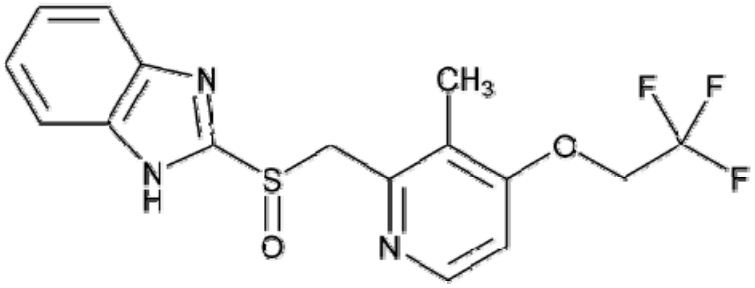
Lansoprazole

USP Method Lansoprazole RS



Original Manufacturer: Novartis (patent expired November 2009)

Brand Name: Prevacid, Helicid, Zoton, Inhibitol, Monolitum, Agopton, Digest, Duogast, Gastrolan, Lanciprol, Lansazol, Lansobene, Lansoloc, Lansoprazol, Lansoptol, Lansor, Lansox, Lanston LFDT, Lenzo, Lanzol, Lanzotec, Lanzul, Lanton, Lanzo, Lanzor, Lanzostad, Laprazol, Limpidex, Ogast, OgastORO, Ogastro, Prosogan, Prosogan FD, pro-ulco, Refluxon, SOLOX, Takepron, Zolt,

Lansoprazole is a proton-pump inhibitor (PPI) in the same pharmacologic class as omeprazole, and prevents the stomach from producing gastric acid.

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Lansoprazole
USP34 – NF29 S1

USP Columns:
YMC-Pack AQ-302 C18 Chromatographic purity 4.6-mm x 15-cm, 5 µm.

Equivalent Column:
Purospher®STAR RP-18 endcapped (5 µm) 150x4.6 mm (1.51455.0001)

Recommended Solvents and Reagents:

Acetonitrile gradient grade for liquid chromatography LiChrosolv® (1.00030)

Methanol for liquid chromatography LiChrosolv® (1.06018)

Water Water for chromatography LiChrosolv® (1.15333)
or freshly purified water from Milli-Q water purification system

Triethylamine: Use a suitable grade with a content of not less than 99.5%. (8.45061)
Phosphoric Acid: Use ACS reagent grade
Sodium Hydroxide :Use ACS reagent grade

USP Standards

Lansoprazole (150 mg)	USP Product Number:1356916
Lansoprazole Related Compound A (25 mg)	USP Product Number:1356927
Lansoprazole Related Compound B (25 mg)	USP Product Number:1356931

USP Method Lansoprazole

Chromatographic purity

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

Solution A: water.

Solution B: Prepare a filtered and degassed mixture of acetonitrile, water, and triethylamine (160:40:1). Adjust with phosphoric acid to a pH of 7.0.

Diluent:

Prepare a mixture of 0.1 N sodium hydroxide solution and methanol (75:25).

Blank solution

Prepare a mixture of Diluent and methanol (9:1).

Mobile phase

Use variable mixtures of Solution A and Solution B as directed for Chromatographic system. Make adjustments if necessary (*see System Suitability under Chromatography 621*).

Resolution solution

Dissolve 5 mg each of USP Lansoprazole RS and USP Lansoprazole Related Compound A RS in 200 mL of methanol. Pipet 1 mL of this solution into a 10-mL volumetric flask, dilute with Diluent to volume, and mix.

System suitability solution

Dissolve a suitable quantity of USP Lansoprazole Related Compound A RS in methanol, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.025 mg per mL. Pipet 1 mL of this solution into a 10-mL volumetric flask, dilute with Diluent to volume, and mix.

Standard solution

Dissolve an accurately weighed quantity of USP Lansoprazole RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having a known concentration of about 25 µg per mL. Pipet 1 mL of this solution into a 10-mL volumetric flask, dilute with Diluent to volume, and mix. The final concentration of the Standard solution is about 2.5 µg per mL.

Test solution

Transfer about 125 mg of Lansoprazole, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix. Pipet 1 mL of this solution into a 10-mL volumetric flask, and dilute with Diluent to volume.

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Chromatographic system (*see Chromatography 621*)

The liquid chromatograph is equipped with a 285-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 0.8 mL per minute. Elution profile as follows.

Time (min)	Solution A (%)	Solution B (%)	Elution
0-40	90→20	10→80	Linear gradient
40-50	20	80	Isocratic
50-51	20→90	80→10	Linear gradient
51-60	90	10	Isocratic

Chromatograph the Resolution solution, and record the peak responses as directed for Procedure: the *resolution, R, between lansoprazole and lansoprazole related compound A is not less than 6.*

Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 3%.

Name	Rel. Response Factor (F)	Approx. Rel. Retention Time	Limit (%)
Lansoprazole RS A	0.82	1.1	0.4
Lansoprazole N-oxide2	1.3	0.8	0.1
Lansoprazole RS B	0.79	1.2	0.1
Other individual impurity	1.00	-	0.1
Lansoprazole RS A = Lansoprazole sulfone = (2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfonyl]benzimidazole)			
Lansoprazole N-oxide = [[(1H-benzimidazole-2-yl)sulfinyl]methyl]-3-methyl-4-(2,2,2-trifluoroethoxy)-pyridine 1-oxide			
Lansoprazole RS B=2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-pyridin-2-yl]methyl]sulfanyl]-1H-benzimidazole			

Procedure

Separately inject equal volumes (about 40 µL) of the Blank solution, the Standard solution and the Test solution into the chromatograph, record the chromatograms, and identify the lansoprazole peak and the peaks due to the impurities listed in Table 1. Measure the areas for the major peaks, excluding the peaks obtained from the Blank solution. Calculate the percentage of each impurity in the portion of Lansoprazole taken by the formula: $100 \times 0.001(1/F)(C_S/C_T)(r_i/r_S)$

in which F is the relative response factor for each impurity peak (see Table 1 for values); 0.001 is the conversion factor from µg per mL to mg per mL; C_S is the concentration, in µg per mL, of USP Lansoprazole RS in the Standard solution; C_T is the concentration, in mg per mL, of Lansoprazole in the Test solution; r_i is the peak response for each impurity obtained from the Test solution; and r_S is the peak response for lansoprazole obtained from the Standard solution: In addition to not exceeding the limits for impurities in Table 1, not more than 0.6% of total impurities is found. Disregard any peak below 0.05%.

USP Method Lansoprazole Assay

Diluent

Prepare a mixture of water, acetonitrile, and triethylamine (60:40:1), and adjust with phosphoric acid to a pH of 10.0.

Mobile phase

Prepare a filtered and degassed mixture of water, acetonitrile, and triethylamine (60:40:1). Adjust with phosphoric acid to a pH of 7.0. Make adjustments if necessary (*see SST under Chromatography 621*).

Resolution solution

Dissolve suitable quantities of USP Lansoprazole RS and USP Lansoprazole Related Compound A RS in Diluent to obtain a solution containing about 0.1 mg of each per mL.

Internal standard solution

Dissolve an accurately weighed quantity of 4¢-ethoxyacetophenone in Diluent to obtain a solution having a known concentration of about 2.5 mg per mL.

Standard preparation

Dissolve an accurately weighed quantity of USP Lansoprazole RS in Internal standard solution to obtain a solution having a known concentration of about 5.0 mg per mL. Transfer 1.0 mL of this solution to a 50-mL volumetric flask, dilute with Diluent to volume, and mix.

Assay preparation

Transfer about 50 mg of Lansoprazole, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with Internal standard solution to volume, and mix. Transfer 1.0 mL of this solution to a 50-mL volumetric flask, dilute with Diluent to volume, and mix.

Chromatographic system *(see Chromatography 621)*

The liquid chromatograph is equipped with a 285-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the Resolution solution, and record the peak responses as directed for Procedure: the resolution, R, between lansoprazole and lansoprazole related compound A is not less than 5. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 1.0%.

Procedure

Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of $C_{16}H_{14}F_3N_3O_2S$ in the portion of Lansoprazole taken by the formula:

$$100(C_S/C_U)(R_U/R_S)$$

in which C_S and C_U are the concentrations, in mg per mL, of lansoprazole in the Standard preparation and the Assay preparation, respectively; and R_U and R_S are the peak response ratios obtained from the Assay preparation and the Standard preparation, respectively.

USP Method for Lansoprazole Assay

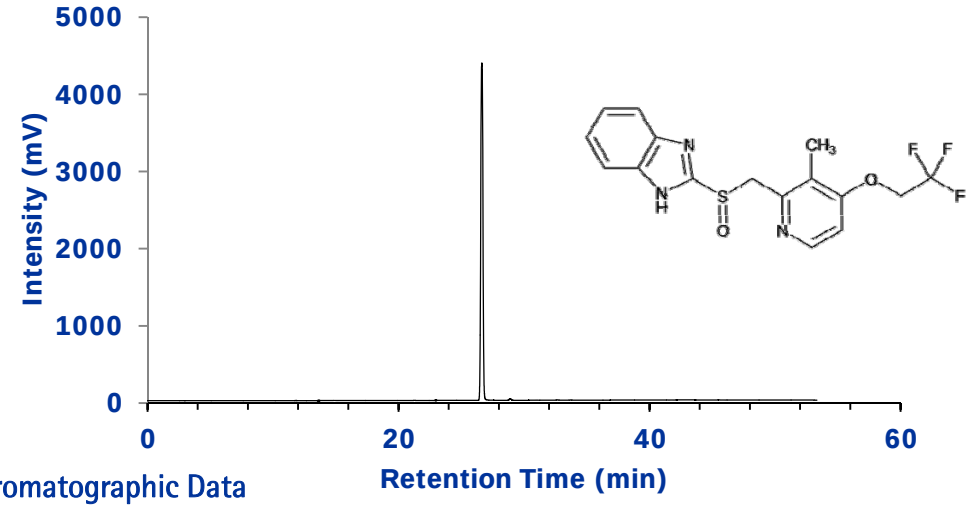
Purospher®STAR RP-18 endcapped

Chromatographic Conditions

Column:	Purospher®STAR RP-18 endcapped (5 µm) 150x4.6 mm	1.51455.0001
Injection:	40 µL	
Detection:	Shimadzu Prominence 2010, UV 285 nm	
Cell:	8 µL	
Flow Rate:	0.8 mL/min	
Mobile Phase (v/v):	Solution A: 100% Water Solution B: Acetonitrile, water, and triethylamine (160:40:1)with a pH of 7.0	
Gradient	See Table	

Time (min)	Solution A (%)	Solution B (%)	Elution
0-40	90→20	10→80	Linear gradient
40-50	20	80	Isocratic
50-51	20→90	80→10	Linear gradient
51-60	90	10	Isocratic

Temperature:	Ambient
Diluent	mixture of 0.1 N sodium hydroxide solution and methanol (75:25). e
Sample:	250 ppm of Lansoprazole



Chromatographic Data

No.	Compound	Time (min)	Tailing Factor (TUSP)	Relative Retention Time (RRT)	Resolution
1	Lansoprazole N-oxide	21.3	1.0	0.8	
2	Lansoprazole	26.6	1.0	1.0	
3	Lansoprazole RS A	28.9	1.1	1.1	8.0
4	Lansoprazole RS B	32.7	1.1	1.2	

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