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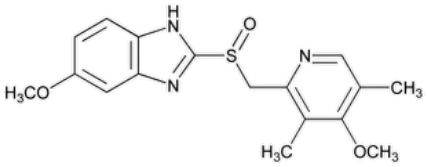
Omeprazole



$C_{17}H_{19}N_3O_3S$ 345.42

1*H*-Benzimidazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-;

5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]benzimidazole CAS RN®: 73590-58-6; UNII: KG60484QX9.

DEFINITION

Omeprazole contains NLT 98.0% and NMT 102.0% of omeprazole ($C_{17}H_{19}N_3O_3S$), calculated on the dried basis.

IDENTIFICATION

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

Change to read:

• **B.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

ASSAY

• **Procedure**

Buffer: Dissolve 0.725 g of monobasic sodium phosphate and 4.472 g of anhydrous dibasic sodium phosphate in 1000 mL of water. Dilute 250 mL of this solution with water to 1000 mL. If necessary, adjust with phosphoric acid to a pH of 7.6.

Mobile phase: Acetonitrile and *Buffer* (1:3)

Diluent: Acetonitrile and 0.01 M sodium borate (1:3)

Standard solution: 0.2 mg/mL of USP Omeprazole RS in *Diluent*

System suitability solution: 0.1 mg/mL of USP Omeprazole RS in *Diluent* from the *Standard solution*

Sample solution: 0.2 mg/mL of Omeprazole in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

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

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of omeprazole ($C_{17}H_{19}N_3O_3S$) in the portion of Omeprazole 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 = concentration of Omeprazole in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: Dissolve 0.725 g of monobasic sodium phosphate and 4.472 g of anhydrous dibasic sodium phosphate in 1000 mL of water. Dilute 250 mL of this solution with water to 1000 mL. Adjust with phosphoric acid to a pH of 7.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to the original conditions, and re-equilibrate the system for about 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
12	75	25
22	50	50
45	50	50
45.1	75	25

Diluent: *Solution A* and *Solution B* (3:1)

System suitability solution: 0.6 mg/mL of USP Omeprazole RS, 0.6 µg/mL each of USP Omeprazole Related Compound A RS, USP Omeprazole Related Compound E RS, USP Omeprazole Related Compound I RS, and 5-methoxy-1*H*-benzimidazol-2-thiol in *Diluent*. [Note—This solution is stable for 14 h when stored at 4°.]

Standard solution: 6.0 µg/mL of USP Omeprazole RS in *Diluent*.[Note—This solution is stable for 14 h when stored at 4°.]

Sample solution: 0.6 mg/mL of Omeprazole in *Diluent*. [Note—Inject within 1 h of preparation.]

Sensitivity solution: 0.3 µg/mL of USP Omeprazole RS from the *Standard solution*

Chromatographic system

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

Mode: LC

Detector: UV 264 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 0.8 mL/min

Injection volume: 40 µL

Autosampler temperature: 4°

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between omeprazole and omeprazole related compound A, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of each impurity 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 in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
5-Methoxy-1*H*-benzimidazol-2-thiol	0.41	1.0	0.15
Omeprazole *N*-oxide (omeprazole related compound E)	0.53	1.34	0.15
Omeprazole sulfone *N*-oxide (omeprazole related compound I)	0.58	1.48	0.15
Desmethoxy omeprazole[a]	0.97	1.0	0.15
Omeprazole	1.0	—	—
Omeprazole sulfone (omeprazole related compound A)	1.07	1.0	0.15
Omeprazole 4-chloro analog[b]	1.16	1.0	0.15
Ufiprazole[c]	1.25	1.0	0.15
Omeprazole thioxo pyrido analogs[d]	1.55 and 1.64	—	—
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 2-[(*RS*)-[(3,5-Dimethylpyridin-2-yl)methyl]sulfinyl]-5-methoxy-1*H*-benzimidazole.

[b] 2-[(*RS*)-[4-Chloro-3,5-dimethylpyridin-2-yl)methyl]sulfinyl]-5-methoxy-1*H*-benzimidazole.

[c] 5-Methoxy-2-((4-methoxy-3,5-dimethylpyridin-2-yl)methylthio)-1*H*-benzimidazole.

[d] Omeprazole related compounds F and G (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). These impurities are controlled in the test for *Limit of Omeprazole Related Compounds F and G*.

SPECIFIC TESTS

• **Completeness of Solution ⟨641⟩**

Sample solution: 20 mg/mL of Omeprazole in methylene chloride

Acceptance criteria: Meets the requirements

- **Limit of Omeprazole Related Compounds F and G**

Sample solution: 20 mg/mL of Omeprazole in methylene chloride

Instrumental conditions

Mode: Vis

Analytical wavelength: 440 nm

Cell: 1 cm

Blank: Methylene chloride

Acceptance criteria: The absorbance is NMT 0.10, corresponding to NMT 350 ppm of the sum of omeprazole related compounds F and G.

- **Loss on Drying ⟨731⟩**

Analysis: Dry a sample under vacuum at 60° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store in a cold place, protected from moisture.
- **USP Reference Standards ⟨11⟩**

USP Omeprazole 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

USP Omeprazole Related Compound E RS

Omeprazole *N*-oxide;
4-Methoxy-2-[[(*RS*)-(5-methoxy-1*H*-benzimidazol-2-yl)sulfinyl]methyl]-3,5-dimethylpyridine 1-oxide.
$C_{17}H_{19}N_3O_4S$ 361.42

USP Omeprazole Related Compound I RS

Omeprazole sulfone *N*-oxide;
4-Methoxy-2-[[(5-methoxy-1*H*-benzimidazol-2-yl)sulfonyl]methyl]-3,5-dimethylpyridine 1-oxide.
$C_{17}H_{19}N_3O_5S$ 377.41

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

Topic/Question	Contact	Expert Committee
OMEPRAZOLE	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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