Esomeprazole Magnesium Delayed-Release Capsules

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In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 3 Expert Committee has revised the Esomeprazole Magnesium Delayed-Release Capsules monograph. *Apparatus 2* in *Dissolution Test 2* is revised to indicate that suitable sinkers may be used if necessary.

The Esomeprazole Magnesium Delayed-Release Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Andrea F. Carney, Scientific Liaison (301-816-8155 or afc@usp.org).

Revision Bulletin
Official: July 1, 2020

Esomeprazole Magnesium Delayed-Release Capsules

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-µm 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 × 10-cm; 5-µm packing L41

Flow rate: 1 mL/min

Injection size: 20 µL

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-µm 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)

Mobile phase: See *Table 2*.

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 ($C_{17}H_{19}N_3O_3S$) 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-µm 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 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 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 ($C_{17}H_{19}N_3O_3S$) 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 ($C_{17}H_{19}N_3O_3S$) 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 ($C_{17}H_{19}N_3O_3S$) 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
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:

$$\text{Result} = (r_U/r_T) \times 100$$

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

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
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.

$C_{17}H_{19}N_3O_4S$ 361.42

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