

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-Jul-2020
 Document Type: USP Monographs
 DocId: GUID-8963B45A-9A27-460A-832E-907225CF2BC7_5_en-US
 DOI: https://doi.org/10.31003/USPNF_M30590_05_01
 DOI Ref: 2a0oy

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Esomeprazole Magnesium Delayed-Release Capsules

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<https://www.uspnf.com/rb/esomeprazole-magnesium-drc-20200626>.

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- μ m 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 $\times$ 15-cm; 5- μ m packing L7

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 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, *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)