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Omeprazole Delayed-Release Capsules

DEFINITION
Omeprazole Delayed-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$).

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

ASSAY
• **Procedure**

Solution A: Dissolve 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: Acetonitrile and methanol (85:15)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	88	12
20	40	60
21	88	12
25	88	12

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.

Standard solution: 0.2 mg/mL of USP Omeprazole RS in *Diluent*, using sonication as necessary

Sample solution: Weigh and mix the contents of NLT 20 Capsules. Transfer an accurately weighed portion of the Capsule content, equivalent to 20 mg of omeprazole, to a 100-mL volumetric flask, add about 50 mL of *Diluent*, and sonicate for 15 min. Cool, dilute with *Diluent* to volume, mix, and pass through a membrane filter of 0.45-µm or finer pore size. [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⟩, System Suitability*.)

Mode: LC

Detector: UV 305 nm

Column: 4.6-mm × 15-cm; 5-µm base-deactivated packing L7

Flow rate: 1.2 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 20,000 theoretical plates

Tailing factor: 0.8–2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) in the portion of Capsules taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Omeprazole RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Acid resistance stage

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 100 rpm

Time: 2 h

Buffer C, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed for *Buffer stage*.

Standard solution: Transfer 50 mg of USP Omeprazole RS to a 250-mL volumetric flask, dissolve in 50 mL of alcohol, and dilute with 0.01 M sodium borate solution to volume. 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.

Sample solution: After 2 h, filter the *Medium* containing the pellets through a sieve with an aperture of NMT 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 min 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 containing 0.02 mg/mL. At level L_1, test 6 units. Test 6 additional units at level L_2, and at level L_3, test an additional 12 units. Continue testing through the three levels unless the results conform at either L_1 or L_2.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in *Medium*, in mg:

$$\text{Result} = T - C_S \times D \times (r_U/r_S)$$

T = labeled quantity of omeprazole in the capsule (mg)

C_S = concentration of USP Omeprazole RS in the *Standard solution* (mg/mL)

D = dilution factor used in preparing the *Sample solution*

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

Tolerances

Level L_1: No individual value exceeds 15% of the omeprazole dissolved.

Level L_2: The average of 12 units is NMT 20% of omeprazole dissolved, and no individual unit is greater than 35% of omeprazole dissolved.

Level L_3: The average of 24 units is NMT 20% of omeprazole dissolved, NMT 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 in *Acid resistance stage* with a new set of Capsules from the same batch. After 2 h, 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 min, determine the amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in the pH 6.8 phosphate buffer by using the following method.

Buffer A (0.235 M dibasic phosphate buffer, pH 10.4)**:** 33.36 g/L of anhydrous dibasic sodium phosphate, adjusted with 2 N sodium hydroxide to a pH of 10.4 ± 0.1

Buffer B (phosphate buffer, pH 6.8)**:** 0.1 N hydrochloric acid and *Buffer A* (5:4), adjusted with 2 N hydrochloric acid or 2 N sodium hydroxide, if necessary, to a pH of 6.8 ± 0.05.

Buffer C (phosphate buffer, pH 7.6)**:** 0.718 g/L of monobasic sodium phosphate and 4.49 g/L of dibasic sodium phosphate, adjusted 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 *Buffer C* to volume, and pass through a membrane filter of 0.5-µm or finer pore size.

Standard solution A (for Capsules labeled to contain 10 mg)**:** Prepare a solution containing 2 mg/mL of USP Omeprazole RS in alcohol. Dilute with *Buffer B* to obtain a solution containing 0.01 mg/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 B (for Capsules labeled to contain 20 or 40 mg)**:** Proceed as directed for *Standard solution A*, except to obtain a solution containing 0.02 mg/mL before mixing with 2 mL of 0.25 M sodium hydroxide.

Sample solution A (for Capsules containing 10 or 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 of 1.2-µm or finer pore size. Protect from light.

Sample solution B (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 *Buffer B*. Mix well, and pass through a membrane filter of 1.2-µm or finer pore size. Protect from light.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.0-mm × 12.5-cm; 5-µm packing L7

Flow rate: 1.0 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution A* or *B*, as appropriate

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times D \times 100$$

r_U = peak response from the appropriate *Sample solution*

r_S = peak response from the appropriate *Standard solution*

C_S = concentration of the appropriate *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

D = dilution factor used in preparing the appropriate *Sample solution*

Tolerances

For Capsules labeled to contain 10 and 20 mg: NLT 75% (*Q*) is dissolved.

For Capsules labeled to contain 40 mg: NLT 70% (*Q*) is dissolved.

The percentages of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved at the time specified conform to *Acceptance Table 1* in *Dissolution* ⟨711⟩.

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 h

Sample solution: After 2 h, 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/mL. Proceed as directed for the *Sample solution* in the *Assay*, starting with "Add about 50 mL of *Diluent*".

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in *Medium*, in mg:

$$\text{Result} = T - C_S \times D \times (r_U/r_S)$$

T = labeled quantity of omeprazole in the capsule (mg)

C_S = concentration of USP Omeprazole RS in the *Standard solution* (mg/mL)

D = dilution factor used in preparing the *Sample solution*

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

Tolerances: See *Table 2*.

Table 2

Level	Criteria
L_1	The average of the 6 units is NMT 10% of omeprazole dissolved.
L_2	The average of the 12 units is NMT 10% of omeprazole dissolved.
L_3	The average of the 24 units is NMT 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 min

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

Tolerances: NLT 75% (*Q*) is dissolved.

The percentage of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved at the time specified conforms to *Acceptance Table 1* in *Dissolution* ⟨711⟩.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Organic Impurities**

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

Standard solution: 1.0 µg/mL of USP Omeprazole RS in *Diluent*

Peak identification solution: 0.2 mg/mL of USP Omeprazole RS, 1.0 µg/mL of USP Omeprazole Related Compound F and G Mixture RS, and 1.0 µg/mL of 5-methoxy-1*H*-benzimidazole-2-thiol in *Diluent*. Sonicate the solution for 15 min, and then heat at 55° for 30 min. [NOTE—The heating step facilitates conversion of omeprazole related compounds F and G into a product with the relative retention time of 0.33. The remaining unconverted omeprazole related compounds F and G may elute as a very broad peak at the relative retention time of about 0.5.]

Analysis

Samples: *Standard solution*, *Peak identification solution*, and *Sample solution*

Chromatograph the *Peak identification solution*, and identify the components on the basis of their relative retention times, given in the *Table 3.*

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

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

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

r_S = peak response for omeprazole from the *Standard solution*

C_S = concentration of USP Omeprazole RS in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Omeprazole related compounds F and G[a]	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
Total impurities	—	—	2.0

[a] These impurities undergo transformation in the solution to form a conversion product, which elutes at the relative retention time of 0.33.

ADDITIONAL REQUIREMENTS

- **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

USP Omeprazole Related Compound F and G Mixture RS

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.

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

Topic/Question	Contact	Expert Committee
OMEPRAZOLE DELAYED-RELEASE CAPSULES	Documentary Standards Support	SM32020 Small Molecules 3

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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