allow the solvent to evaporate, and examine the plate under short-wavelength UV light: the chromatograms show principal spots at about the same R_F value. Estimate the intensities of any secondary spots observed in the chromatogram of the *Test solution* by comparison with the spots in the chromatograms of the *Standard solutions:* no secondary spot from the chromatogram of the *Test solution* is larger or more intense than the principal spot obtained from *Standard solution B* (0.3%), and the sum of the intensities of all secondary spots obtained from the *Test solution* is not more intense than the principal spot obtained from *Standard solution A* (1.0%).

METHOD 2—

Diluent—Use *Mobile phase.*

Phosphate buffer, Mobile phase, System suitability solution, and *Chromatographic system*—Proceed as directed in the *Assay.*

Test solution—Dissolve an accurately weighed quantity of Omeprazole in *Diluent* to obtain a solution containing about 0.16 mg per mL. [NOTE—Prepare this solution fresh.]

Procedure—Inject equal volumes (about 40 µL) of the *Test solution* and *Diluent* into the chromatograph, and allow the *Test solution* to elute for not less than two times the retention time of omeprazole. Record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Omeprazole taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity, and r_s is the sum of the responses of all of the peaks: not more than 0.3% of any individual impurity is found, and the sum of all impurities is not more than 1.0%.

Assay—

Phosphate buffer—Dissolve 0.725 g of monobasic sodium phosphate and 4.472 g of anhydrous dibasic sodium phosphate in 300 mL of water, dilute with water to 1000 mL, and mix. Dilute 250 mL of this solution with water to 1000 mL. If necessary, adjust the pH with phosphoric acid to 7.6.

Mobile phase—Prepare a filtered and degassed mixture of *Phosphate buffer* and acetonitrile (3:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of 0.01 M sodium borate and acetonitrile (3:1).

Standard preparation—Dissolve an accurately weighed quantity of USP Omeprazole RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.2 mg per mL.

Assay preparation—Transfer about 100 mg of Omeprazole, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix.

System suitability solution—Dilute a volume of *Standard preparation* with *Diluent* to obtain a solution containing about 0.1 mg of USP Omeprazole RS per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L7. The flow rate is about 0.8 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the capacity factor, k', is not less than 6.0; the column efficiency is not less than 3000 theoretical plates; the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{17}H_{19}N_3O_3S$ in the portion of Omeprazole taken by the formula:

$$500C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Omeprazole 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.

Omeprazole Delayed-Release Capsules

» Omeprazole Delayed-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$).

Packaging and storage—Preserve in tight, light-resistant containers. Store between 15° and 30°.

Labeling—When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

USP Reference standards ⟨11⟩**—**
USP Omeprazole RS

Identification— 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⟩**—**

TEST 1—

ACID RESISTANCE STAGE—

Medium: 0.1 N hydrochloric acid; 500 mL.

Apparatus 2: 100 rpm.

Time: 2 hours.

pH 7.6 Phosphate buffer, Mobile phase, and *Chromatographic system*—Proceed as directed for *Buffer stage.*

Standard solution—Transfer about 50 mg of USP Omeprazole RS, accurately weighed, to a 250-mL volumetric flask, dissolve in 50 mL of alcohol, dilute with 0.01 M sodium borate solution to volume, and mix. Transfer 10.0 mL of this solution into a 100-mL volumetric flask, add 20 mL of alcohol, dilute with 0.01 M sodium borate solution to volume, and mix.

Test solution—After 2 hours, filter the *Medium* containing the pellets through a sieve with an aperture of not more than 0.2 mm. Collect the pellets on the sieve, and rinse them with water. Using approximately 60 mL of 0.01 M sodium borate solution, carefully transfer the pellets quantitatively to a 100-mL volumetric flask. Sonicate for about 20 minutes until the pellets are broken up. Add 20 mL of alcohol to the flask, dilute with 0.01 M sodium borate solution to volume, and mix. Dilute an appropriate amount of this solution with 0.01 M sodium borate solution to obtain a solution having a concentration of about 0.02 mg per mL. At level L_1, test 6 units. Test 6 additional units at level L_2, and at level L_3, an additional 12 units are tested. Continue testing through the three levels unless the results conform at either L_1or L_2.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in the *Medium* by the formula:

$$T - CD(r_U / r_S)$$

in which T is the labeled quantity, in mg, of omeprazole in the capsule; C is the concentration, in mg per mL, of USP Omeprazole RS in the *Standard solution; D* is the dilution factor used in preparing the *Test solution;* and r_U and r_S are the omeprazole

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peak responses obtained from the *Test solution* and the *Standard solution,* respectively.

Tolerances—Level L_1: no individual value exceeds 15% of omeprazole dissolved. Level L_2: the average of 12 units is not more than 20% of omeprazole dissolved, and no individual unit is greater than 35% of omeprazole dissolved. Level L_3: the average of 24 units is not more than 20% of omeprazole dissolved, not more than 2 units are greater than 35% of omeprazole dissolved, and no individual unit is greater than 45% of omeprazole dissolved.

BUFFER STAGE—

Medium: pH 6.8 phosphate buffer, 900 mL.

Proceed as directed for *Acid resistance stage* with a new set of capsules from the same batch. After 2 hours, add 400 mL of 0.235 M dibasic sodium phosphate to the 500 mL of 0.1 N hydrochloric acid medium in the vessel. Adjust, if necessary, with 2 N hydrochloric acid or 2 N sodium hydroxide to a pH of 6.8 ± 0.05.

Apparatus 2: 100 rpm.

At the end of 30 minutes, determine the amount of $C_{17}H_{19}N_3O_3S$ dissolved in pH 6.8 phosphate buffer by employing the following method.

pH 10.4, 0.235 M Dibasic sodium phosphate—Dissolve 33.36 g of anhydrous dibasic sodium phosphate in 1000 mL of water, and adjust with 2 N sodium hydroxide to a pH of 10.4 ± 0.1.

pH 6.8 Phosphate buffer—Add 400 mL of 0.1 N hydrochloric acid to 320 mL of *pH 10.4, 0.235 M Dibasic sodium phosphate,* and adjust with 2 N hydrochloric acid or 2 N sodium hydroxide, if necessary, to a pH of 6.8 ± 0.05.

pH 7.6 Phosphate buffer—Dissolve 0.718 g of monobasic sodium phosphate and 4.49 g of dibasic sodium phosphate in 1000 mL of water. Adjust with 2 N hydrochloric acid or 2 N sodium hydroxide, if necessary, to a pH of 7.6 ± 0.1. Dilute 250 mL of this solution with water to 1000 mL.

Mobile phase—Transfer 340 mL of acetonitrile to a 1000-mL volumetric flask, dilute with *pH 7.6 Phosphate buffer* to volume, and pass through a membrane filter having a 0.5-µm or finer porosity. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution 1 (for Capsules labeled 10 mg)—Dissolve an accurately weighed quantity of USP Omeprazole RS in alcohol to obtain a solution having a known concentration of about 2 mg per mL. Dilute with *pH 6.8 Phosphate buffer* quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.01 mg per mL. Immediately add 2 mL of 0.25 M sodium hydroxide to 10 mL of this solution, and mix. [NOTE—Do not allow the solution to stand before adding the sodium hydroxide solution.]

Standard solution 2 (for Capsules labeled 20 mg and 40 mg)—Proceed as directed for *Standard solution 1,* except to obtain a solution having a known concentration of about 0.02 mg per mL before mixing with 2 mL of 0.25 M sodium hydroxide.

Test solution 1 (for Capsules containing 10 mg and 20 mg)—Immediately transfer 5.0 mL of the solution under test to a test tube containing 1.0 mL of 0.25 M sodium hydroxide. Mix well, and pass through a membrane filter having a 1.2-µm or finer porosity. Protect from light.

Test solution 2 (for Capsules labeled 40 mg)—Immediately transfer 5.0 mL of the solution under test to a test tube containing 2.0 mL of 0.25 M sodium hydroxide and 5 mL of *pH 6.8 Phosphate buffer.* Mix well, and pass through a membrane filter having a 1.2-µm or finer porosity. Protect from light.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.0-mm × 12.5-cm analytical column that contains 5-µm packing L7. The flow rate is about 1.0 mL per minute. Chromatograph the appropriate *Standard solution,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 2000 theoretical plates, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the appropriate *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved by the formula:

$$VCD(r_U / r_S)$$

in which V is the volume of *Medium* in each vessel; C is the concentration, in mg per mL, of USP Omeprazole RS in the appropriate *Standard solution; D* is the dilution factor used in preparing the appropriate *Test solution;* and r_U and r_S are the omeprazole peak responses obtained from the appropriate *Test solution* and the *Standard solution,* respectively.

Tolerances—For Capsules labeled 10 and 20 mg, not less than 75% *(Q)* of the labeled amount of $C_{17}H_{19}N_3O_3S$ is dissolved in 30 minutes. For Capsules labeled 40 mg, not less than 70% *(Q)* of the labeled amount of $C_{17}H_{19}N_3O_3S$ is dissolved in 30 minutes. The requirements are met if the quantities dissolved from the product conform to *Acceptance Table 1*.

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.*

ACID RESISTANCE STAGE—

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 2 hours.

Procedure—After 2 hours, remove each sample from the basket, and quantitatively transfer into separate volumetric flasks to obtain a solution having a final concentration of about 0.2 mg per mL. Proceed as directed for the *Assay preparation* in the *Assay,* starting with "Add about 50 mL of *Diluent*". Calculate the quantity, in mg, of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in the *Medium* by the formula:

$$T - CD(r_U / r_S)$$

in which T is the assayed quantity, in mg, of omeprazole in the capsule; C is the concentration, in mg per mL, of USP Omeprazole RS in the *Standard solution; D* is the dilution factor used in preparing the *Test solution;* and r_U and r_S are the omeprazole peak responses obtained from *Test solution* and *Standard solution,* respectively.

Tolerances—It complies with the following *Acceptance Table:*

Acceptance Table

Level	Criterion
L_1	the average of the 6 units is not more than 10% of omeprazole dissolved
L_2	the average of the 12 units is not more than 10% of omeprazole dissolved
L_3	the average of the 24 units is not more than 10% of omeprazole dissolved

BUFFER STAGE—

Medium: 0.05 M pH 6.8 phosphate buffer; 900 mL (see *Reagents, Indicators, and Solutions*).

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Proceed as directed for *Acid resistance stage* with a new set of capsules from the same batch. After 2 hours, replace the acid *Medium* with the buffer *Medium* and continue the test for 45 more minutes. Determine the amount of $C_{17}H_{19}N_3O_3S$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 305 nm on portions of the solutions under test passed through a 0.2-µm nylon filter, in comparison with a Standard solution having a known concentration of USP Omeprazole RS in the same *Medium.*

Tolerances—It complies with *Acceptance Table 1* under *Dissolution* ⟨711⟩. Not less than 75% *(Q)* of the labeled amount of $C_{17}H_{19}N_3O_3S$ is dissolved in 45 minutes.

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

Chromatographic purity—

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

Standard solution—Prepare as directed for the *Standard preparation* in the *Assay.*

Test solution—Use the *Assay preparation.*

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all of the peak responses. Calculate the percentage of each impurity in the portion of Capsules taken by the formula:

$$10(C/A)(1/F)(r_i / r_S)$$

in which *C* is the concentration, in µg per mL, of USP Omeprazole RS in the *Standard solution; A* is the quantity, in mg, of omeprazole in the portion of Capsules taken, as determined in the *Assay; F* is the relative response factor (see *Table 1* below for values); r_i is the peak response for each impurity obtained from the *Test solution;* and r_S is the peak response for omeprazole obtained from the *Standard solution.* In addition to not exceeding the limits for each impurity in *Table 1,* not more than 2.0% of total impurities is found.

Table 1

Name	Relative Retention Time	Relative Response Factor *(F)*	Limit (%)
Thioxopyrido conversion product[1]	0.33	1.6	0.5
5-methoxy-1*H*-benzimidazole-2-thiol	0.64	3.1	0.5
Any other individual impurity	—	1.0	0.5

[1]Formed in the solution from two isomers: 1,3-dimethyl-8-methoxy-12-thioxopyrido[1′,2′:3,4]imidazo[1,2-*a*]benzimidazol-2(12*H*)-one and 1,3-dimethyl-9-methoxy-12-thioxopyrido[1′,2′:3,4]imidazo[1,2-*a*]benzimidazol-2(12*H*)-one.

Assay—

Diluent—Dissolve 7.6 g of sodium borate decahydrate in about 800 mL of water. Add 1.0 g of edetate disodium, and adjust with 50% sodium hydroxide solution to a pH of 11.0 ± 0.1. Transfer the solution to a 2000-mL volumetric flask, add 400 mL of dehydrated alcohol, and dilute with water to volume.

Solution A—Prepare a filtered and degassed solution of 6.0 g of glycine in 1500 mL of water. Adjust with 50% sodium hydroxide solution to a pH of 9.0, and dilute with water to 2000 mL.

Solution B—Use a filtered and degassed mixture of acetonitrile and methanol (85:15).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve, by sonicating, an accurately weighed quantity of USP Omeprazole RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.2 mg per mL.

Assay preparation—Weigh and mix the contents of not fewer than 20 Capsules. Transfer an accurately weighed portion of the mixture, equivalent to about 20 mg of omeprazole, to a 100-mL volumetric flask, add about 50 mL of *Diluent,* and sonicate for 15 minutes. Cool, dilute with *Diluent* to volume, mix, and pass through a membrane filter having 0.45-µm or finer porosity. [NOTE—Bubbles may form just before bringing the solution to volume. Add a few drops of dehydrated alcohol to dissipate the bubbles if they persist for more than a few minutes.]

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 305-nm detector and a 4.6-mm × 15-cm column that contains 5-µm base-deactivated packing L7. The flow rate is about 1.2 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* %	*Solution B* %	Elution
0–20	88→40	12→60	linear gradient
20–21	40→88	60→12	linear gradient
21–25	88	12	isocratic

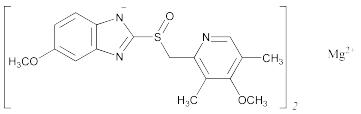
Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 20,000 theoretical plates; the tailing factor is not less than 0.8 and not more than 2; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of omeprazole ($C_{17}H_{19}N_3O_3S$) in the portion of Capsules taken by the formula:

$$DC(r_U / r_S)$$

in which *D* is the dilution factor of the *Assay preparation; C* is the concentration, in mg per mL, of USP Omeprazole 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.

Omeprazole Magnesium



$C_{34}H_{36}MgN_6O_6S_2$ 713.12

(*RS*)-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole, magnesium salt (2:1).

5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl]benzimidazole, (*RS*), magnesium salt (2:1) [95382-33-5].

» Omeprazole Magnesium contains not less than 97.5 percent and not more than 102.0 percent of $C_{34}H_{36}MgN_6O_6S_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers, protected from light. Store at room temperature.

USP Reference standards ⟨11⟩**—**

USP Omeprazole RS

USP Omeprazole Magnesium RS

USP Omeprazole Related Compound A RS

Omeprazole sulfone, 5-methoxy-2-[[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfonyl]-1*H*-benzimidazole. $C_{17}H_{19}N_3O_4S$ 361.42 [CAS-88546-55-8].

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The *Test solution,* prepared and tested as directed in the test for *Content of magnesium,* exhibits a significant absorption at the magnesium emission line at 285.2 nm.

Color of solution—Prepare a solution of Omeprazole Magnesium in methanol having a concentration of 20 mg per mL, and filter. Determine the absorbance of this solution at 440 nm, in 1-cm cells, using methanol as the blank: the absorbance is no greater than 0.1.

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