

Ph. Eur. Monograph 2232: Losartan Potassium Related Substances on Luna® 5 µm C18(2)

Laura Nakasone¹, Heiko Behr², and Dr. Bryan Tackett¹

¹Phenomenex, Inc., 411 Madrid Ave., Torrance, CA 90501 USA

²Phenomenex Ltd. Deutschland, Zeppelinstr. 5, 63741 Aschaffenburg, Germany

Overview

Losartan potassium belongs to a class of drugs called angiotensin receptor blockers (ARBs). It is an oral medication beneficial for treating hypertension. There is an increase in interest recently in the effectiveness of Losartan potassium in lowering high blood pressure.

In this application note we demonstrate the effective identification and separation of Losartan potassium from its impurities and related substances according to Ph.Eur. Monograph 2232. To meet system suitability requirements, the peak-to-valley ratio must be a minimum of 2 between Impurity A and Impurity G for reference solution (b). The peak-to-valley ratio is defined as H_p/H_v , where H_p = height above the baseline of the peak due to impurity M and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity G.

We used the fully porous Luna 5 µm C18(2) column and compared it to the Kromasil 5 µm C18 column originally used in the monograph. Both columns met system suitability and all peaks due to impurities J, K, L, M, and G were identified (**Figure 4**), with the Luna C18(2) column providing a larger peak-to-valley ratio, indicative of increased separation.

All reference solutions were prepared as indicated in Ph. Eur. Monograph 2232 for Losartan potassium. Losartan potassium Certified Reference Standard (CRS) (catalog no. Y0001062), Losartan for System Suitability CRS (catalog no. Y0001076), Losartan Impurity D CRS (catalog no. Y0001072), and Triphenylmethanol (Impurity G) (catalog no. Y0001654) were purchased from the European Directorate for the Quality of Medicines & HealthCare (EDQM) Council of Europe.

LC-UV Conditions

Column: Kromasil® 5 µm C18, 250 x 4.6 mm
Luna 5 µm C18(2), 250 x 4.6 mm ([00G-4252-E0](#))

Pressure: 239 bar (Kromasil)
237 bar (Luna)

Mobile Phase: A: Dilute 1.0 mL of phosphoric acid to 1000 mL with water
B: Acetonitrile

Gradient: Time (min)	%B
0	25
5	25
30	90
40	90

Flow Rate: 1.3 mL/min

Injection: 10 µL

Temperature: 35 °C

Detector: UV @ 220 nm

System: Agilent® 1260 Binary UHPLC

Figure 1. Structure of Losartan Potassium

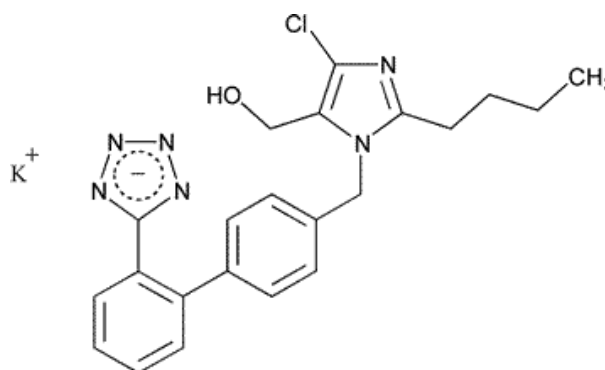
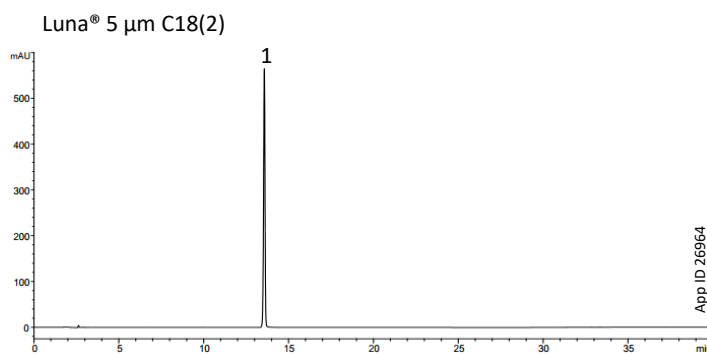
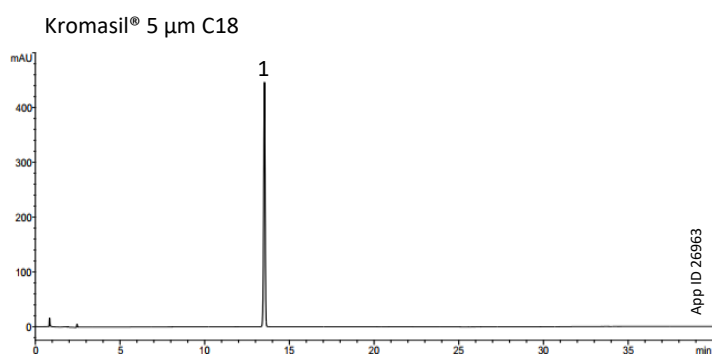


Table 1. Preparation of Test and Reference Solutions

Solution	Composition
Test Solution	Dissolve 30.0 mg of the Losartan Potassium CRS in methanol and dilute to 100.0 mL with the same solvent.
Reference Solution (a)	Dilute 1.0 mL of the Test Solution to 100.0 mL with methanol. Dilute 1.0 mL of this solution to 10.0 mL with methanol.
Reference Solution (b)	Dissolve 6.0 mg of triphenylmethanol (Impurity G) in 100.0 mL of methanol. Dilute 1.0 mL of the solution to 100.0 mL with methanol. Use 1.0 mL of this solution to dissolve the contents of a vial of Losartan for System Suitability CRS (containing impurities J, K, L and M) and sonicate for 5 min.
Reference Solution (c)	Dissolve 3.0 mg of Losartan Impurity D CRS in methanol and dilute to 100.0 mL with the same solvent. Dilute 1.5 mL of this solution to 100.0 mL with methanol.

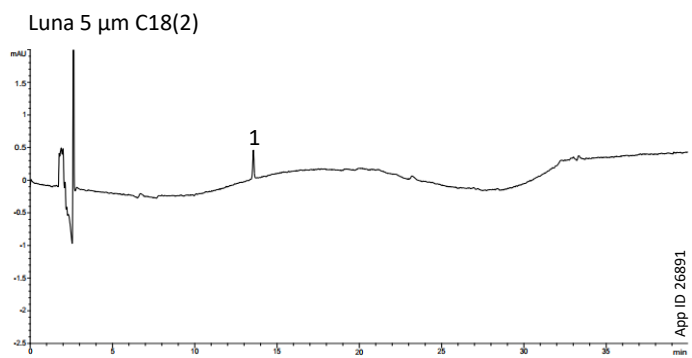
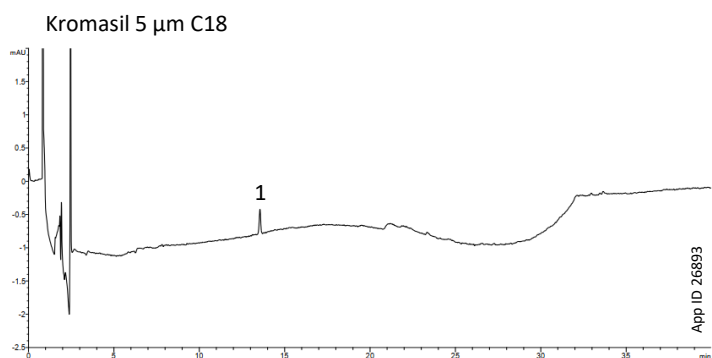
Figure 2. Chromatograms for Test Solution



Peak No.	Analyte	Retention Time (min)	Area	Height	Symmetry Factor
1	Losartan Potassium	13.528	2664.1	448.3	1.114

Peak No.	Analyte	Retention Time (min)	Area	Height	Symmetry Factor
1	Losartan Potassium	13.578	3346.4	566.4	1.158

Figure 3. Chromatograms for Reference Solution (a)

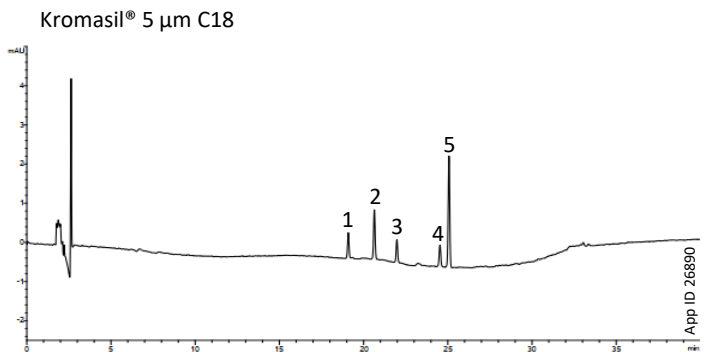


Peak No.	Analyte	Retention Time (min)	Area	Height	Symmetry Factor
1	Losartan Potassium	13.554	2.3	3.7e-1	1.067

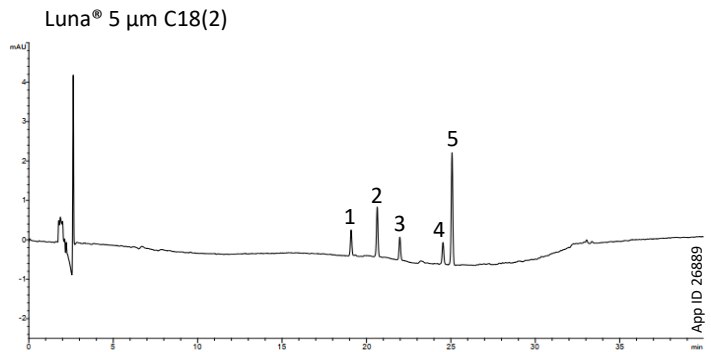
Peak No.	Analyte	Retention Time (min)	Area	Height	Symmetry Factor
1	Losartan Potassium	13.564	2.5	4.4e-1	1.038



Figure 4. Chromatograms for Reference Solution (b)

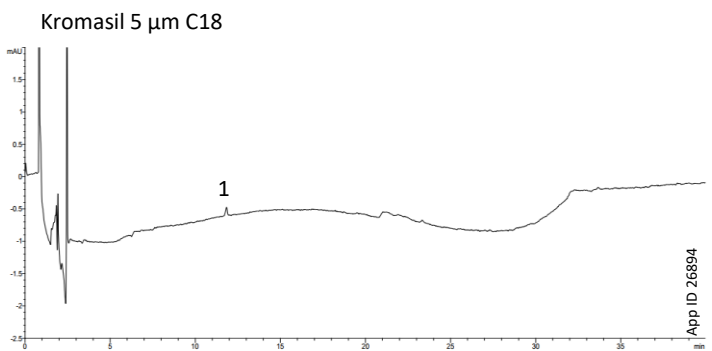


Peak No.	Analyte	Retention Time (min)	RRT to Losartan	Area	Height	Symmetry Factor	Peak-to-Valley Ratio
1	Impurity J	18.90	1.40	3.8	6.3e-1	1.04	-
2	Impurity K	20.48	1.51	7.8	1.3	1.04	-
3	Impurity L	21.88	1.62	3.7	6.0e-1	1.04	-
4	Impurity M	24.51	1.81	3.7	5.7e-1	0.97	37.78
5	Impurity G	25.04	1.85	7	1.1	1.06	-

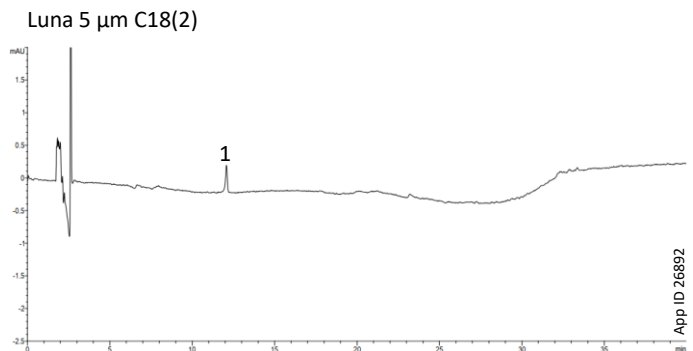


Peak No.	Analyte	Retention Time (min)	RRT to Losartan	Area	Height	Symmetry Factor	Peak-to-Valley Ratio
1	Impurity J	19.09	1.41	3.9	6.5e-1	1.0	-
2	Impurity K	20.64	1.52	8.0	1.3	1.06	-
3	Impurity L	21.98	1.62	3.8	5.9e-1	0.96	-
4	Impurity M	24.54	1.81	3.7	5.5e-1	1.02	55.00
5	Impurity G	25.07	1.85	718.2	2.8	1.04	-

Figure 5. Chromatograms for Reference Solution (c)



Peak No.	Analyte	Retention Time (min)	RRT to Losartan	Area	Height	Symmetry Factor
1	Impurity D	11.84	0.88	9.0e-1	1.3e-1	1.30



Peak No.	Analyte	Retention Time (min)	RRT to Losartan	Area	Height	Symmetry Factor
1	Impurity D	11.84	0.88	9.0e-1	1.3e-1	1.30



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t: +61 (0)2-9428-6444
auiinfo@phenomenex.com

Austria

t: +43 (0)1-319-1301
anfrage@phenomenex.com

Belgium

t: +32 (0)2 503 4015 (French)
t: +32 (0)2 511 8666 (Dutch)
beinfo@phenomenex.com

Canada

t: +1 (800) 543-3681
info@phenomenex.com

China

t: +86 400-606-8099
cninfo@phenomenex.com

Czech Republic

t: +420 272 017 077
cz-info@phenomenex.com

Denmark

t: +45 4824 8048
nordicinfo@phenomenex.com

Finland

t: +358 (0)9 4789 0063
nordicinfo@phenomenex.com

France

t: +33 (0)1 30 09 21 10
franceinfo@phenomenex.com

Germany

t: +49 (0)6021-58830-0
anfrage@phenomenex.com

Hong Kong

t: +852 6012 8162
hkinfo@phenomenex.com

India

t: +91 (0)40-3012 2400
indiainfo@phenomenex.com

Indonesia

t: +62 21 5010 9707
indoinfo@phenomenex.com

Ireland

t: +353 (0)1 247 5405
eireinfo@phenomenex.com

Italy

t: +39 051 6327511
italiainfo@phenomenex.com

Japan

t: +81 (0) 120-149-262
jpinfo@phenomenex.com

Luxembourg

t: +31 (0)30-2418700
nlinfo@phenomenex.com

Mexico

t: 01-800-844-5226
tecnicomx@phenomenex.com

The Netherlands

t: +31 (0)30-2418700
nlinfo@phenomenex.com

New Zealand

t: +64 (0)9-4780951
nzinfo@phenomenex.com

Norway

t: +47 810 02 005
nordicinfo@phenomenex.com

Poland

t: +48 22 104 21 72
pl-info@phenomenex.com

Portugal

t: +351 221 450 488
ptinfo@phenomenex.com

Singapore

t: +65 800-852-3944
sginfo@phenomenex.com

Slovakia

t: +420 272 017 077
sk-info@phenomenex.com

Spain

t: +34 91-413-8613
espinfo@phenomenex.com

Sweden

t: +46 (0)8 611 6950
nordicinfo@phenomenex.com

Switzerland

t: +41 (0)61 692 20 20
swissinfo@phenomenex.com

Taiwan

t: +886 (0) 0801-49-1246
twinfo@phenomenex.com

Thailand

t: +66 (0) 2 566 0287
thaiinfo@phenomenex.com

United Kingdom

t: +44 (0)1625-501367
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t: +1 (310) 212-0555
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