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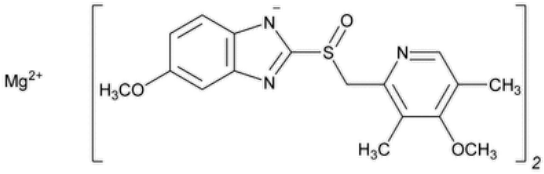
Omeprazole Magnesium



$C_{34}H_{36}MgN_6O_6S_2$ 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) CAS RN®: 95382-33-5; UNII: 426QFE7XLK.

DEFINITION

Omeprazole Magnesium contains NLT 97.5% and NMT 102.0% of omeprazole magnesium ($C_{34}H_{36}MgN_6O_6S_2$), calculated on the anhydrous basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B.** The *Sample 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.

Add the following:

▲• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Solution A: 0.181 g/L of sodium phosphate monobasic and 1.118 g/L of sodium phosphate dibasic anhydrous in water. If necessary, adjust with phosphoric acid to a pH of 7.6.

Solution B: Mix 11 mL of 0.25 M sodium phosphate tribasic with 22 mL of 0.5 M sodium phosphate dibasic, and dilute with water to 100 mL.

Mobile phase: Acetonitrile and *Solution A* (35:65)

Standard solution: 0.05 mg/mL of USP Omeprazole RS prepared as follows. Transfer 10 mg of USP Omeprazole RS to a 200-mL volumetric flask, and dissolve in 10 mL of methanol. Add 10 mL of *Solution B*, and dilute with water to volume.

Sample solution: 0.05 mg/mL of Omeprazole Magnesium prepared as follows. Transfer 10 mg of Omeprazole Magnesium to a 200-mL volumetric flask, and dissolve in 10 mL of methanol. Add 10 mL of *Solution B*, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.0-mm × 12.5-cm or 4.6-mm × 15-cm; 5-µm packing L7. [Note—Alternatively, a 3.9-mm × 15-cm column; 4-µm packing L1 may be used.]

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

▲**Tailing factor:** NMT 1.5▲ (USP 1-May-2021)

Relative standard deviation: NMT ▲1.0%▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of omeprazole magnesium ($C_{34}H_{36}MgN_6O_6S_2$) in the portion of Omeprazole Magnesium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times [M_{r1}/(2 \times M_{r2})] \times 100$$

r_U = peak response of omeprazole 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)

C_U = concentration of Omeprazole Magnesium in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of omeprazole magnesium, 713.12

M_{r2} = molecular weight of omeprazole, 345.42

Acceptance criteria: 97.5%–102.0% on the anhydrous basis

OTHER COMPONENTS

• **Content of Magnesium**

Lanthanum solution: Transfer 58.7 g of lanthanum oxide to a 1000-mL volumetric flask, wet the substance with some water, and dissolve by cautious addition of 250 mL of hydrochloric acid in 20- to 30-mL portions, cooling between the additions. Add water while stirring, cool to room temperature, and dilute with water to volume. [Note—Store the solution in a plastic bottle.]

Standard stock solution: 1000 µg/mL of magnesium in water, from a commercially prepared atomic absorption standard solution. [Note—Store the solution in a plastic bottle.]

Standard solution A: Transfer 10.0 mL of *Standard stock solution* to a 500-mL volumetric flask, add 50 mL of 1 N hydrochloric acid, and dilute with water to volume. Transfer 20.0 mL of this solution to a 200-mL volumetric flask, and dilute with water to volume. [Note—This solution contains 2 µg/mL of magnesium.]

Standard solution B: Combine 5.0 mL of *Standard solution A* and 4.0 mL of *Lanthanum solution*, and dilute with water to 100.0 mL (0.1 µg/mL).

Standard solution C: Combine 10.0 mL of *Standard solution A* and 4.0 mL of *Lanthanum solution*, and dilute with water to 100.0 mL (0.2 µg/mL).

Standard solution D: Combine 15.0 mL of *Standard solution A* and 4.0 mL of *Lanthanum solution*, and dilute with water to 100.0 mL (0.3 µg/mL).

Standard solution E: Combine 20.0 mL of *Standard solution A* and 4.0 mL of *Lanthanum solution*, and dilute with water to 100.0 mL (0.4 µg/mL).

Standard solution F: Combine 25.0 mL of *Standard solution A* and 4.0 mL of *Lanthanum solution*, and dilute with water to 100.0 mL (0.5 µg/mL). [Note—Concentrations of the *Standard solutions* and the *Sample solution* may be modified to fit the linear or working range of the instrument. When using instruments with a linear calibration graph, the number of *Standard solutions* can be reduced.]

Sample solution: Transfer 250 mg of Omeprazole Magnesium to a 100-mL volumetric flask, add 20 mL of 1 N hydrochloric acid, swirl until dissolved, and dilute with water to volume. Allow to stand for 30 min. Transfer 10.0 mL of this solution to a 200-mL volumetric flask, and dilute with water to volume. Transfer 10.0 mL of the solution to another 100-mL volumetric flask, add 4.0 mL of *Lanthanum solution*, and dilute with water to volume.

Blank: Transfer 4.0 mL of *Lanthanum solution* to a 100-mL volumetric flask, and dilute with water to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption spectrophotometry

Flame: Air–acetylene

Analytical wavelength: 285.2 nm

Analysis

Samples: *Standard solution B*, *Standard solution C*, *Standard solution D*, *Standard solution E*, *Standard solution F*, *Sample solution*, and *Blank*

Determine the concentration, C_S, in µg/mL, of magnesium in the *Sample solution* using the calibration graph.

Calculate the percentage of magnesium in the portion of Omeprazole Magnesium taken:

$$\text{Result} = (C_S/C_U) \times [100/(100 - F)] \times 100$$

C_S = concentration of magnesium in the *Sample solution* as calculated above (µg/mL)

C_U = concentration of Omeprazole Magnesium in the *Sample solution* (µg/mL)

F = content of water in Omeprazole Magnesium, as determined in *Specific Tests, Water Determination* (%)

Acceptance criteria: 3.30%–3.55% of magnesium content on the anhydrous basis

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and *Solution A* (27.5: 72.5) ▲▲ (USP 1-May-2021) [Note—To improve the resolution, the composition may be changed to 1:3, if necessary.]

System suitability solution: 0.04 mg/mL each of USP Omeprazole RS and USP Omeprazole Related Compound A RS in *Mobile phase* ▲▲ (USP 1-May-2021)

Sample solution: 0.16 mg/mL of Omeprazole Magnesium in *Mobile phase*.[Note—Prepare this solution fresh.]

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.0-mm × 12.5-cm or 4.6-mm × 15-cm; 5-µm packing L7. [Note—Alternatively, a 3.9-mm × 15-cm column; 4-µm packing L1 may be used.]

Flow rate: 0.8–1.0 mL/min

Injection volume: 50 µL

Run time: NLT 4.5 times the retention time of omeprazole

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 3 between omeprazole related compound A and omeprazole

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Omeprazole Magnesium taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Omeprazole *N*-oxide[a]	0.45	0.1
▲▲ (USP 1-May-2021) Omeprazole related compound A	0.8	0.1
Omeprazole	1.0	—
Any other individual impurity	—	0.1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Total impurities	—	0.5

[a] 4-Methoxy-2-[[(*RS*)-(5-methoxy-1*H*-benzimidazol-2-yl)sulfinyl]methyl]-3,5-dimethylpyridine 1-oxide.

SPECIFIC TESTS

- **Water Determination ⟨921⟩, *Method I*:** 7%–10%
- **Optical Rotation ⟨781S⟩, *Procedures, Specific Rotation***

  Sample solution: 10 mg/mL, in methanol

  Acceptance criteria: +0.5° to −0.5°, measured at 20°
- **Color of Solution**

  Analysis: Prepare a solution of Omeprazole Magnesium in methanol having a concentration of 20 mg/mL, and filter. Determine the absorbance of this solution at 440 nm, in 1-cm cells, using methanol as the blank.

  Acceptance criteria: The absorbance is NMT 0.1.

ADDITIONAL REQUIREMENTS

- **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

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

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

Chromatographic Database Information: Chromatographic Database

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