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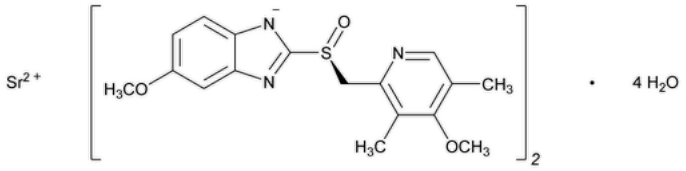
Esomeprazole Strontium



$C_{34}H_{36}N_6O_6S_2Sr \cdot 4H_2O$ Tetrahydrate: 848.50
$C_{34}H_{36}N_6O_6S_2Sr$ Anhydrous: 776.44

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

(−)-5-Methoxy-2-{(*S*)-[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfinyl}-1*H*-benzimidazole strontium salt tetrahydrate CAS RN®: 934714-36-0.

DEFINITION

Esomeprazole Strontium contains NLT 98.0% and NMT 102.0% of esomeprazole strontium ($C_{34}H_{36}N_6O_6S_2Sr$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

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

• **C.**

Sample solution: 1 mg/mL of Esomeprazole Strontium in 20% acetonitrile (v/v)

Acceptance criteria: The *Sample solution* imparts a red color to the nonluminous flame.

ASSAY

• **Procedure**

Buffer: Dissolve 1.12 g of dibasic sodium phosphate anhydrous and 0.18 g of monobasic sodium phosphate anhydrous in 1000 mL of water. If necessary, adjust with phosphoric acid to a pH of 7.6.

Solution A: Acetonitrile and *Buffer* (10:30)

Solution B: Acetonitrile and *Buffer* (20:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
25	0	100
50	0	100

Return to the original conditions, and re-equilibrate the system for about 5 min.

System suitability solution: 0.5 mg/mL of USP Omeprazole RS and 0.5 µg/mL of USP Omeprazole Related Compound A RS in *Solution A*

Standard solution: 0.5 mg/mL of USP Omeprazole RS in *Solution A*

Sample solution: 0.5 mg/mL of Esomeprazole Strontium in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 5 µL

System suitability

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

Suitability requirements

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

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of esomeprazole strontium ($C_{34}H_{36}N_6O_6S_2Sr$) in the portion of Esomeprazole Strontium 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 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 Esomeprazole Strontium in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of esomeprazole strontium, 776.44

M_{r2} = molecular weight of omeprazole, 345.42

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

OTHER COMPONENTS

• **Content of Strontium**

Solution A: 37.2 mg/mL of edetate sodium in water

Solution B: 24.9 mg/mL of cupric sulfate in water

Solution C: *Solution A* and *Solution B* (1:1)

Buffer: Transfer 54 g of ammonium chloride to a 1000-mL volumetric flask, add 350 mL of ammonium hydroxide, and dilute with water to volume.

Sample: 400 mg of Esomeprazole Strontium

Analysis: Transfer the *Sample* to a suitable flask, dissolve in 30 mL of methanol, add 40 mL of *Buffer*, and mix. Add 0.5 mL of pH 7.0 phosphate buffer and 1 mL of *Solution C*, and mix. Titrate with 0.05 M edetate disodium VS to a potentiometric endpoint (see *Titrimetry ⟨541⟩*). Perform a blank determination. Each mL of 0.05 M edetate disodium VS is equivalent to 4.381 mg of strontium.

Acceptance criteria: 10.8%–11.8% on the dried basis

IMPURITIES

• **Organic Impurities**

Buffer, Solution A, Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 500 µg/mL of USP Omeprazole RS and 0.5 µg/mL of USP Omeprazole Related Compound A RS in *Solution A*

Standard solution: 0.5 µg/mL each of USP Omeprazole RS and USP Omeprazole Related Compound A RS, and 0.25 µg/mL of (*S*)-binol in *Solution A*

Sample solution: 500 µg/mL of Esomeprazole Strontium in *Solution A*

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

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

Relative standard deviation: NMT 10% for each peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of omeprazole related compound A and (*S*)-binol in the portion of Esomeprazole Strontium taken:

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

r_U = peak response of omeprazole related compound A or (*S*)-binol from the *Sample solution*

r_S = peak response of omeprazole related compound A or (*S*)-binol from the *Standard solution*

C_S = concentration of USP Omeprazole Related Compound A RS or (*S*)-binol in the *Standard solution* (µg/mL)

C_U = concentration of Esomeprazole Strontium in the *Sample solution* (µg/mL)

Calculate the percentage of each unspecified impurity in the portion of Esomeprazole Strontium taken:

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

r_U = peak response of each unspecified impurity from the *Sample solution*

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

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Omeprazole sulfone (omeprazole related compound A)	0.7	0.1
Esomeprazole	1.0	—
(*S*)-Binol[a]	3.9	0.05
Any individual unspecified impurity	—	0.10
Total impurities	—	0.3

[a] 1-(2-Hydroxynaphthalen-1-yl)naphthalene-2-ol.

- **Enantiomeric Purity**

Solution A: Dissolve 1.42 g of dibasic sodium phosphate anhydrous in 900 mL of water. Adjust with phosphoric acid to a pH of 6.5 and dilute with water to 1000 mL.

Solution B: Acetonitrile

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20	90	10
25	70	30
30	70	30

Return to the original conditions, and re-equilibrate the system for about 5 min.

Buffer: Prepare as directed in the *Assay*.

Diluent: Acetonitrile and *Buffer* (10:30)

System suitability solution: 0.005 mg/mL of USP Omeprazole RS in *Diluent*

Sample solution: 0.5 mg/mL of Esomeprazole Strontium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.0-mm × 15-cm; 5-µm packing L41

Column temperature: 30°

Flow rate: 0.8 mL/min

Injection volume: 5 µL

Run time: 4 times the retention time of esomeprazole

System suitability

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

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 5 between the esomeprazole and *R*-enantiomer peaks

Relative standard deviation: NMT 10% for each peak

Analysis

Sample: *Sample solution*

Calculate the percentage of the *R*-enantiomer in the portion of Esomeprazole Strontium taken:

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

r_U = peak response of the *R*-enantiomer from the *Sample solution*

r_T = sum of the peak responses of esomeprazole and *R*-enantiomer from the *Sample solution*

Acceptance criteria: NMT 0.1% of the *R*-enantiomer

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry at 125° to constant weight.

Acceptance criteria: 7.5%–9.5%

- **Color of Solution**

Sample solution: 20 mg/mL of Esomeprazole Strontium in acetone

Analysis: Determine the absorbance of the *Sample solution* at 440 and 650 nm, in 1-cm cells, using acetone as the blank.

Acceptance criteria: NMT 0.2 at 440 and 650 nm

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers protected from light.
- **USP Reference Standards ⟨11⟩**

USP Esomeprazole Strontium RS

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

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

Topic/Question	Contact	Expert Committee
ESOMEPRAZOLE STRONTIUM	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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