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

meloxicam peak in the chromatogram of the *System sensitivity solution* is not less than 10.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Determine the relative retention times for the impurity peaks relative to that of the meloxicam peak. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$(5000/3)(1/F)(C/W)(A/L)(r_i / r_S)$$

in which F is the relative response factor for each impurity and is equal to 2.7 for the impurity with a relative retention time of about 0.5 (meloxicam related compound B [2-amino-5-methylthiazole]) and 1.0 for all other impurities; C is the concentration, in mg per mL, of USP Meloxicam RS in the *Standard solution; W* is the weight, in mg, of powdered Tablets taken to prepare the *Test solution; A* is the average weight of a Tablet; L is the labeled amount, in mg, of meloxicam in each Tablet; r_i is the peak response obtained for each impurity in the *Test solution;* and r_S is the peak response for meloxicam in the *Standard solution:* not more than 0.15% of meloxicam related compound B is found; not more than 0.2% of any individual unknown impurity is found; and not more than 0.5% of total impurities is found.

Assay—

Solution A—Dissolve 2.0 g of dibasic ammonium phosphate in 1 L of water, and adjust with phosphoric acid to a pH of 7.0 ± 0.1.

Solution B—Mix 650 mL of methanol and 100 mL of isopropyl alcohol.

Mobile phase—Prepare a filtered and degassed mixture of *Solution A* and *Solution B* (63:37). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock preparation—[NOTE—The *Standard stock preparation* is prepared so that the final concentration of meloxicam, in mg per mL, is approximately equivalent to the concentration of the *Assay stock preparation.*] Transfer a suitable quantity of USP Meloxicam RS, accurately weighed, to a 50-mL volumetric flask, dissolve in 1 mL of 1 N sodium hydroxide and 30 mL of methanol, and dilute with methanol to volume. Transfer 10 mL of the resulting solution to a 100-mL volumetric flask, add 10 mL of 1 N sodium hydroxide, and dilute with methanol to volume.

Standard preparation—Transfer 15 mL of the *Standard stock preparation* to a 25-mL volumetric flask, and dilute with water to volume.

Assay stock preparation—Transfer 10 Tablets to a 1000-mL volumetric flask, add about 100 mL of 1 N sodium hydroxide, shake to disperse the Tablets, and add 800 mL of methanol. Sonicate the solution for about 15 minutes, then stir for 30 minutes. Dilute with methanol to volume, and mix. Filter the resulting solution, and use the filtrate.

Assay preparation—Transfer 15 mL of the *Assay stock preparation* to a 25-mL volumetric flask, and dilute with water to volume.

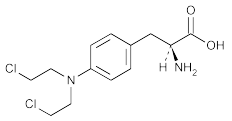
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector, a guard column that contains packing L1, and a 4-mm ×10-cm column that contains packing L1. The flow rate is about 0.8 mL per minute. The column temperature is maintained at 40°. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the meloxicam peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* to the chromatograph, record the chromatograms, and measure the responses for the meloxicam peak. Calculate the quantity, in mg, of meloxicam ($C_{14}H_{13}N_3O_4S_2$) in the portion of Tablets taken by the formula:

$$5000(C/3)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Meloxicam RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Melphalan



$C_{13}H_{18}Cl_2N_2O_2$ 305.20
L-Phenylalanine, 4-bis(2-chloroethyl)amino]-.
L-3-[*p*-[Bis(2-chloroethyl)amino]phenyl]alanine [148-82-3].

» Melphalan contains not less than 93.0 percent and not more than 100.5 percent of $C_{13}H_{18}Cl_2N_2O_2$, calculated on the dried and ionizable chlorine-free basis.

Caution—Handle Melphalan with exceptional care because it is a highly potent agent.

Packaging and storage—Preserve in tight, light-resistant, glass containers.

USP Reference standards ⟨11⟩**—**
USP Melphalan Hydrochloride RS

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 5 µg per mL.

Medium: methanol.

B: To 1 mL of 1 in 10,000 solution in alcohol in a glass-stoppered test tube add 1 mL of pH 4.0 acid phthalate buffer (see under *Solutions* in the section *Reagents, Indicators, and Solutions*), 1 mL of a 1 in 20 solution of 4-(*p*-nitrobenzyl)pyridine in acetone, and 1 mL of saline TS. Heat on a water bath at 80° for 20 minutes, and cool quickly. Add 10 mL of alcohol and 1 mL of 1 N potassium hydroxide: a violet to red-violet color is produced.

C: Heat 100 mg with 10 mL of 0.1 N sodium hydroxide on a water bath for 10 minutes: the resulting solution, after acidification with 2 N nitric acid, responds to the tests for *Chloride* ⟨191⟩.

Specific rotation ⟨781S⟩: between −30° and −36°.

Test solution: 7 mg per mL, in methanol, prepared with the aid of gentle heating.

Loss on drying ⟨731⟩: Dry it in vacuum at 105° to constant weight: it loses not more than 7.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.3%.

Ionizable chlorine—Dissolve about 500 mg of Melphalan, accurately weighed, in a mixture of 75 mL of water and 2 mL of nitric acid, allow to stand for 2 minutes, and titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically: not more than 1.0 mL of 0.1 N silver nitrate is required for each 500 mg of test specimen.

Nitrogen content ⟨461⟩**—**Determine the nitrogen content as directed under *Method II*, using about 325 mg of Melphalan, accurately weighed, and 0.1 N sulfuric acid VS for the titration: not less than 8.90% and not more than 9.45% of N is found, calculated on the dried basis.