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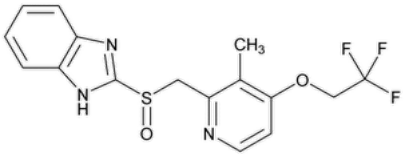
Lansoprazole



$C_{16}H_{14}F_3N_3O_2S$ 369.36

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

2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]-methyl]sulfinyl]benzimidazole CAS RN®: 103577-45-3; UNII: 0K5C5T2QPG.

DEFINITION

Lansoprazole contains NLT 98.0% and NMT 102.0% of $C_{16}H_{14}F_3N_3O_2S$.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Sample solution: 10 µg/mL in methanol

Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

Mobile phase: Acetonitrile, water, and triethylamine (40:60:1). Adjust with phosphoric acid to a pH of 7.0.

Diluent: Acetonitrile, water, and triethylamine (40:60:1). Adjust with phosphoric acid to a pH of 10.0.

System suitability solution: 0.1 mg/mL of USP Lansoprazole RS and 0.1 mg/mL of USP Lansoprazole Related Compound A RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Lansoprazole RS in *Diluent*

Sample solution: 0.1 mg/mL of Lansoprazole in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 5 between lansoprazole and lansoprazole related compound A, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) in the portion of Lansoprazole 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 Lansoprazole RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

Inorganic Impurities

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

Organic Impurities

- **Procedure**

[Note—Store and inject the lansoprazole solutions at or below 5° using a cooled autosampler. The solutions are stable for about 24 h when stored at 5°.]

Solution A: Water

Solution B: Acetonitrile, water, and triethylamine (160:40:1). Adjust with phosphoric acid to a pH of 7.0.

Diluent: Methanol and 0.1 N sodium hydroxide (1:3)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
40	20	80
50	20	80
51	90	10
60	90	10

System suitability solution: Prepare a solution containing 25 µg/mL of USP Lansoprazole RS and 25 µg/mL of USP Lansoprazole Related Compound A RS in methanol. Transfer 1 mL of this solution into a 10-mL volumetric flask, and dilute with *Diluent* to volume.

Standard solution: Prepare a solution containing 25 µg/mL of USP Lansoprazole RS and 25 µg/mL of USP Lansoprazole Related Compound B RS in methanol. Transfer 1 mL of this solution into a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Sample solution: 2.5 mg/mL of Lansoprazole in methanol. Transfer 1 mL of this solution into a 10-mL volumetric flask, and dilute with *Diluent* to volume.

Blank: Methanol and *Diluent* (1:9)

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 0.8 mL/min

Injection size: 40 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 6 between lansoprazole and lansoprazole related compound A

Relative standard deviation: NMT 3%

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Identify the lansoprazole peak and the peaks due to the impurities listed in *Table 2*. Measure the areas for the major peaks, excluding peaks obtained from the *Blank*.

Calculate the percentage of lansoprazole related compound B in the portion of Lansoprazole taken:

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

r_U = peak response for lansoprazole related compound B from the *Sample solution*

r_S = peak response for lansoprazole related compound B from the *Standard solution*

C_S = concentration of USP Lansoprazole Related Compound B RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of lansoprazole *N*-oxide, lansoprazole sulfone, and any other individual impurity in the portion of Lansoprazole taken:

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

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response for lansoprazole from the *Standard solution*

C_S = concentration of USP Lansoprazole RS in the *Standard solution* (µg/mL)

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

F = relative response factor for each impurity (see *Table 2*)

Acceptance criteria

Individual impurities: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lansoprazole *N*-oxide[a]	0.8	1.3	0.1
Lansoprazole	1.0	—	—
Lansoprazole related compound A (lansoprazole sulfone)[b]	1.1	0.82	0.4
Lansoprazole related compound B (lansoprazole sulfide)[c]	1.2	—	0.1
Other individual impurity	—	1.00	0.1
Total impurities	—	—	0.6

[a] [[(1*H*-Benzimidazole-2-yl)sulfinyl]methyl]-3-methyl-4-(2,2,2-trifluoroethoxy)-pyridine 1-oxide.

[b] 2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfonyl]benzimidazole.

[c] 2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-pyridin-2-yl]methyl]sulfanyl]-1*H*-benzimidazole.

SPECIFIC TESTS

• **Water Determination, *Method Ia*⟨921⟩**

Sample: 1.0 g

[Note—Use 50 mL of a dehydrated mixture of pyridine and ethylene glycol (9:1 to 8:2) as the solvent.]

Acceptance criteria: NMT 0.1%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature, and protect from excessive heat.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Lansoprazole RS

USP Lansoprazole Related Compound A RS

2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfonyl]benzimidazole.

$C_{16}H_{14}F_3N_3O_3S$ 385.36

USP Lansoprazole Related Compound B RS

▲2-{[(3-Methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methyl]thio}benzimidazole monohydrate.

$C_{16}H_{14}F_3N_3OS \cdot H_2O$ 371.38▲ (ERR 1-Jul-2021)

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

Chromatographic Database Information: Chromatographic Database

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