and record each weight. Introduce each of the samples to the middle of the dissolution vessels, and rinse each beaker with about 20 mL of the *Medium* withdrawn from the vessel. Carefully lower the paddle to the appropriate height and start the rotation. After completion of the dissolution, pass a 20-mL aliquot through a nylon filter having a 0.45-µm porosity, discarding the first 3 mL of the filtrate.

Procedure—Determine the amount of $C_{14}H_{13}N_3O_4S_2$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 362 nm on the *Test solution* in comparison with the *Standard solution,* using *Medium* as the blank. Calculate the percentage of $C_{14}H_{13}N_3O_4S_2$ released by the formula:

$$\frac{A_U \times C_S \times 900 \times d \times 100}{A_S \times W_U \times LC}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and the *Standard solution,* respectively; C_S is the concentration, in mg per mL, of the *Standard solution; d* is the density, in g per mL, of the Oral Suspension; W_U is the weight, in mg, of the Oral Suspension taken; 900 is the volume, in mL of the *Medium;* 100 is the conversion factor to percentage; and *LC* is the label claim, in mg per mL.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{14}H_{13}N_3O_4S_2$ is dissolved in 15 minutes.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**The total aerobic microbial count does not exceed 100 cfu per g or 100 cfu per mL. The total yeasts and molds count does not exceed 50 cfu per g or 50 cfu per mL. It meets the requirements of the test for the absence of *Escherichia coli.*

Chromatographic purity—

Buffer, Mobile phase, and *Diluent*—Proceed as directed in the *Assay.*

Related compound standard stock solution—Proceed as directed for *Related compound standard stock preparation* in the *Assay.*

Sensitivity solution—Dilute the *Related compound standard stock solution* with *Diluent* to a final concentration of about 0.08 µg per mL.

Related compound standard solution—Dilute *Related compound standard stock preparation* with *Diluent* to a final concentration of about 0.5 µg per mL.

Test solution—Proceed as directed for *Assay preparation* in the *Assay.*

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in the *Assay.* Chromatograph the *Sensitivity solution* (about 10 µL), and record the peak responses as directed for *Procedure* at 260 nm: the relative standard deviation of three replicate injections is not more than 10% for meloxicam related compound B. Chromatograph the *Related compound standard solution* (about 10 µL), and record the peak responses as directed for *Procedure* at 260 nm: the tailing factor for meloxicam related compound B is not more than 2.0.

Procedure—Separately inject equal volumes (about 10 µL) of the *Related compound standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and record the peak areas at 260 nm and 360 nm. The run time is about 20 minutes or two times the retention time of meloxicam. Calculate the percentage of meloxicam related compound B in the portion of Oral Suspension taken by the formula:

$$(5000/L)(C/V)(r_U / r_S)$$

in which L is the label claim, in mg per mL; C is the concentration, in mg per mL, of USP Meloxicam Related Compound B RS in the *Related compound standard solution; V* is the volume, in mL, of Oral Suspension taken to prepare the *Test solution;* r_U is the peak area obtained for meloxicam related compound B in the *Test solution* at 260 nm; and r_S is the peak area for meloxicam related compound B in the *Related compound standard solution* at 260 nm. Calculate the percentage of each unknown degradation product in the portion of Oral Suspension taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the area of any unknown degradant at 360 nm; r_s is the sum of areas of meloxicam and all impurities in the *Test solution* at 360 nm. Not more than 0.15% of meloxicam related compound B is found; not more than 0.2% of any individual unknown degradation product is found; and not more than 0.5% of total degradation products is found.

Assay—

Buffer—Dissolve 2 g of monohydrate citric acid and 2 g of boric acid in 1000 mL of water, and adjust with dihydrate trisodium citrate to a pH of 2.9.

Mobile phase—Mix 565 mL of *Buffer,* 260 mL of methanol, and 200 mL of acetonitrile. Degas the solution, and then dissolve 200 mg of sodium dodecyl sulfate in 1000 mL of the resulting solution.

Diluent—Dissolve 3 g of boric acid and 1.5 g of dihydrate trisodium citrate in 1000 mL of water, and adjust with 2 M sodium hydroxide to a pH of 8.3. Mix 420 mL of the resulting buffer with 420 mL of methanol and 160 mL of acetonitrile.

Standard stock preparation—Transfer about 67 mg of USP Meloxicam RS, accurately weighed, into a 100-mL volumetric flask. Add 3.0 mL of dimethylformamide. Swirl the flask, and allow to stand for about 5 minutes. Add 15 mL of methanol. Dilute with *Diluent* to just below volume. Sonicate for 30 minutes, and mix until dissolved. Cool to room temperature. Dilute with *Diluent* to volume.

Standard preparation—Dilute *Standard stock preparation* with *Diluent* to a final concentration of about 0.27 mg per mL.

Related compound standard stock preparation—Transfer about 21 mg of USP Meloxicam Related Compound B RS, accurately weighed, into a 100-mL volumetric flask. Add 3.0 mL of dimethylformamide, 15 mL of methanol, and about 60 mL of *Diluent.* Sonicate, and mix until dissolved. Cool to room temperature. Dilute with *Diluent* to volume. Dilute further with *Diluent* to a concentration of about 8.4 µg per mL.

System suitability solution—Transfer a volume of Oral Suspension, equivalent to about 15 mg of meloxicam, accurately weighed, to a 50-mL volumetric flask. Add 3.0 mL of *Related compound standard stock preparation.* Add 3.0 mL of dimethylformamide. Swirl the flask, and allow to stand for about 5 minutes. Add 15 mL of methanol. Dilute with *Diluent* to just below volume. Sonicate for 30 minutes, mixing the flask vigorously

about every 5 minutes. Cool to room temperature. Dilute with *Diluent* to volume. Mix, and allow particulates to settle. Pass through a 0.45-µm membrane filter with a fiberglass prefilter.

Assay preparation—Transfer an accurately meaured volume of Oral Suspension, equivalent to about 15 mg of meloxicam, to a 50-mL volumetric flask. Add 3.0 mL of dimethylformamide. Swirl the flask, and allow to stand for about 5 minutes. Add 15 mL of methanol. Dilute with *Diluent* to just below volume. Sonicate for 30 minutes, mixing the flask vigorously about every 5 minutes. Cool to room temperature. Dilute with *Diluent* to volume. Mix, and allow particulates to settle. Pass through a 0.45-µm membrane filter with a fiberglass prefilter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a programmable dual wavelength detector, a single wavelength detector in series, or a photodiode array detector capable of detecting wavelengths from 190 nm to 400 nm, or equivalent, and a 4-mm × 12.5-cm analytical column that contains 5-µm packing L1. The column temperature is maintained at 40°. The flow rate is about 1.0 mL per minute. The run time is about 20 minutes or two times the retention time of meloxicam. Chromatograph the *System suitability solution* (about 10 µL), and record the peak responses as directed for *Procedure* at 360 nm and 260 nm: at 360 nm the resolution, *R,* between meloxicam and any other adjacent peak is not less than 1.5. The tailing factor for the meloxicam peak is not more than 2.0. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure* at 360 nm: the relative standard deviation for replicate injections of the *Standard preparation* is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and record the peak areas at 360 nm. Calculate the amount of meloxicam ($C_{14}H_{13}N_3O_4S_2$), in mg per mL, in the portion of Oral Suspension taken by the formula:

$$50(C/V)(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Meloxicam RS in the *Standard preparation; V* is the volume, in mL, of Oral Suspension taken to prepare the *Assay preparation;* r_U is the peak area obtained for meloxicam in the *Assay preparation* at 360 nm; and r_S is the peak area for meloxicam in the *Standard solution* at 360 nm.

Meloxicam Tablets

» Meloxicam Tablets contain 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

Identification—

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

0.1 N Methanolic sodium hydroxide—Dilute 100 mL of 1 N sodium hydroxide with methanol to 1000 mL.

Test solution—Transfer a portion of finely powdered Tablets, equivalent to about 50 mg of meloxicam, to a suitable flask. Add 5 mL of *0.1 N Methanolic sodium hydroxide,* and mix. Add 20 mL of methanol, and stir for about 15 minutes. Filter the mixture to remove insoluble material, and use the filtrate.

Standard solution—Transfer about 20 mg of USP Meloxicam RS, accurately weighed, to a 10-mL volumetric flask, dissolve in 2 mL of *0.1 N Methanolic sodium hydroxide,* dilute with methanol to volume, and mix.

Developing solvent system—Prepare a mixture of chloroform, methanol, and ammonia water (25%) (80:20:1).

Procedure—Proceed as directed in the chapter.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩**—**

Medium: pH 7.5 phosphate buffer (prepared by dissolving 6.81 g of potassium dihydrogen phosphate in 800 mL of water, adjusting the pH to 7.5 with 0.5 N sodium hydroxide, and diluting with water to 1 L); 900 mL.

Apparatus 2: 75 rpm.

Time: 30 minutes.

Determine the amount of meloxicam dissolved by employing the following method.

Standard solution—

FOR TABLETS LABELED TO CONTAIN 7.5 MG—Transfer about 33.3 mg of USP Meloxicam RS, accurately weighed, to a 100-mL volumetric flask. Add 5.0 mL of methanol, 1.0 mL of 0.1 N sodium hydroxide, dilute with *Medium* to volume, and mix. Transfer 5.0 mL to a 100-mL volumetric flask, dilute with *Medium* to volume, and mix. Transfer 25.0 mL of the resulting solution to a 50-mL volumetric flask, dilute with *Medium* to volume, and mix.

FOR TABLETS LABELED TO CONTAIN 15 MG—Transfer about 33.3 mg of USP Meloxicam RS, accurately weighed, to a 100-mL volumetric flask. Add 5.0 mL of methanol, 1.0 mL of 0.1 N sodium hydroxide, dilute with *Medium* to volume, and mix. Transfer 5.0 mL to a 100-mL volumetric flask, dilute with *Medium* to volume, and mix.

Test solution—Use portions of the solution under test passed through a suitable 10-µm filter, discarding the first few mL.

Procedure—Determine the percentage of the labeled amount of meloxicam dissolved by employing UV absorption, using a suitable spectrophotometer, at the wavelength of maximum absorbance at about 362 nm, using 1-cm cuvettes, on the *Test solution* in comparison with the *Standard solution* using *Medium* as blank. Calculate the percentage of meloxicam dissolved by the formula:

$$\frac{A_U \times C_S \times 900 \times 100}{A_S \times LC}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and the *Standard solution*, respectively; C_S is the concentration, in mg per mL, of the *Standard solution;* 900 is the volume, in mL, of *Medium;* 100 is the conversion factor to percentage; and *LC* is the Tablet label claim, in mg.

Tolerances—Not less than 70% *(Q)* of the labeled amount of meloxicam is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Related compounds—

Solution A, Solution B, and *Mobile phase*—Proceed as directed in the *Assay.*

Standard solution—Use the *Standard preparation* from the *Assay.*

System sensitivity solution—Transfer 4 mL of the *Standard solution* to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 5 mL of the resulting solution to a 50-mL volumetric flask, add 5 mL of 1 N sodium hydroxide, and dilute with methanol to volume.

Test solution—Use the *Assay preparation.*

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in the *Assay,* except to chromatograph the *Standard solution* and the *System sensitivity solution:* the tailing factor for the meloxicam peak is not more than 2.0; the relative standard deviation for replicate injections of the *Standard solution* is not more than 2.0%; and the signal-to-noise ratio of the