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Lansoprazole Delayed-Release Capsules

DEFINITION

Lansoprazole Delayed-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$).

IDENTIFICATION

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

[Note—The UV spectra of the major peaks of the *Sample solution* and the *Standard solution* as obtained in the *Assay* may also be used to meet the *Acceptance criteria*.]

Standard solution: 10 µg/mL of USP Lansoprazole RS in methanol

Sample solution: Nominally equivalent to 10 µg/mL of lansoprazole prepared as follows. Powder a portion of Capsule contents equivalent to 5 mg of lansoprazole. Add 5 mL of methanol, shake well, and centrifuge. To 0.1 mL of the supernatant, add 10 mL of methanol.

Acceptance criteria: The UV absorption spectra exhibit a maximum between 281 and 286 nm.

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

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 each of USP Lansoprazole RS and USP Lansoprazole Related Compound A RS in *Diluent*

Standard stock solution: 3.0 mg/mL of USP Lansoprazole RS in a mixture of acetonitrile and 0.1 M sodium hydroxide (2:3)

Standard solution: 0.09 mg/mL of USP Lansoprazole RS in *Diluent*, from *Standard stock solution*

Sample stock solution: Transfer the contents of NLT 10 Capsules, equivalent to 300 mg of lansoprazole, to a 100-mL volumetric flask. Add 60.0 mL of 0.1 M sodium hydroxide and sonicate until completely disintegrated. Add 20.0 mL of acetonitrile and sonicate for about 20 min, dilute with acetonitrile to volume, allow to settle, and use a clear supernatant.

Sample solution: Nominally 0.09 mg/mL of lansoprazole prepared as follows. Transfer 3.0 mL of the *Sample stock solution* to a 100-mL volumetric flask and dilute with *Diluent* to volume. Pass the solution through a PVDF filter having a 0.5-µm pore size or another suitable filter, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Flow rate: 1 mL/min

Injection volume: 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*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) in the portion of Capsules taken:

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

r_U = peak response of lansoprazole from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩, *Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method A Procedure*

Test 1

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 75 rpm

Time: 60 min

Acid stage standard solution: (L × 0.08/500) mg/mL of USP Lansoprazole RS in *Acid stage medium*, where L is the label claim, in mg/Capsule

[Note—An amount of methanol NMT 0.5% of the total volume of the *Acid stage standard solution* may be used to dissolve USP Lansoprazole RS prior to dilution with *Acid stage medium*.]

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 306 nm

Blank: *Acid stage medium*

Analysis: Withdraw a 25-mL aliquot, leaving the remaining 475 mL in the vessel for use in the *Buffer stage*, and proceed immediately as directed for *Buffer stage sample solution*. Use a filtered portion of the aliquot as an *Acid stage sample solution*.

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) dissolved during the *Acid stage*:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Acid stage sample solution*

A_S = absorbance of the *Acid stage standard solution*

C_S = concentration of USP Lansoprazole RS in the *Acid stage standard solution* (mg/mL)

L = label claim of lansoprazole (mg/Capsule)

V = volume of *Acid stage medium*, 500 mL

Tolerances: NMT 10% of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 buffer; 900 mL. Proceed as directed in *Buffer stage sample solution*.

Apparatus 2: 75 rpm

Time: 60 min

Buffer concentrate: Dissolve 65.4 g of monobasic sodium phosphate, 28.2 g of sodium hydroxide, and 12 g of sodium dodecyl sulfate in 4 L of water.

Blank solution: *Acid stage medium* and *Buffer concentrate* (19:17). Adjust, if necessary, with either phosphoric acid or sodium hydroxide solution to a pH of 6.8.

Buffer stage standard solution: (L × 0.7/900) mg/mL of USP Lansoprazole RS in the *Blank solution*, where L is the label claim in mg/Capsule

[Note—An amount of methanol NMT 2% of the total volume of the *Buffer stage standard solution* may be used to dissolve USP Lansoprazole RS prior to dilution with *Blank solution*.]

Buffer stage sample solution: Add 425 mL of *Buffer concentrate* to the remaining 475 mL of solution in each vessel from the *Acid stage*. Adjust, if necessary, with either phosphoric acid or sodium hydroxide solution to a pH of 6.8, and pass through a suitable filter.

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: About 286 and 650 nm

Blank: *Blank solution*

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Determine the percentage of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) dissolved using the difference between the absorbances at the wavelengths of about 286 nm and 650 nm.

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = difference between absorbances of the *Buffer stage sample solution*

A_S = difference between absorbances of the *Buffer stage standard solution*

C_S = concentration of USP Lansoprazole RS in the *Buffer stage standard solution* (mg/mL)

L = label claim of lansoprazole (mg/Capsule)

V = volume of *Buffer stage medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Acid stage: Proceed as directed in *Dissolution Test 1*.

Tolerances: NMT 10% of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) is dissolved.

Buffer stage: Proceed as directed in *Dissolution Test 1*, except for the *Time*.

Time: 45 min

Tolerances: NLT 80% (Q) of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

Standard solution: 12 µg/mL of USP Lansoprazole RS in a mixture of acetonitrile and 0.1 M sodium hydroxide (7:3)

Sample solution: Transfer the contents of 1 Capsule to a 100-mL volumetric flask, add 30 mL of 0.1 M sodium hydroxide, and sonicate to disintegrate. Add 65 mL of acetonitrile, cool, and dilute with acetonitrile to volume. Centrifuge a portion of the suspension and pass through a membrane filter having a 0.5-µm or finer pore size. Further dilute a portion of the filtrate with a mixture of acetonitrile and 0.1 M sodium hydroxide (7:3) to obtain a solution having a nominal concentration of about 12 µg/mL of lansoprazole.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 294 nm

Cell: 1 cm

Blank: Acetonitrile and 0.1 M sodium hydroxide (7:3)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lansoprazole ($C_{16}H_{14}F_3N_3O_2S$) in the Capsule taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

[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). Adjust with phosphoric acid to a pH of 10.0.

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

Table 1

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

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

Standard solution: 2 µg/mL of USP Lansoprazole RS in *Diluent*. Use sonication to dissolve.

Sensitivity solution: 0.25 µg/mL of USP Lansoprazole RS in *Diluent*, from the *Standard solution*

Sample solution: Nominally 250 µg/mL of lansoprazole prepared as follows. Transfer a portion of Capsules contents, equivalent to about 25 mg of lansoprazole, to a 100-mL volumetric flask. Add 70 mL of *Diluent* and sonicate with occasional shaking for about 30 min, maintaining the temperature below 10°. Dilute with *Diluent* to volume, and pass the solution through a PVDF filter having a 0.45-µm pore size or another suitable filter, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

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

Autosampler temperature: 5°

Flow rate: 0.8 mL/min

Injection volume: 40 µL

System suitability

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

Suitability requirements

Resolution: NLT 6 between lansoprazole and lansoprazole related compound A, *System suitability solution*

Relative standard deviation: NMT 10.0%, *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 Capsules 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 lansoprazole from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lansoprazole *N*-oxide[a]	0.8	1.3	0.2
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	1.0	0.2
Other individual impurity	—	1.00	0.2
Total impurities	—	—	1.5

[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.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **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

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

Topic/Question	Contact	Expert Committee
LANSOPRAZOLE DELAYED-RELEASE CAPSULES	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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