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Esomeprazole Magnesium Delayed-Release Capsules

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DEFINITION

Esomeprazole Magnesium Delayed-Release Capsules contain an amount of Esomeprazole Magnesium equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$).

IDENTIFICATION

• A.

Buffer: Prepare a pH 6.0 phosphate buffer containing 26.6 g/L of [dibasic sodium phosphate dihydrate](#) and 55.2 g/L of [monobasic sodium phosphate monohydrate](#) in [water](#).

Diluent: Prepare a pH 11.0 diluent as follows. Dissolve 5.24 g of [tribasic sodium phosphate dodecahydrate](#) in [water](#). Add 110 mL of 0.5 M [dibasic sodium phosphate](#) solution, and dilute with [water](#) to 1000 mL.

Mobile phase: Transfer 150 mL of acetonitrile and 85 mL of the *Buffer* to a 1000-mL volumetric flask, and dilute with [water](#) to volume.

Standard stock solution: Prepare a solution containing 0.2 mg/mL of [USP Omeprazole RS](#) by dissolving a suitable amount first in [alcohol](#), using 20% of the final volume, and then diluting with *Diluent* to volume.

Standard solution: 0.02 mg/mL of [USP Omeprazole RS](#) from the *Standard stock solution* in [water](#)

Sample stock solution: Transfer a portion of the Capsule content, equivalent to 20 mg of esomeprazole, to a 200-mL volumetric flask, add 120 mL of *Diluent*, and shake for 20 min to dissolve the pellets. Sonicate for a few min, if needed, to completely dissolve. Add 40 mL of [alcohol](#), and sonicate for a few min. Cool, and dilute with *Diluent* to volume. Pass a portion of the solution through a filter of 1- μ m pore size.

Sample solution: 0.01 mg/mL of esomeprazole from the *Sample stock solution* in [water](#)

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 302 nm

Column: 4.0-mm \times 10-cm; 5- μ m packing L41

Flow rate: 1 mL/min

Injection size: 20 μ L

System suitability

Sample: *Standard solution*

[NOTE—The elution order is the *R*-enantiomer, followed by the esomeprazole peak, which is the *S*-enantiomer.]

Suitability requirements

Resolution: NLT 1.0 between the enantiomer peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the ratio of the retention times of the esomeprazole peak in the *Standard solution* and the *Sample solution*:

$$\text{Result} = (t_U/t_S)$$

t_U = retention time of esomeprazole from the *Sample solution*

t_S = retention time of esomeprazole from the *Standard solution*

Acceptance criteria: 0.98–1.02

ASSAY

• PROCEDURE

Buffer: Prepare a pH 7.3 phosphate buffer by mixing 10.5 mL of 1.0 M [monobasic sodium phosphate buffer](#) and 60 mL of 0.5 M [dibasic sodium phosphate](#) buffer, and diluting with [water](#) to 1000 mL.

Diluent: Prepare as directed in *Identification* test A.

Mobile phase: Mix 350 mL of acetonitrile and 500 mL of the *Buffer*. Dilute with [water](#) to 1000 mL.

Standard solution: Transfer 10 mg of [USP Omeprazole RS](#) to a 250-mL volumetric flask, and dissolve in about 10 mL of [alcohol](#). Add 40 mL of *Diluent*, and dilute with [water](#) to volume. This solution contains 0.04 mg/mL of [USP Omeprazole RS](#).

Sample stock solution: Mix the contents of NLT 20 Capsules. Transfer a portion of the Capsule content, equivalent to 20 mg of esomeprazole, to a 100-mL volumetric flask, add 60 mL of *Diluent*, and shake for 20 min to dissolve the pellets. Sonicate for a few min, if needed, to completely dissolve. Add 20 mL of [alcohol](#), and sonicate for a few min. Cool, and dilute with *Diluent* to volume. Pass a portion of the solution through a filter of 1-μm pore size.

Sample solution: 0.04 mg/mL of esomeprazole from the *Sample stock solution* in [water](#). Store this solution protected from light.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 302 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 1 mL/min

Injection size: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) in the portion of the 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 esomeprazole in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Medium: [0.1 N hydrochloric acid](#); 300 mL. After 2 h, continue with a pH 6.8 phosphate buffer as follows. To the vessel, add 700 mL of 0.086 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 .

Apparatus 2: 100 rpm

Time: 30 min in a pH 6.8 phosphate buffer

Standard solution: Prepare a solution containing 2 mg/mL of [USP Omeprazole RS](#) in [alcohol](#). Dilute this solution with [pH 6.8 phosphate buffer](#) to obtain a solution containing $(L/1000)$ mg/mL, where L is the label claim, in mg/Capsule. Immediately add 2.0 mL of 0.25 M [sodium hydroxide](#) to 10.0 mL of this solution, and mix. [NOTE—Do not allow the solution to stand before adding the sodium hydroxide solution.]

Sample solution: After 30 min in pH 6.8 phosphate buffer, pass a portion of the solution under test through a suitable filter. Transfer 5.0 mL of the filtrate to a suitable glassware containing 1.0 mL of 0.25 M [sodium hydroxide](#). Mix well. Protect from light.

Buffer, Mobile phase, System suitability, and Chromatographic system: Proceed as directed in the Assay.

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 1000 mL

Tolerances: NLT 75% (Q) of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

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

Acid resistance stage

Acid stage medium: [0.1 N hydrochloric acid](#); 300 mL

Apparatus 2: 100 rpm. ▲Use a suitable sinker, if necessary.▲ (RB 1-Jul-2020)

Time: 2 h

Solution A: Prepare a 0.05 M ammonium acetate buffer pH 7.6 as follows. Dissolve 3.85 g of [ammonium acetate](#) in 1000 mL of [water](#), and adjust with a diluted [ammonia](#) solution to a pH of 7.6.

Solution B: Use [acetonitrile](#).

Mobile phase: See [Table 1](#). Return to original conditions and re-equilibrate the system for 5 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
5	77	23
8	77	23
10	50	50

Diluent: Dissolve 7.6 g of [sodium borate](#) 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: 0.12 mg/mL of [USP Omeprazole RS](#) in *Diluent*, using sonication at a temperature between 10° and 15° to dissolve. Protect this solution from light.

Sample solution: After 2 h, drain the *Acid stage medium* from each vessel and carefully transfer the pellets into a suitable volumetric flask (use a 100-mL flask for 20-mg Capsules and a 200-mL flask for 40-mg Capsules). Add *Diluent* to about 70% of the final volume, and sonicate at a temperature between 10° and 15° for about 20 min with intermittent shaking. Allow to cool, dilute with *Diluent* to volume, mix, and pass through a PVDF or other suitable filter of 0.45-µm or finer pore size. Further dilute 5 mL of this solution with *Diluent* to 10 mL. Protect this solution from light.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 302 nm

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

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage, *T*, of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) retained:

$$\text{Result} = (r_u/r_s) \times C_s \times D \times (1/L) \times 100$$

r_u = peak response of esomeprazole from the *Sample solution*

r_s = peak response of omeprazole from the *Standard solution*

C_s = concentration of [USP Omeprazole RS](#) in the *Standard solution* (mg/mL)

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

L = label claim (mg/Capsule)

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

$$\text{Result} = A - T$$

A = esomeprazole content as a percentage of the labeled amount, as determined in the Assay

T = percentage of the labeled amount of esomeprazole retained, as determined above

[NOTE—If T is greater than A , then consider the result to be zero.]

Tolerances: NMT 10% of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer. Proceed as directed in *Acid resistance stage* with a new set of Capsules. After 2 h with *Acid stage medium*, continue with a pH 6.8 phosphate buffer as follows. To the vessel, add 700 mL of 0.086 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 .

Apparatus 2: 100 rpm. ▲Use a suitable sinker, if necessary.▲ (RB 1-Jul-2020)

Time: 30 min

Solution A: Prepare a 0.05 M ammonium acetate buffer pH 7.6 as follows. Dissolve 3.85 g of [ammonium acetate](#) in 1000 mL of [water](#), and adjust with a [diluted ammonia solution](#) to a pH of 7.6 ± 0.05 .

Mobile phase: [Acetonitrile](#) and *Solution A* (27:73)

Diluent: 0.086 M [dibasic sodium phosphate](#) buffer and 0.1 N hydrochloric acid (70:30). Adjust with [2 N hydrochloric acid](#) or [2 N sodium hydroxide](#), if necessary, to a pH of 6.8 ± 0.05 .

Standard stock solution: Prepare a solution containing 0.4 mg/mL of [USP Omeprazole RS](#) as follows. Dissolve first in [alcohol](#), using 10% of the final volume, and then dilute with *Diluent* to volume. Protect this solution from light.

Standard solution: Dilute the *Standard stock solution* with *Diluent* to obtain a solution containing $(L/1000)$ mg/mL, where L is the label claim, in mg/Capsule. Immediately transfer 10 mL of this solution to a test tube containing 2.0 mL of 0.25 M [sodium hydroxide](#), and mix. Protect this solution from light.

Sample solution: After 30 min, pass a portion of the solution under test through a PVDF or other suitable filter of 0.45- μ m pore size. Immediately transfer 5.0 mL of the filtrate to a test tube containing 1.0 mL of 0.25 M [sodium hydroxide](#). Mix well. Protect this solution from light.

Chromatographic system: Proceed as directed in *Acid resistance stage*, except use a flow rate of 1.0 mL/min.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Capsule)

D = dilution factor used to prepare the *Sample solution*

V = volume of *Medium*, 1000 mL

Tolerances: NLT 80% (Q) of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

[NOTE—Use only glass bowls.]

Acid resistance stage

Acid stage medium: [0.1 N hydrochloric acid](#); 300 mL

Apparatus 2: 100 rpm (*Acid stage medium*)

Time: 2 h

Buffer: Prepare a 25 mM potassium phosphate buffer pH 8.0 as follows. Dissolve 3.4 g of [monobasic potassium phosphate](#) in 1000 mL of [water](#), add 8.0 mL of [triethylamine](#), and adjust with [phosphoric acid](#) to a pH of 8.0.

Solution A: *Buffer* : methanol (90:10)

Solution B: [Acetonitrile](#) : [methanol](#) (50:50)

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	85	15
3	65	35
4	65	35
4.5	20	80
5.5	20	80
6	85	15
8	85	15

Diluent 1: 0.3 N [sodium hydroxide](#) : [methanol](#) (10:90)

Diluent 2: [0.1 N sodium hydroxide](#) : [methanol](#) (75:25)

[NOTE—Protect all standard and sample solutions from light.]

Standard stock solution: 0.4 mg/mL of [USP Omeprazole RS](#) prepared as follows. Dissolve a suitable amount of [USP Omeprazole RS](#) in a suitable volumetric flask containing 30% volume of 0.3 N [sodium hydroxide](#), sonicate as needed to dissolve, and dilute to volume with *Diluent 1*.

Standard solution: Dilute the *Standard stock solution* with *Diluent 2* to obtain a solution containing (L/500) mg/mL, where L is the label claim, in mg/Capsule.

Sample solution: After 2 h, drain the *Acid stage medium* from each vessel carefully without losing any pellet. Add 250 mL of 0.25 N [sodium hydroxide](#) to each vessel and run the dissolution apparatus at 200 rpm for 30 min or until the pellet is completely dissolved. Centrifuge a portion of this solution at 3000 rpm for 10 min. Transfer 5.0 mL of this solution to a 10-mL volumetric flask and dilute to volume with *Diluent 2*.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 305 nm

Column: 4.6-mm × 20-mm; 5-μm packing [L1](#)

[NOTE—A suitable L1 guard column may be used.]

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage, *T*, of the labeled amount of esomeprazole (C₁₇H₁₉N₃O₃S) retained:

$$\text{Result} = (r_U/r_S) \times C_S \times D \times (1/L) \times V \times 100$$

r_U = peak response of esomeprazole from the *Sample solution*

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

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

D = dilution factor used to prepare the *Sample solution*

L = label claim (mg/Capsule)

V = volume of 0.25 N [sodium hydroxide](#), 250 mL

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

$$\text{Result} = A - T$$

A = esomeprazole content as a percentage of the labeled amount, as determined in the Assay

T = percentage of the labeled amount of esomeprazole retained, as determined above

[NOTE—If T is greater than A , then consider the result to be zero.]

Tolerances: NMT 10% of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

Buffer stage

Buffer stock solution: Prepare a 76 g/L solution of sodium phosphate tribasic in [water](#).

Buffer stage medium: [0.1 N hydrochloric acid](#) : *Buffer stock solution* (3:1). Adjust with [1 N hydrochloric acid](#) or [1 N sodium hydroxide](#), if necessary, to pH 6.8.

Apparatus 2: 100 rpm

Time: 30 min

Standard solution: Dilute the *Standard stock solution* with *Buffer stage medium* to obtain a solution containing ($L/1000$) mg/mL, where L is the label claim, in mg/Capsule. Immediately transfer 5 mL of this solution to a test tube containing 1.0 mL of 0.25 N [sodium hydroxide](#), and mix.

Sample solution: Proceed as directed in *Acid resistance stage* with a new set of Capsules. After 2 h with *Acid stage medium*, continue with *Buffer stage medium* as follows. Completely drain the vessel of *Acid stage medium* carefully without losing any pellet. Add 1000 mL of preheated *Buffer stage medium* to each vessel. After 30 min, pass a portion of the solution under test through a full flow or other suitable filter of 10- μ m pore size. Immediately transfer 5 mL of the filtrate to a test tube containing 1 mL of 0.25 N [sodium hydroxide](#), and mix.

Chromatographic system: Proceed as directed in *Acid resistance stage*, except use *Injection volume* of 20 μ L.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times C_S \times D \times (1/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Omeprazole RS](#) from the *Standard solution* (mg/mL)

D = dilution factor used to prepare the *Sample solution*

L = label claim (mg/Capsule)

V = volume of *Buffer stage medium*, 1000 mL

Tolerances: NLT 75% (Q) of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

Test 4: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 4*.

Acid resistance stage

Acid stage medium: [0.1 N hydrochloric acid](#), 300 mL

Apparatus 2: 100 rpm

Time: 2 h

Buffer: 2.72 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with 50% [potassium hydroxide](#) or [20% phosphoric acid TS](#) to a pH of 8.0.

Solution A: *Buffer* and [acetonitrile](#) (85:15)

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 3](#).

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	65	35
18	45	55
19	100	0
24	100	0

Diluent: 10 mM [sodium borate](#) and 1.3 mM [edetate disodium](#) as follows. Transfer 7.6 g of [sodium borate](#) to a 2-L volumetric flask and dissolve in 800 mL of [water](#). Add 1.0 g of [edetate disodium](#), and adjust with 50% [sodium hydroxide](#) or [acetic acid](#) to a pH of 11.0 ± 0.1. Add 400 mL of [ethanol](#), and dilute to volume with [water](#).

Standard solution: 0.23 mg/mL of [USP Esomeprazole Magnesium RS](#) as follows. Transfer 23 mg of [USP Esomeprazole Magnesium RS](#) to a 100-mL volumetric flask containing approximately 80 mL of *Diluent* and sonicate with intermittent vigorous shaking until dissolved. Dilute with *Diluent* to volume.

Sample solution: After 2 h, drain the *Acid stage medium* from each vessel and carefully transfer the pellets into a suitable volumetric flask (use a 100-mL flask for 20-mg Capsules and a 200-mL flask for 40-mg Capsules). Add *Diluent* to about 80% of the final volume, stir for NLT 2 h and NMT 3 h, and dilute with *Diluent* to volume. Mix by inverting the flask and shaking multiple times. Pass a portion of the *Sample solution* through a suitable filter of 0.2-µm pore size and discard the first few milliliters.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 305 nm

Column: 4.6-mm × 15-cm; 5 µm packing [L1](#)

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 1.2 mL/min

Injection volume: 15 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage, *T*, of the labeled amount of esomeprazole (C₁₇H₁₉N₃O₃S) retained:

$$\text{Result} = (r_U/r_S) \times C_S \times (1/L) \times V \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of esomeprazole from the *Sample solution*

r_S = peak response of esomeprazole from the *Standard solution*

C_S = concentration of [USP Esomeprazole Magnesium RS](#) in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of the *Sample solution*, 100 mL (20-mg Capsules) and 200 mL (40-mg Capsules)

M_{r1} = molecular weight of esomeprazole, 690.84

M_{r2} = molecular weight of esomeprazole magnesium trihydrate, 767.17

Calculate the percentage of the labeled amount of esomeprazole (C₁₇H₁₉N₃O₃S) dissolved:

$$\text{Result} = A - T$$

A = esomeprazole content as a percentage of the labeled amount of esomeprazole, as determined in the Assay

T = percentage of the labeled amount of esomeprazole retained, as determined above

[NOTE—If *T* is greater than *A*, then consider the result to be zero.]

Tolerances: NMT 10% of the labeled amount of esomeprazole (C₁₇H₁₉N₃O₃S) is dissolved.

Buffer stage

Buffer: 23.1 g/L of [dibasic sodium phosphate](#) in [water](#)

Buffer stage medium: [0.1 N hydrochloric acid](#) and *Buffer* (30:70). Adjust with [2 N hydrochloric acid](#) or [2 N sodium hydroxide](#) to a pH of 6.8, if necessary, 1000 mL.

Apparatus 2: 100 rpm

Time: 45 min

Solution A: Combine 10.5 mL of 1.0 M [monobasic sodium phosphate](#) and 60 mL of 0.5 M [dibasic sodium phosphate](#) in a 1-L volumetric flask, and dilute to volume with [water](#). Adjust with [2 N sodium hydroxide](#) or [phosphoric acid](#) to a pH of 7.3, if necessary.

Mobile phase: *Solution A*, [acetonitrile](#), and [water](#) (50:35:15)

Diluent: 5.24 g/L of [tribasic sodium phosphate](#) in 110 mL of 0.5 M [dibasic sodium phosphate](#) and diluted with [water](#) to volume. Adjust with [2 N sodium hydroxide](#) or [phosphoric acid](#) to a pH of 11.0, if necessary.

System suitability solution: 0.04 mg/mL of [USP Omeprazole RS](#) prepared as follows. Transfer 10 mg of [USP Omeprazole RS](#) to a 250-mL volumetric flask containing 10 mL of [methanol](#), add 40 mL of *Diluent*, and dilute with [water](#) to volume.

Standard stock solution: 2 mg/mL of [USP Omeprazole RS](#) in [ethanol](#)

Standard solution: Dilute the *Standard stock solution* to obtain a solution containing (L/1000 mg/mL), where L is the label claim, in mg/Capsule, with *Buffer stage medium*. Immediately transfer 10 mL of this solution to a test tube containing 2 mL of 0.25 M [sodium hydroxide](#).

Sample solution: Prepare by placing a new set of Capsules in vessels containing 300 mL of *Acid stage medium*. After 2 h with *Acid stage medium*, add 700 mL of *Buffer* to each vessel and adjust with [2 N hydrochloric acid](#) or [2 N sodium hydroxide](#) to a pH of 6.8. After 45 min immediately withdraw a suitable amount of solution from each vessel and pass through a suitable filter 0.45-µm pore size. Pass the filtrate through a suitable filter of 0.2-µm pore size. Transfer 5 mL of the filtrate to a suitable container containing 1 mL of 0.25 M [sodium hydroxide](#).

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 302 nm

Column: 4.6-mm x 15-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of esomeprazole from the *Sample solution*

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

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

L = label claim (mg/Capsule)

V = volume of the *Buffer stage medium*, 1000 mL

Tolerances: NLT 75% (Q) of the labeled amount of esomeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved.

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Buffer: Prepare a pH 7.6 phosphate buffer by mixing 5.2 mL of 1.0 M [monobasic sodium phosphate](#) buffer and 63 mL of 0.5 M [dibasic sodium phosphate](#) buffer, and diluting with [water](#) to 1000 mL.

Solution A: Mix 100 mL of [acetonitrile](#) and 100 mL of the *Buffer*. Dilute with [water](#) to 1000 mL.

Solution B: Mix 800 mL of [acetonitrile](#) and 10 mL of the *Buffer*. Dilute with [water](#) to 1000 mL.

Mobile phase: See [Table 4](#).

Table 4

Time (min)	Solution A (%)	Solution B (%)
0	100	0

Time (min)	Solution A (%)	Solution B (%)
10	80	20
30	0	100
31	100	0
45	100	0

Diluent: Prepare as directed in *Identification* test A.

System suitability stock solution: 1 mg/mL each of [USP Omeprazole RS](#) and [USP Omeprazole Related Compound A RS](#) in [methanol](#)

System suitability solution: 1 µg/mL each of [USP Omeprazole RS](#) and [USP Omeprazole Related Compound A RS](#) from *System suitability stock solution*, in a mixture of *Diluent* and [water](#) (1:4)

Sample solution: Transfer a portion of the powdered pellets (about 80–90 mg), from the Capsule content, to a 200-mL volumetric flask, add 20 mL of methanol, and shake for 30 s. Add 40 mL of *Diluent*, shake for 30 s by hand, and sonicate for a few min. Cool, and dilute with [water](#) to volume. Pass a portion of the solution through a filter of 0.45-µm pore size. [NOTE—The solution is stable for 3 h if stored protected from light.]

Chromatographic system
(See [Chromatography \(621\), System Suitability](#).)

Mode: LC
Detector: UV 302 nm
Column: 4.6-mm × 10-cm; 3-µm packing L1
Flow rate: 1 mL/min
Injection size: 20 µL

System suitability
Sample: *System suitability solution*
[NOTE—See [Table 5](#) for the relative retention times.]
Suitability requirements

Resolution: NLT 2.5 between omeprazole related compound A and omeprazole

Analysis
Sample: *Sample solution*
Calculate the percentage of any individual impurity in the portion of the Capsules taken:

Result = $(r_U/r_T) \times 100$

r_U = peak response for each impurity
 r_T = sum of all peak responses

Acceptance criteria: See [Table 5](#).

Table 5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Omeprazole sulfone ^a	0.93	0.5
Omeprazole	1.00	—
Any other individual impurity	—	0.2
Total impurities	—	2

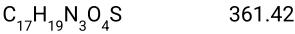
^a Omeprazole related compound A.

- ADDITIONAL REQUIREMENTS**
- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at room temperature.
 - **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 Esomeprazole Magnesium RS](#)

[USP Omeprazole RS](#)

[USP Omeprazole Related Compound A RS](#)

Omeprazole sulfone; 5-Methoxy-2-[[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfonyl]-1*H*-benzimidazole.



Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

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

Chromatographic Database Information: [Chromatographic Database](#)

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