# Lisinopril Assay and Related Substances Method per IP Monograph

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## Overview

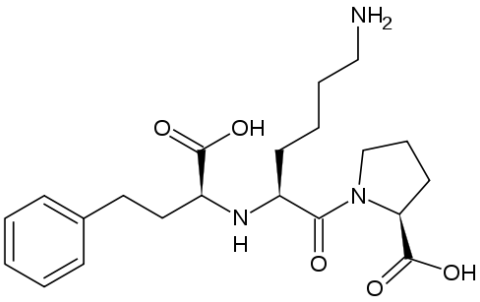
Lisinopril is an orally active angiotensin-converting enzyme (ACE) inhibitor used for the treatment of hypertension, heart failure, and acute myocardial infarction. The development of a quick and efficient analysis of Lisinopril and its related substances is of interest for generic drug manufacturers. In this application note, we report the separation of Lisinopril and its related substances using a Luna™ 5 µm C8(2) column and a Kinetex™ 5 µm C8 column according to the Indian Pharmacopoeia (IP) Monograph for Lisinopril.

System suitability per IP Monograph for the Lisinopril Assay is theoretical plates not less than (NLT) 180, a tailing factor not more than (NMT) 2.0, and a percent relative standard deviation (%RSD) of NMT 2.0 % for Lisinopril. System suitability per IP Monograph for Lisinopril Related Substances is a tailing factor NMT 3.0 for Lisinopril.

The results above clearly show that the system suitability criteria (tailing factor, area %RSD, and theoretical plates) for both assay and related substances per the IP monograph for Lisinopril were met with both the Luna 5 µm C8(2) and Kinetex 5 µm C8 columns. While the data demonstrates that the use of either column would be acceptable, the core-shell Kinetex C8 column provided shorter run times, while the Luna C8(2) column provided slightly better peak shape.

All solutions were prepared as indicated in the IP Monograph for Lisinopril. Lisinopril RS (Catalog No. 1368609) was purchased from USP.

**Figure 1.** Lisinopril




## LC-UV Conditions - Assay

**Column:** Luna 5 µm C8(2) (00G-4249-E0)
Kinetex 5 µm C8 (00G-4608-E0)
**Dimensions:** 250 x 4.6 mm
**Mobile Phase:** Acetonitrile / Buffer (4:96, v/v)

Buffer: 2.76 g of Monobasic Sodium Phosphate was dissolved in 900 mL of water in a 1000 mL volumetric flask. Adjusted pH to 5.0 with 1N Sodium Hydroxide and diluted with water to volume.

**Flow Rate:** 1 mL/min (Isocratic)
**Injection Volume:** 20 µL
**Temperature:** 50 °C
**Detector:** UV @ 210 nm
**System:** Waters® ACQUITY Arc® HPLC

## LC-UV Conditions - Organic Impurities

**Column:** Luna 5 µm C8(2) (00G-4249-E0)
Kinetex 5 µm C8 (00G-4608-E0)
**Dimensions:** 250 x 4.6 mm
**Mobile Phase:** A: Acetonitrile / Buffer (30:970, v/v)
B: Acetonitrile / Buffer (200:800, v/v)

Buffer: 0.02 M Sodium Dihydrogen Phosphate, adjusted to pH 5.0 with 5 % w/v solution of Sodium Hydroxide and filtered.

**Gradient:**

| Time (min) | %B |
|---|---|
| 0.00 | 0 |
| 35.0 | 30 |
| 45.0 | 30 |
| 55.0 | 100 |
| 65.0 | 0 |
| 75.0 | 0 |

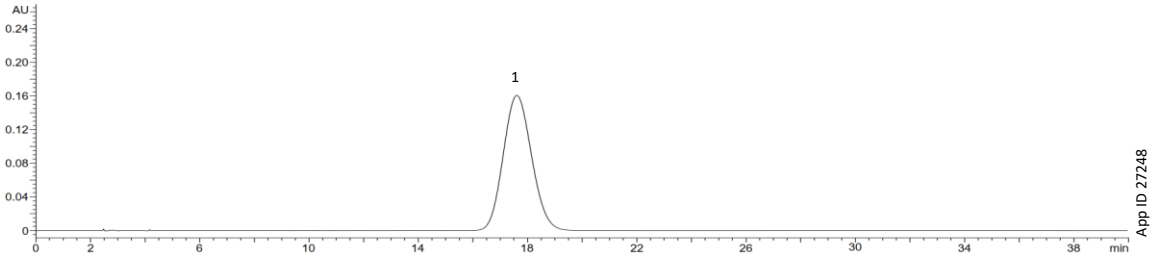
**Flow Rate:** 1.8 mL/min
**Injection Volume:** 20 µL
**Temperature:** 50 °C
**Detector:** UV @ 210 nm
**System:** Waters ACQUITY Arc HPLC

**Table 1.** Preparation of Solutions

| Solution | Composition |
|---|---|
| Reference Solution – Assay | 30 mg of Lisinopril RS was transferred into a 100 mL volumetric flask. 70 mL of water was added and sonicated to dissolve. Made up to volume with water. (0.3 mg/mL) |
| Reference Solution (a) – Related Substances | 0.2 % solution of Lisinopril RS in Mobile Phase A |
| Reference Solution (b) – Related Substances | Dilute 1 mL of Reference Solution (a) – Related Substances to 100 mL with Mobile Phase A (0.02 mg/mL) |

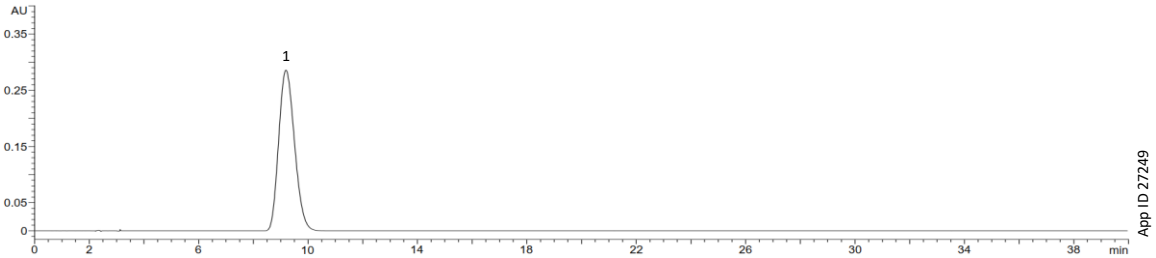
**Figure 2.** Reference Solution – Assay

Luna™ 5 µm C8(2) Column




| Peak No. | Analyte | Retention Time (min) | Area | Area %RSD | Tailing Factor | Theoretical Plates |
|---|---|---|---|---|---|---|
| 1 | Lisinopril | 17.64 | 11571239 | 0.04 | 1.11 | 1303 |
| N = 6 Injections | | | | | | |

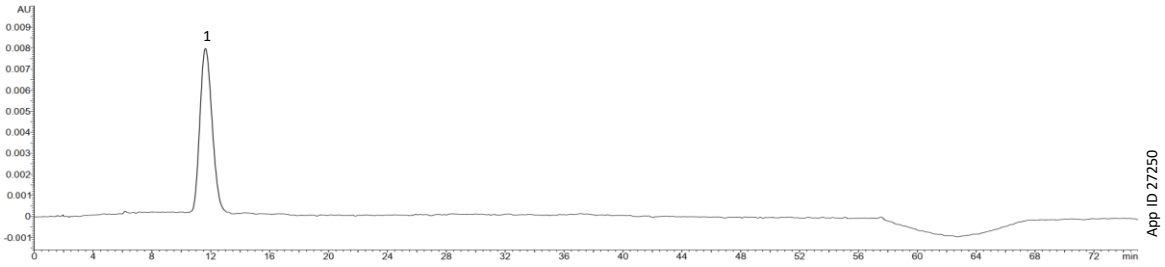
Kinetex™ 5 µm C8 Column




| Peak No. | Analyte | Retention Time (min) | Area | Area %RSD | Tailing Factor | Theoretical Plates |
|---|---|---|---|---|---|---|
| 1 | Lisinopril | 9.20 | 11393656 | 0.35 | 1.19 | 1160 |
| N = 6 Injections | | | | | | |

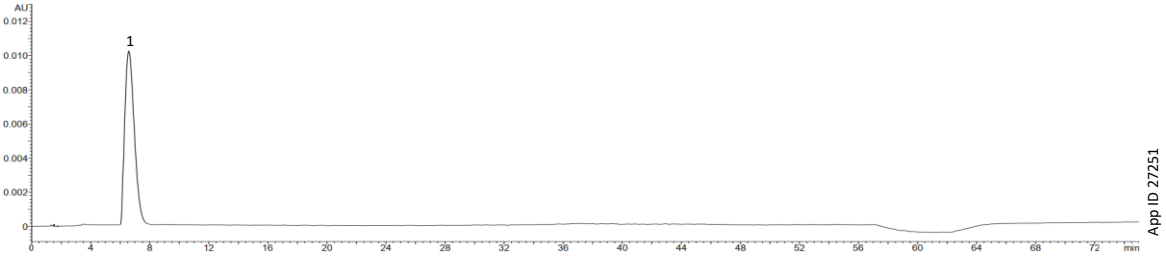
**Figure 3.** Reference Solution (b) – Related Substances

Luna™ 5 µm C8(2) Column




| Peak No. | Analyte | Retention Time (min) | Area | Area %RSD | Tailing Factor |
|---|---|---|---|---|---|
| 1 | Lisinopril | 11.63 | 453512 | 0.30 | 1.19 |
| N = 6 Injections | | | | | |

Kinetex™ 5 µm C8 Column




| Peak No. | Analyte | Retention Time (min) | Area | Area %RSD | Tailing Factor |
|---|---|---|---|---|---|
| 1 | Lisinopril | 6.58 | 458008 | 0.13 | 1.41 |
| N = 6 Injections | | | | | |

## Need a different column size or sample preparation format?

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