Improve Your European Pharmacopoeia (Ph. Eur.) and United States (USP) Monographs

- Reduce run times
- Achieve higher resolution
- Stay within Allowable Adjustments

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...breaking with tradition℠

High-throughput productivity is of critical importance for laboratories undertaking testing for generic drugs following the quality standards and test procedures of the United States Pharmacopeia (USP) and European Pharmacopoeia Monographs (Ph. Eur.). This guide provides analysts with solutions to standard USP and Ph. Eur. Monographs and also incorporates cutting edge Kinetex® core-shell LC columns to provide shorter separation times and improved resolution while meeting all the quality standards of the United States Pharmacopoeia and European Pharmacopoeia Monographs.

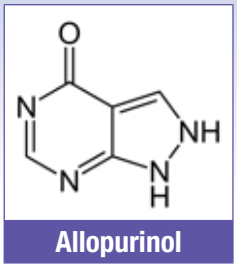
Table of Contents

European Pharmacopoeia (Ph. Eur.) Monographs for Generic Drugs

Allopurinol and Related Substances

Ph. Eur. monograph 0576

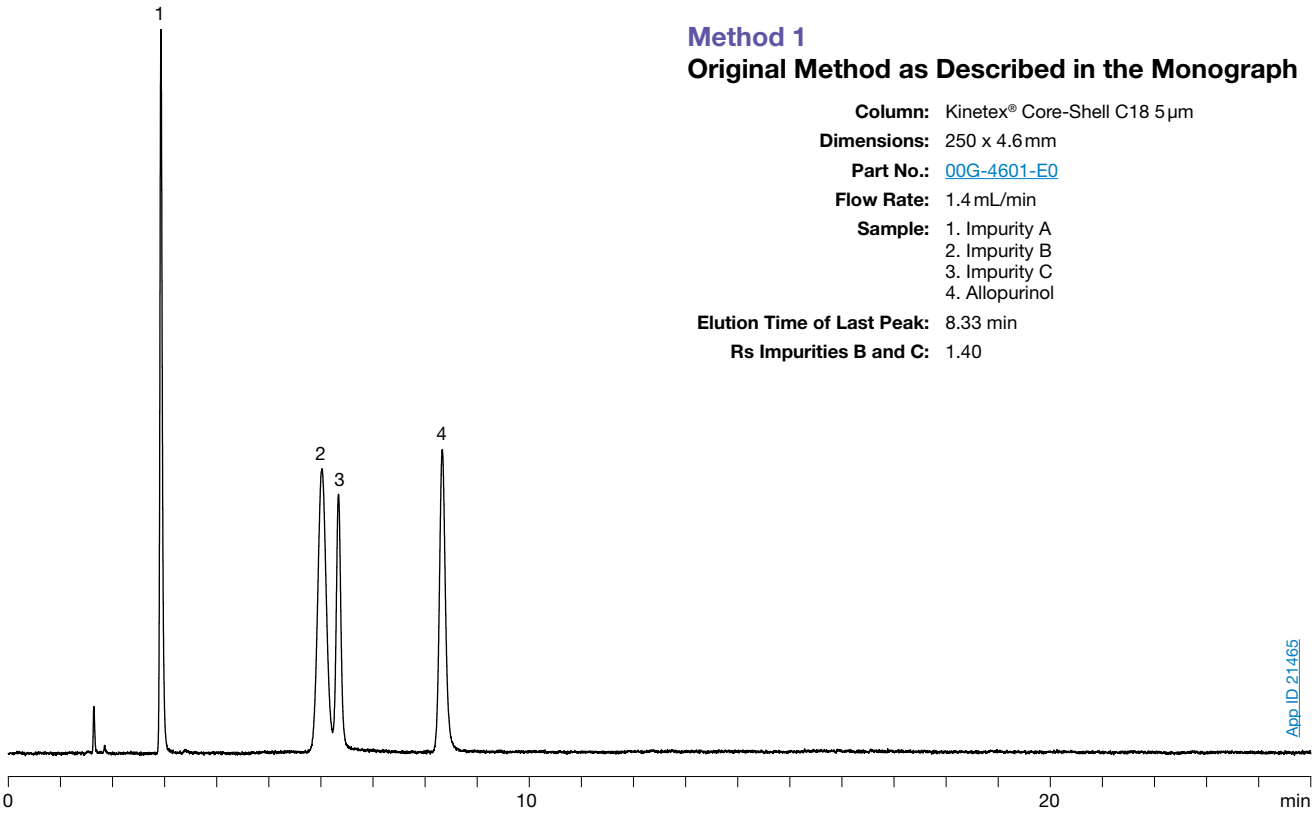
The related substances test of the Ph. Eur. Monograph 0576 outlines the separation of all relevant impurities from Allopurinol. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Allopurinol

Ph. Eur. Monograph 0576 Details	
Test Solution (a)	Dissolve 25.0 mg of Allopurinol CRS* in 2.5 mL of a 4 g/L solution of sodium hydroxide R and dilute immediately to 50.0 mL with the mobile phase
Reference Solution	**(a)** Dilute 2.0 mL of the test solution (a) to 100.0 mL with the mobile phase. Dilute 5 mL of this solution to 100.0 mL with the mobile phase. **(b)** Dissolve 5.0 mg of Allopurinol Impurity A CRS*, 5.0 mg of Allopurinol Impurity B CRS* and 5.0 mg of Allopurinol Impurity C CRS* in 5.0 mL of a 4 g/L solution of sodium hydroxide R and dilute immediately to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase.
Column	
Size	250 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	1.25 g/L solution of potassium dihydrogen phosphate R
Flow Rate	1.4 mL/min
Detection	Spectrophotometer @ 230 nm
Injection	20 µL (reference solution (a) and (b))
Run Time	Twice the retention time of Allopurinol
Elution Order	1. Impurity A 2. Impurity B 3. Impurity C 4. Allopurinol (about 10 min)
System Suitability	
Reference Solution (b)	Minimum resolution of 1.1 between peaks due to Impurities B and C

* Allopurinol CRS (A0350000), Allopurinol Impurity A CRS (A0350010), Allopurinol Impurity B CRS (A0350020) and Allopurinol Impurity C CRS (A0350030) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).



Method 1

Original Method as Described in the Monograph

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 1.4 mL/min
Sample: 1. Impurity A
2. Impurity B
3. Impurity C
4. Allopurinol
Elution Time of Last Peak: 8.33 min
Rs Impurities B and C: 1.40

Adjustments for Meeting System Suitability

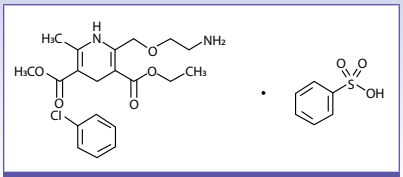
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 0576 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 0576 Details Table
Wavelength of Detector	No deviations permitted	230 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)
Column Temperature	± 10 °C	Ambient (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	250 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.4 mL/min (as specified)

Amlodipine Besylate and Related Substances

Ph. Eur. monograph 1491

The related substances test of the Ph. Eur. Monograph 1491 outlines the separation of all relevant impurities from Amlodipine Besylate. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Amlodipine Besylate

Ph. Eur. Monograph 1491 Details

Reference Solution (b)	Dissolve 2.5 mg of Amlodipine Impurity B CRS* and 2.5 mg of Amlodipine Impurity G CRS* in the mobile phase and dilute to 25 mL with the mobile phase. Dilute 1.0 mL of the solution to 10.0 mL with the mobile phase.
Column	
Size	250 x 4.0 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	30 °C
Mobile Phase	2.3 g/L solution of Ammonium acetate R, methanol R (30:70 V/V)
Flow Rate	1.5 mL/min
Detection	Spectrophotometer @ 237 nm
Injection	20 µL
Run Time	Twice the retention time of Amlodipine
Relative Retention with Reference to Amlodipine (about 20 min)**	
Impurity G	about 0.21
Impurity B	about 0.25
System Suitability	
Reference Solution (b)	Minimum resolution of 2.0 between peaks due to Impurities G and B

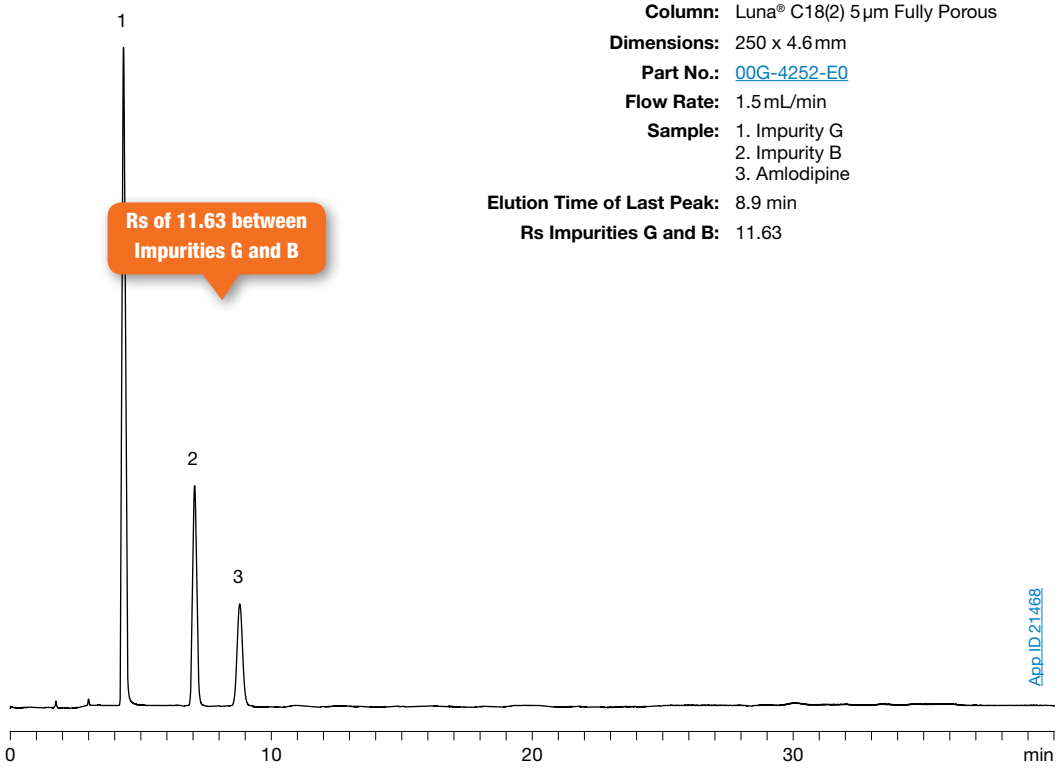
* Amlodipine Impurity B CRS (Y0001069) and Amlodipine Impurity G CRS (Y0001070) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

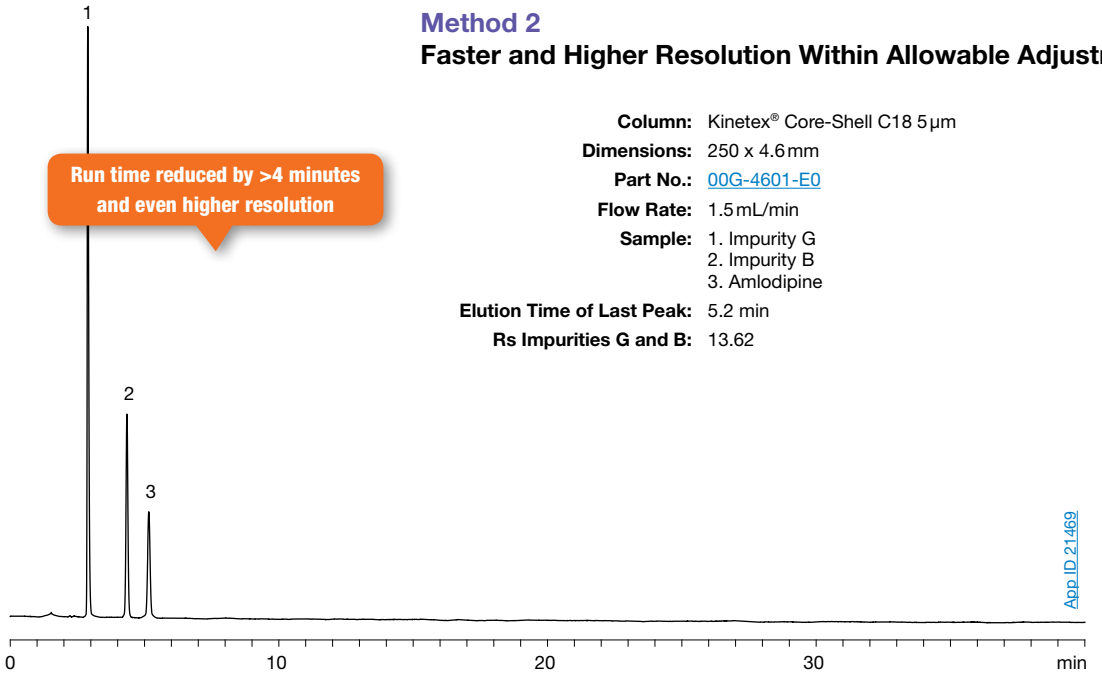
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Alternative Method Within Allowable Adjustments

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4252-E0
Flow Rate: 1.5 mL/min
Sample: 1. Impurity G
2. Impurity B
3. Amlodipine
Elution Time of Last Peak: 8.9 min
Rs Impurities G and B: 11.63





Method 2
Faster and Higher Resolution Within Allowable Adjustments

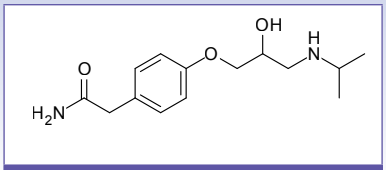
Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 1.5 mL/min
Sample: 1. Impurity G
2. Impurity B
3. Amlodipine
Elution Time of Last Peak: 5.2 min
Rs Impurities G and B: 13.62

Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1491 Details Table	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1491 Details Table	As specified
Wavelength of Detector	No deviations permitted	237 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 10 °C	30 °C (as specified)	As specified
Stationary Phase	No change of the identity of the sub-stituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	250 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)	As specified
Flow Rate	± 50 %	1.5 mL/min (as specified)	As specified

Atenolol and Related Substances

Ph. Eur. monograph 0703



Atenolol

The related substances test of the Ph. Eur. Monograph 0703 outlines the separation of all relevant impurities from Atenolol. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.

Ph. Eur. Monograph 0703 Details	
Reference Solution (a)	Dissolve 2 mg of Atenolol for system suitability CRS* (containing Impurities B, F, G, I and J) in 1 mL mobile phase
Column	
Size	125 x 4.0 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Dissolve 1.0 g of sodium octanesulphonate R and 0.4 g of tetrabutylammonium hydrogen sulfate R in 1 L of a mixture of 20 volumes of tetrahydrofuran R, 180 volumes methanol R2 and 800 volumes of 3.4 g/L solution of potassium dihydrogen phosphate R; adjust the apparent pH to 3.0 with phosphoric acid R.
Flow Rate	0.6 mL/min
Detection	Spectrophotometer @ 226 nm
Injection	10 µL
Run Time	5 times the retention time of Atenolol
Relative Retention with Reference to Atenolol (about 8 min)**	
Impurity B	about 0.3
Impurity J	about 0.7
Impurity I	about 0.8
Impurity F	about 2.0 (pair of peaks)
Impurity G	about 3.5
System Suitability	
Reference Solution (a)	Minimum resolution of 1.4 between peaks due to Impurities J and I

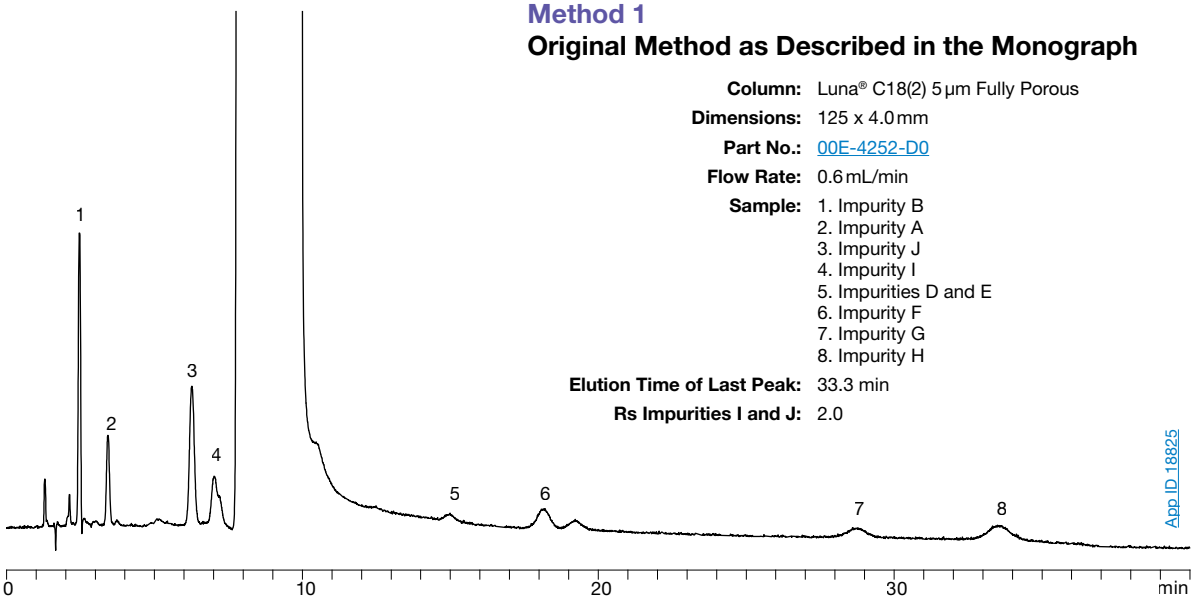
* Atenolol for system suitability CRS (Y0001089) was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

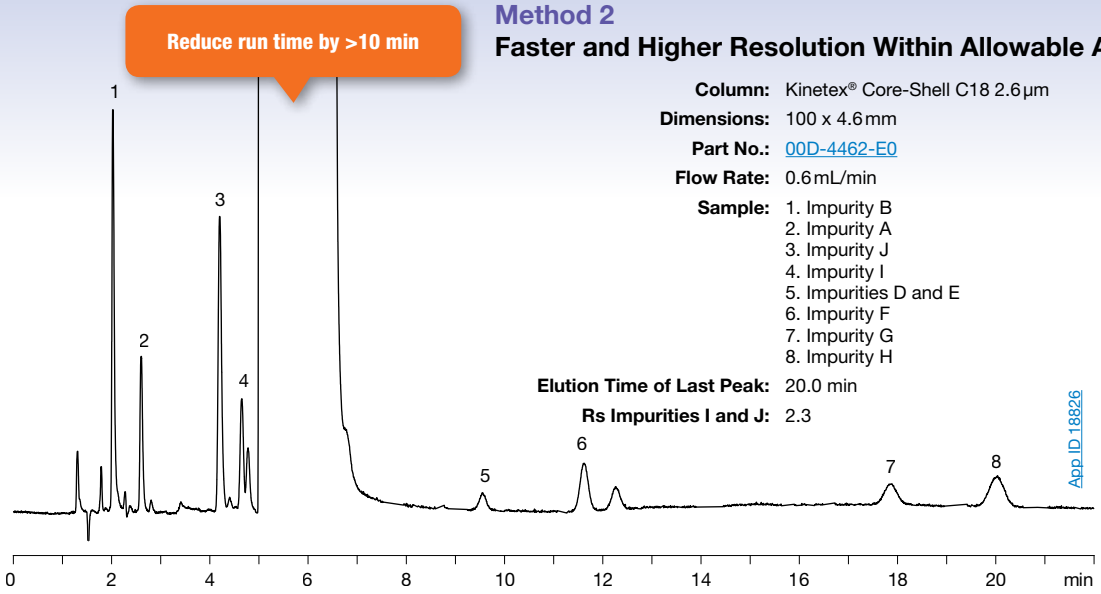
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method as Described in the Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 125 x 4.0 mm
Part No.: 00E-4252-D0
Flow Rate: 0.6 mL/min
Sample: 1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H
Elution Time of Last Peak: 33.3 min
Rs Impurities I and J: 2.0

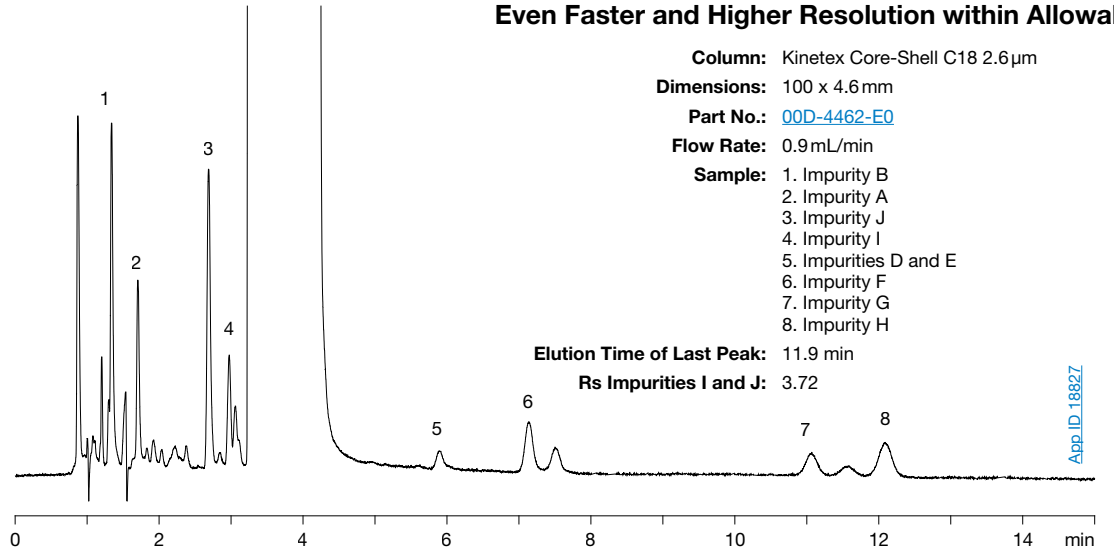




Method 2
Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 0.6 mL/min
Sample:
1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H

Elution Time of Last Peak: 20.0 min
Rs Impurities I and J: 2.3



Method 3
Even Faster and Higher Resolution within Allowable Adjustments

Column: Kinetex Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 0.9 mL/min
Sample:
1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H

Elution Time of Last Peak: 11.9 min
Rs Impurities I and J: 3.72

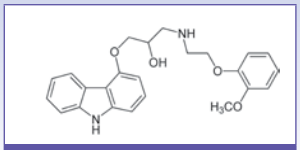
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2	Method 3
Mobile Phase pH	± 0.2 units	3 (as specified)	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 0703 Details Table	As specified	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 0703 Details Table	As specified	As specified
Wavelength of Detector	No deviations permitted	226 nm (as specified)	As specified	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)	As specified	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	End-capped octadecylsilyl silica gel for chromatography (as specified)	As specified	As specified
Column Length	± 70 %	125 mm (as specified)	100 mm (-20 %)	100 mm (-20 %)
Column Internal Diameter	± 25 %	4.0 mm (as specified)	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)	2.6 µm (-48 %)	2.6 µm (-48 %)
Flow Rate	± 50 %	0.6 mL/min (as specified)	As specified	0.9 mL/min (+ 50 %)

Carvedilol and Related Substances

Ph. Eur. monograph 1745

The Ph. Eur. Monograph 1745 outlines the separation of Carvedilol from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.

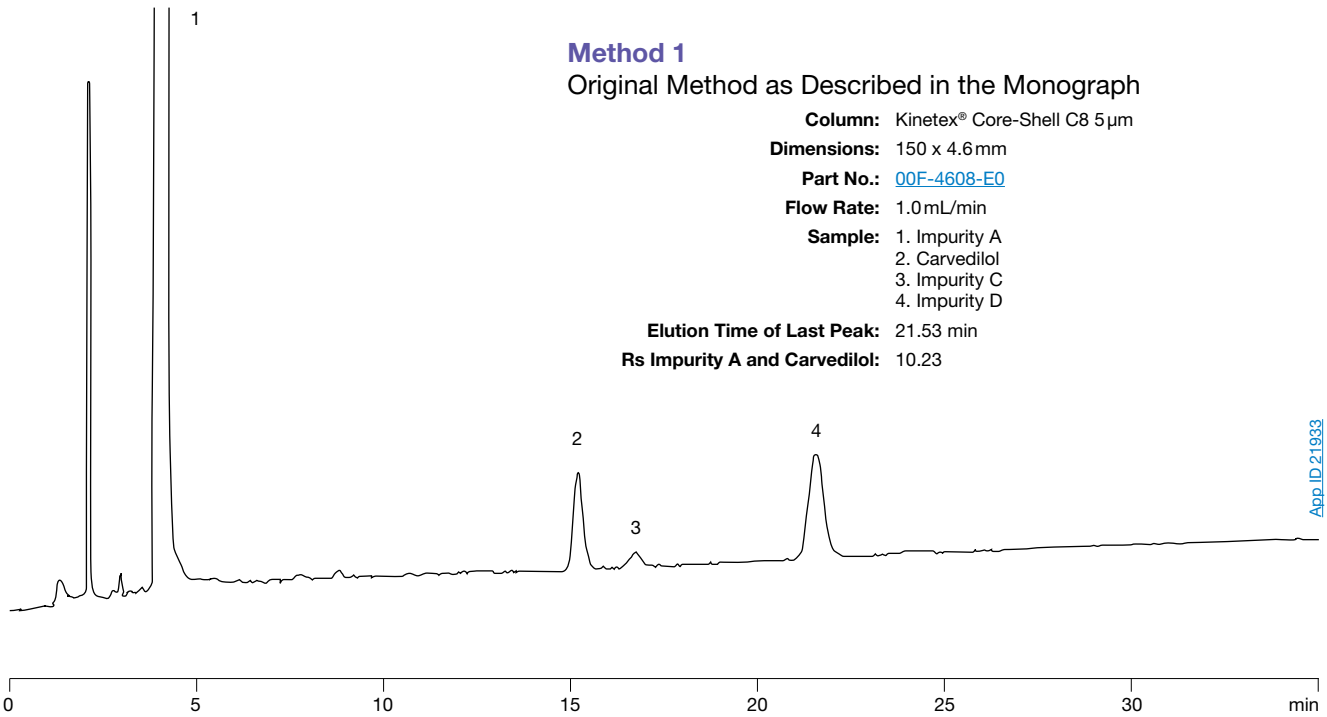


Carvedilol

Ph. Eur. Monograph 1745 Details	
Reference Solution	**(b)** Dissolve 5 mg of Carvedilol Impurity C CRS* in 5.0 mL of the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 4.0 mL of the solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase. **(c)** Dissolve 5 mg of Carvedilol for system suitability CRS* (containing Impurities A and D) in the mobile phase and dilute to 50.0 mL with the mobile phase.
Column	
Size	150 x 4.6 mm
Stationary Phase	End-capped octylsilyl silica gel for chromatography R (5 µm)
Temperature	55 °C
Mobile Phase	Dissolve 1.77 g of potassium dihydrogen phosphate R in water and dilute to 650 mL with the same solvent; adjust to pH 2.0 with phosphoric acid R and add 350 mL of acetonitrile R
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 240 nm
Injection	20 µL
Run Time	6 times the retention time of Carvedilol
Relative Retention with Reference to Carvedilol (about 4 min)**	
Impurity A	about 0.5
Impurity C	about 2.9
Impurity D	about 3.8
System Suitability	
Reference Solution (b)	Minimum resolution of 3.5 between peaks due to Impuritiy A and Carvedilol

*Carvedilol Impurity C CRS (Y0000103) and Carvedilol for system suitability CRS (Y0001426) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.



Method 1

Original Method as Described in the Monograph

Column: Kinetex® Core-Shell C8 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4608-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Carvedilol
3. Impurity C
4. Impurity D
Elution Time of Last Peak: 21.53 min
Rs Impurity A and Carvedilol: 10.23

Adjustments for Meeting System Suitability

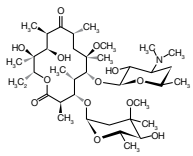
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	2.0 (as specified)
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1745 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1745 Details Table
Wavelength of Detector	No deviations permitted	240 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)
Column Temperature	± 10 °C	55 °C (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	150 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.0 mL/min (as specified)

Clarithromycin and Related Substances

Ph. Eur. monograph 1651

The Ph. Eur. Monograph 1651 outlines the separation of Clarithromycin from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Clarithromycin

Ph. Eur. Monograph 1651 Details	
Reference Solution	**(d)** Dissolve 15 mg of Clarithromycin for peak identification CRS* in 5 mL of acetonitrile and dilute to 10 mL with water
Column	
Size	100 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (3.5 µm)
Temperature	40 °C
Mobile Phase	A: 4.76 g/L solution of potassium dihydrogen phosphate adjusted to pH 4.4 with dilute phosphoric acid B: Acetonitrile
Gradient	**Time (min)** **%B** 0 – 32 min 25 → 60 32- 34 min 60
Flow Rate	1.1 mL/min
Detection	Spectrophotometer @ 205 nm
Injection	10 µL
Relative Retention with Reference to Clarithromycin (about 11 min)**	
Impurity A	about 0.42
Impurity J	about 0.63
Impurity L	about 0.74
Impurity B	about 0.79
Impurity M	about 0.81
Impurity C	about 0.89
Impurity D	about 0.96
Impurity N	about 1.15
Impurity E	about 1.27
Impurity F	about 1.33
Impurity P	about 1.35
Impurity O	about 1.41
Impurity K	about 1.59
Impurity G	about 1.59
Impurity H	about 1.82
System Suitability	
Peak-to-Valley Ratio	Minimum 3.0, where Hp = height above the baseline of the peak due to Impurity D and Hv = height above the baseline of the lowest point of the curve separating this peak from the peak due to Clarithromycin in the chromatogram obtained with reference solution D

* Ph. Eur. Standard Clarithromycin for peak identification CRS Y0000321 was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allée Kastner CS 30026F - 67081 STRASBOURG (France).

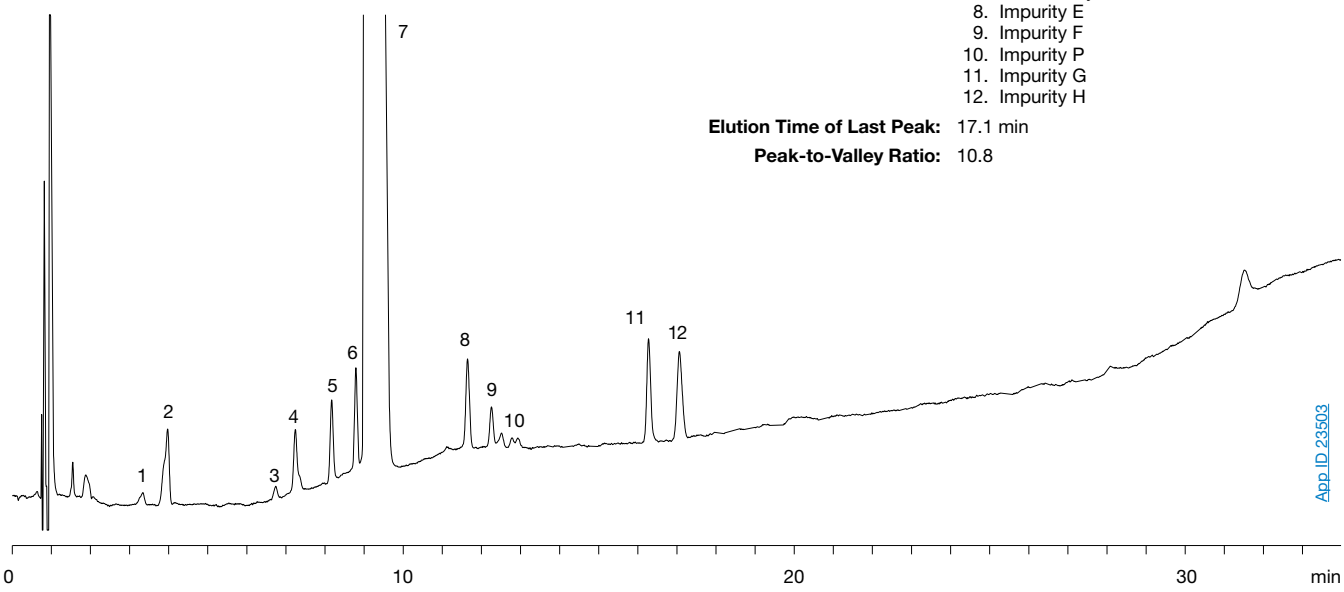
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Achieve improved sensitivity and resolution using Kinetex Core-Shell Columns

Method 1
Original Method as Described in the Monograph

Column: Kinetex® Core-Shell XB-C18 3.5 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4744-E0
Flow Rate: 1.1 mL/min
Sample:
1. Impurity I
2. Impurity A
3. Impurity L
4. Impurity B
5. Impurity C
6. Impurity D
7. Clarithromycin
8. Impurity E
9. Impurity F
10. Impurity P
11. Impurity G
12. Impurity H

Elution Time of Last Peak: 17.1 min
Peak-to-Valley Ratio: 10.8



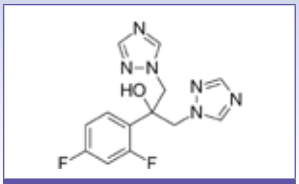
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1651 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1651 Details Table
Wavelength of Detector	No deviations permitted	205 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	1 µL (as specified)
Column Temperature	± 10 °C	40 °C (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	100 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	3.5 µm (as specified)
Flow Rate	± 50 %	1.1 mL/min (as specified)

Fluconazole and Related Substances

Ph. Eur. monograph 2287

The Ph. Eur. Monograph 2287 outlines the separation of Fluconazole from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Fluconazole

Ph. Eur. Monograph 2287 Details

Reference Solution	**(b)** Dissolve 5.0 mg of Fluconazole for peak identification CRS* (containing Impurity A) in the mobile phase, sonicate if necessary, and dilute to 10 mL with the mobile phase **(c)** Dissolve 3.0 mg of Fluconazole Impurity B CRS* in the mobile phase, sonicate if necessary, and dilute to 100 mL with the mobile phase **(d)** Dissolve 3.0 mg of Fluconazole Impurity C CRS* in the mobile phase and dilute to 20 mL with the mobile phase
Column	
Size	150 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R1 (5 µm)
Temperature	40 °C
Mobile Phase	Acetonitrile R, 0.63 g/L solution of ammonium formate R (14:86 V/V)
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 260 nm
Injection	20 µL
Run Time	3.5 times the retention time of Fluconazole
Relative Retention with Reference to Fluconazole (about 11 min)**	
Impurity B	about 0.4
Impurity A	about 0.5
Impurity C	about 0.8
System Suitability	
Reference Solution (a)	Minimum resolution of 3.0 between peaks due to Impurity C and Fluconazole

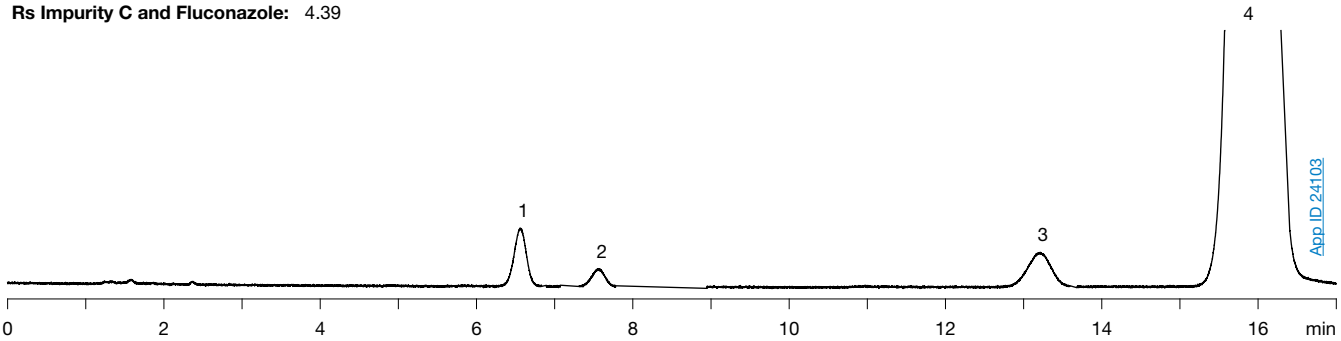
* Fluconazole for peak identification CRS (Y0000558), Fluconazole Impurity B CRS (Y0000573) and Fluconazole Impurity C CRS (Y0000574) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

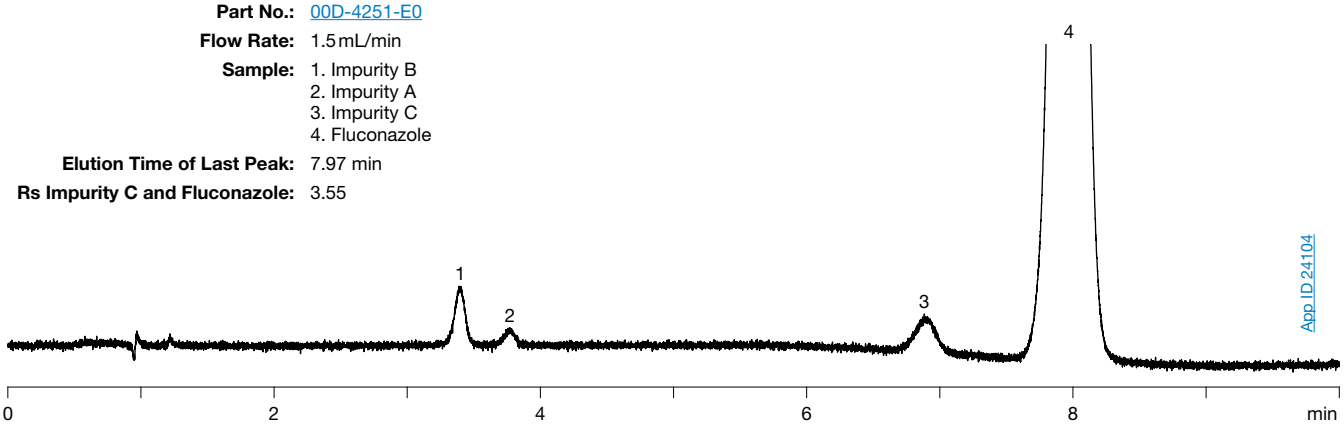
Original Method as Described in the Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity B
2. Impurity A
3. Impurity C
4. Fluconazole
Elution Time of Last Peak: 15.9 min
Rs Impurity C and Fluconazole: 4.39



Method 2
Faster Method Within Allowable Adjustments

Column: Luna C18(2) 3 µm Fully Porous
Dimensions: 100 x 4.6 mm
Part No.: 00D-4251-E0
Flow Rate: 1.5 mL/min
Sample: 1. Impurity B
2. Impurity A
3. Impurity C
4. Fluconazole
Elution Time of Last Peak: 7.97 min
Rs Impurity C and Fluconazole: 3.55



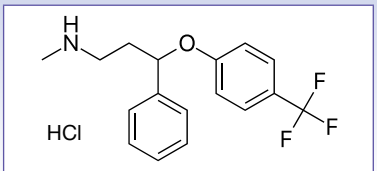
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 2287 Details Table	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 2287 Details Table	As specified
Wavelength of Detector	No deviations permitted	260 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 10 °C	40 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	150 mm (as specified)	100 mm (-33.3 %)
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	-50 %	5 µm (as specified)	3 µm (-40 %)
Flow Rate	± 50 %	1.0 mL/min (as specified)	1.5 mL/min (+50 %)

Fluoxetine Hydrochloride and Related Substances

Ph. Eur. monograph 1104

The Ph. Eur. Monograph 1104 outlines the separation of Fluoxetine from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Fluoxetine Hydrochloride

Ph. Eur. Monograph 1104 Details

Reference Solution	Dissolve 22 mg of Fluoxetine Hydrochloride CRS* in 10.0 mL of a 0.5 M sulfuric acid. Heat at about 85° C for 3 h. Allow to cool. The resulting solution contains considerable quantities of Impurity A and usually also contains 4-trifluoromethylphenol. To 0.4 mL of this solution add 28.0 mg of Fluoxetine hydrochloride CRS*, about 1 mg of Fluoxetine Impurity B CRS* and about 1 mg Fluoxetine Impurity C CRS*, then dilute to 25.0 mL with mobile phase.
Column	
Size	150 x 4.6 mm
Stationary Phase	Octylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Mix 8 volumes of methanol R, 30 volumes of tetrahydrofuran R, and 62 volumes of a solution of trimethylamine R prepared as follows: to 10 mL of trimethylamine R, add 980 mL of water R, mix and adjust to pH 6.0 with phosphoric acid R (about 4.5 mL) and dilute to 1000 mL with water R.
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 215 nm
Injection	10 µL
Run Time	3 times the retention time of Fluoxetine
Relative Retention with Reference to Fluoxetine (about 10-18 min)**	
Impurity A	about 0.24
Impurity B	about 0.27
Impurity C	about 0.90
System Suitability	
Peak-to-Valley Ratio	Minimum 11, where Hp = height above the baseline of the peak due to Impurity C and Hv = height above the baseline of the lowest point of the curve separating this peak from the peak due to Fluoxetine.

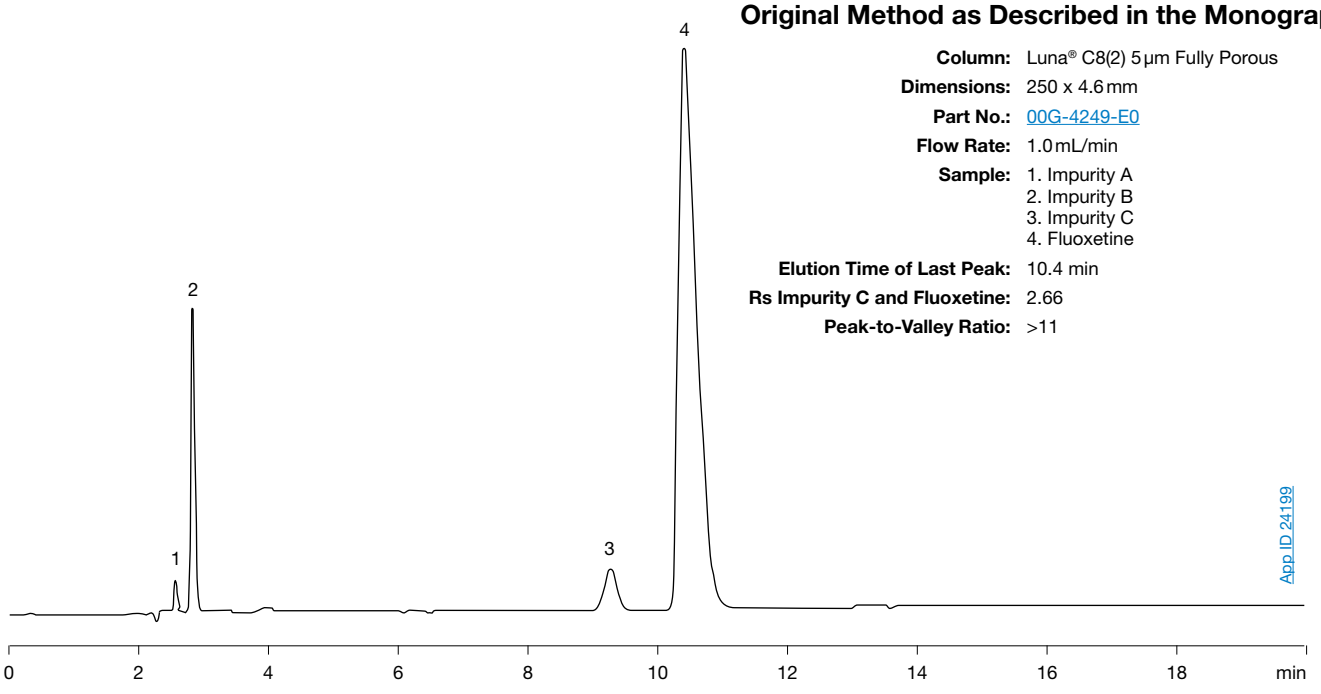
* Fluoxetine hydrochloride CRS (F0253000), Fluoxetine Impurity B CRS (F0253020) and Fluoxetine Impurity C CRS (F0253030) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

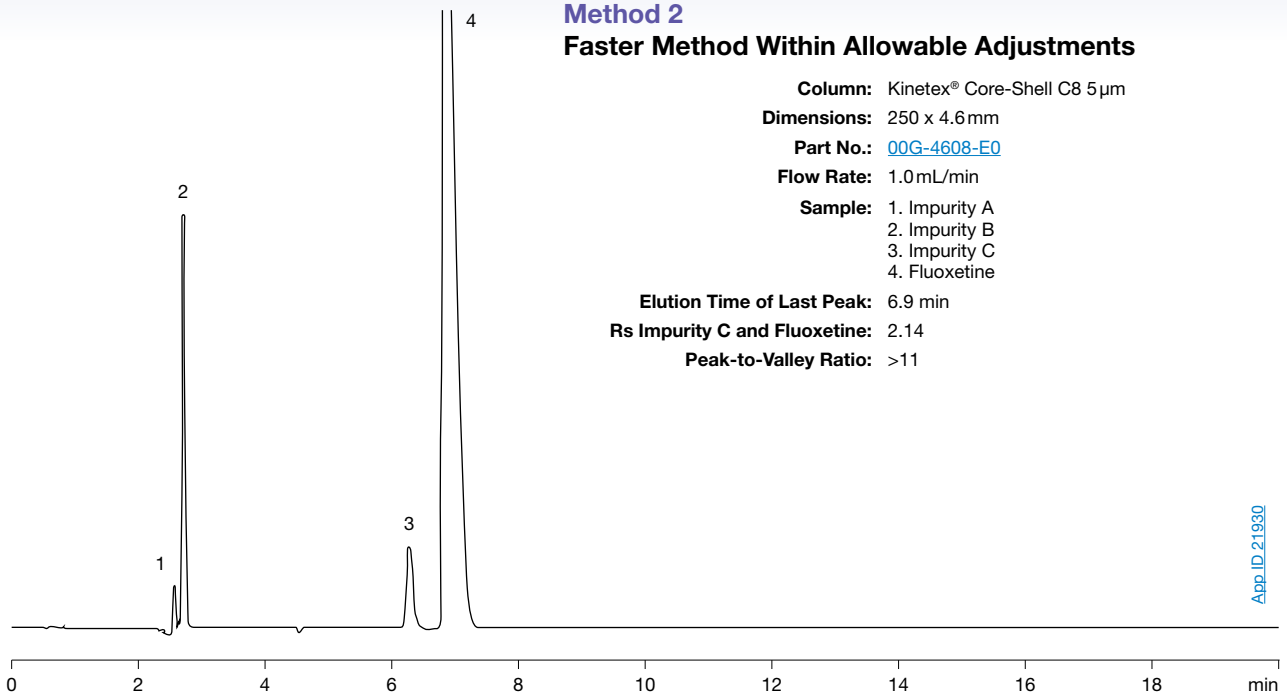
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method as Described in the Monograph

Column: Luna® C8(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4249-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Impurity B
3. Impurity C
4. Fluoxetine
Elution Time of Last Peak: 10.4 min
Rs Impurity C and Fluoxetine: 2.66
Peak-to-Valley Ratio: >11





Method 2
Faster Method Within Allowable Adjustments

Column: Kinetex® Core-Shell C8 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4608-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Impurity B
3. Impurity C
4. Fluoxetine
Elution Time of Last Peak: 6.9 min
Rs Impurity C and Fluoxetine: 2.14
Peak-to-Valley Ratio: >11

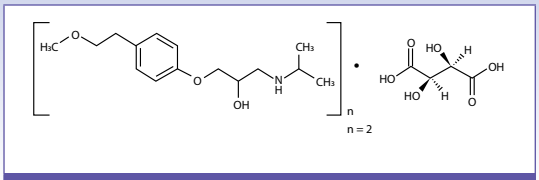
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	6 (as specified)	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1104 Details Table	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1104 Details Table	As specified
Wavelength of Detector	No deviations permitted	215 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	250 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	-50 %	5 µm (as specified)	As specified
Flow Rate	± 50 %	1.0 mL/min (as specified)	As specified

Metoprolol Tartrate and Related Substances

Ph. Eur. monograph 1028

The Ph. Eur. Monograph 1028 outlines the separation of Metoprolol Tartrate from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Metoprolol Tartrate

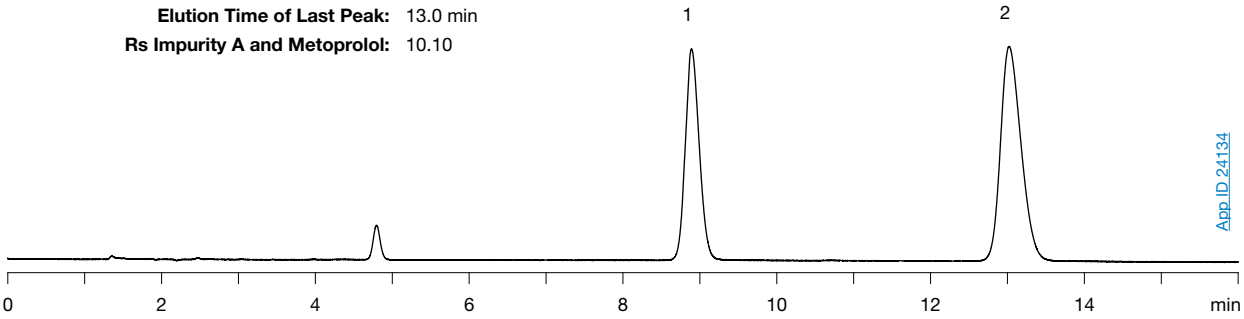
Ph. Eur. Monograph 1028 Details	
Reference Solution (a) and Impurity G	Dissolve 1.5 mg of Metoprolol Impurity A CRS*, 2.5 mg of Metoprolol Tartrate CRS* and 1.5 mg of Metoprolol impurity G in the mobile phase and dilute to 50.0 mL with the mobile phase.
Column	
Size	150 x 3.9 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Dissolve 3.9 g of ammonium acetate R in 810 mL of water R, add 2.0 mL of trimethylamine R, 10.0 mL of glacial acetic acid R, 3.0 mL of phosphoric acid R and 146 mL of acetonitrile R and mix
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 280 nm
Injection	20 µL
Run Time	3 times the retention time of Metoprolol
Elution Order	1. Impurity G 2. Impurity A 3. Metoprolol Tartrate
System Suitability	
Reference Solution (a)	Minimum resolution of 6.0 between peaks due to Impurity A and Metoprolol

* Metoprolol impurity A CRS (Y0000145) and Metoprolol Tartrate CRS (M1830000) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1

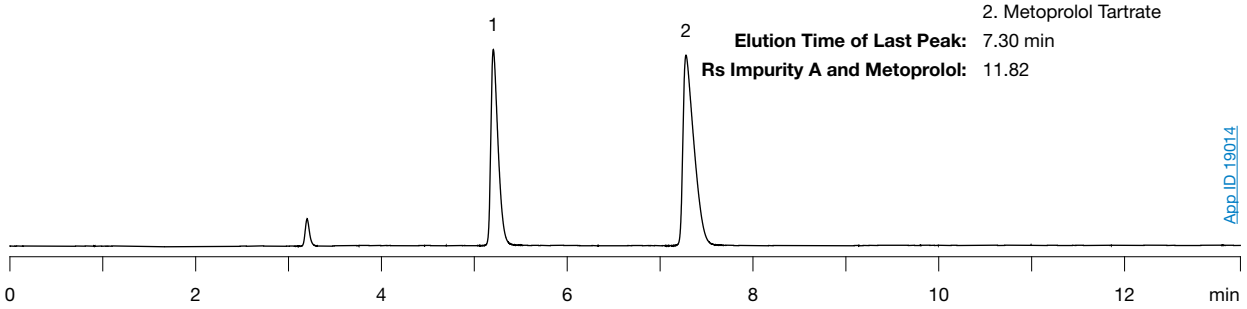
Original Method as Described in the Monograph within Allowable Adjustments

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Metoprolol Tartrate
Elution Time of Last Peak: 13.0 min
Rs Impurity A and Metoprolol: 10.10



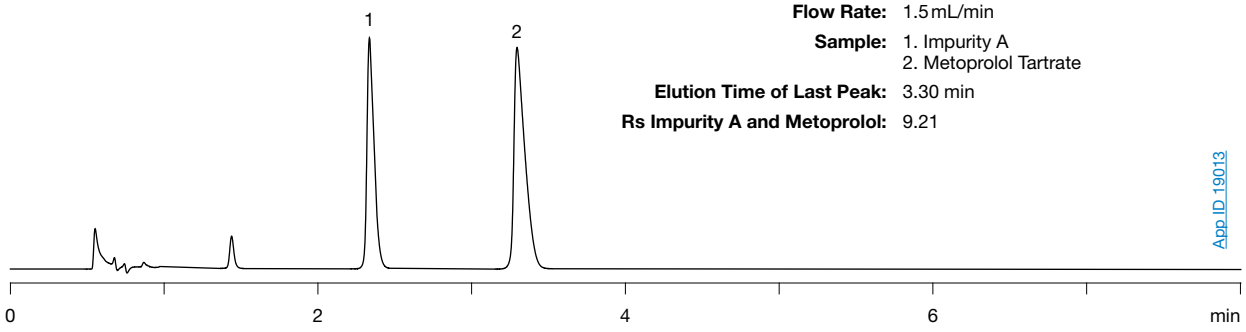
Method 2
Faster Method Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4462-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Metoprolol Tartrate
Elution Time of Last Peak: 7.30 min
Rs Impurity A and Metoprolol: 11.82



Method 3
Even Faster Method within Allowable Adjustments

Column: Kinetex Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 1.5 mL/min
Sample: 1. Impurity A
2. Metoprolol Tartrate
Elution Time of Last Peak: 3.30 min
Rs Impurity A and Metoprolol: 9.21



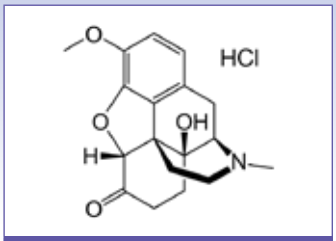
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2	Method 3
Mobile Phase pH	± 0.2 units	As specified	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1028 Details Table	As specified	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1028 Details Table	As specified	As specified
Wavelength of Detector	No deviations permitted	280 nm (as specified)	As specified	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	End-capped octadecylsilyl silica gel for chromatography (as specified)	As specified	As specified
Column Length	± 70 %	150 mm (as specified)	150 mm (as specified)	100 mm (-33 %)
Column Internal Diameter	± 25 %	4.6 mm (+18 %)	4.6 mm (+18 %)	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)	2.6 µm (-48 %)	2.6 µm (-48 %)
Flow Rate	± 50 %	1.0 mL/min (as specified)	As specified	1.5 mL/min (+ 50 %)

Oxycodone Hydrochloride and Related Substances

Ph. Eur. monograph 1793

The Ph. Eur. Monograph 1793 outlines the separation of Oxycodone Hydrochloride from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Oxycodone Hydrochloride

Ph. Eur. Monograph 1793 Details

Test Solution	Dissolve 0.100 g of Oxycodone Hydrochloride CRS* in a 1 % V/V solution of dilute acetic acid R and dilute to 50.0 mL with the same solvent
Reference Solution	**(a)** Dissolve 20.0 mg of Oxycodone Impurity D CRS* in a 1.0 % V/V solution of dilute acetic acid R and dilute to 10.0 mL with the same solution **(b)** To 1.0 mL of the test solution, add 1 mL of reference solution (a) and dilute to 100.0 mL with a 1 % V/V solution of dilute acetic acid R. Dilute 1.0 mL of the solution to 10.0 mL with a 1.0 % V/V solution of dilute acetic acid R.
Column	
Size	150 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	40 °C
Mobile Phase	A: Mix 830 mL of a 1.1 g/L solution of sodium heptanesulfonate monohydrate R previously adjusted to pH 2.0 with a mixture of equal volumes of phosphoric acid R and water R, with 70 mL of acetonitrile R and 100 mL of methanol R B: Mix 600 mL of a 1.1 g/L solution of sodium heptanesulfonate monohydrate R previously adjusted to pH 2.0 with a mixture of equal volumes of phosphoric acid R and water R, with 150 mL of acetonitrile R and 250 mL of methanol R
Gradient	**Time (min)** **%B** 0 – 60 min 0 - 50
Flow Rate	1.5 mL/min
Detection	Spectrophotometer @ 230 nm
Injection	20 µL
Relative Retention with Reference to Oxycodone (about 24 min)**	
Impurity B	about 0.7
System Suitability	
Reference Solution (a)	Minimum resolution of 3.0 between peaks due to Oxycodone and Impurity D

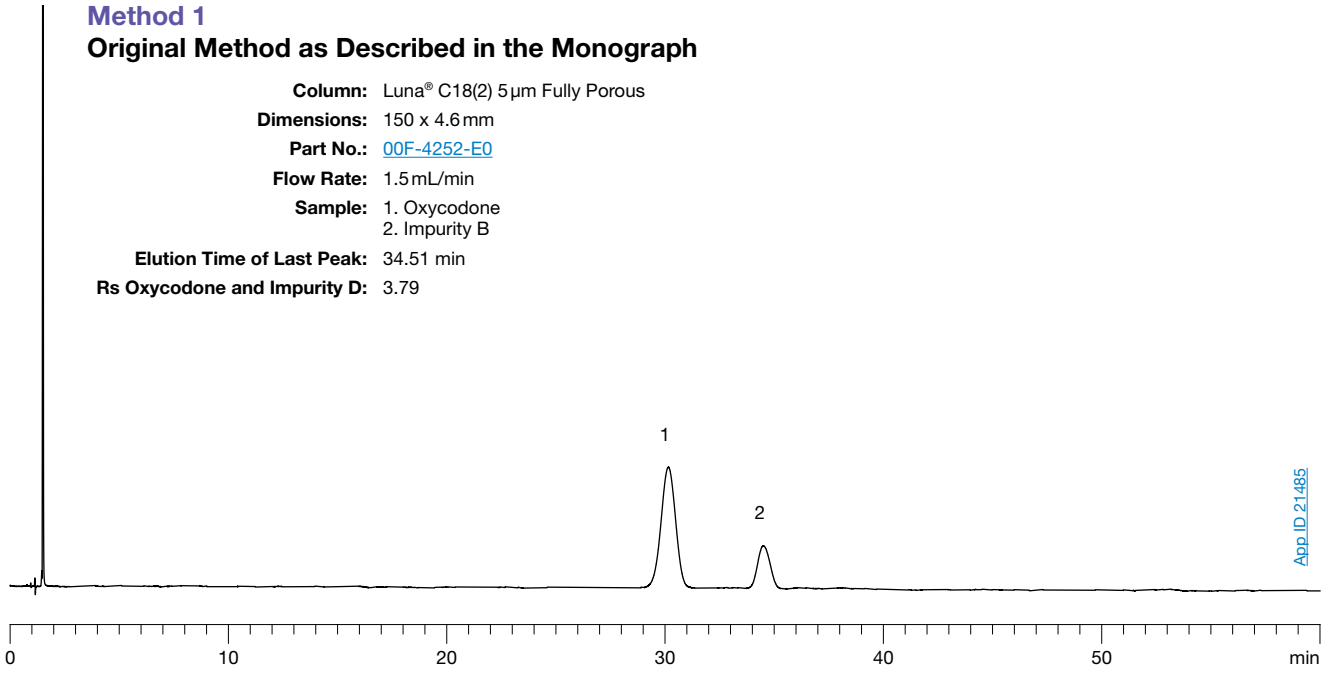
* Oxycodone Hydrochloride CRS (Y0000492) and Oxycodone Impurity D CRS (Y0000453) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

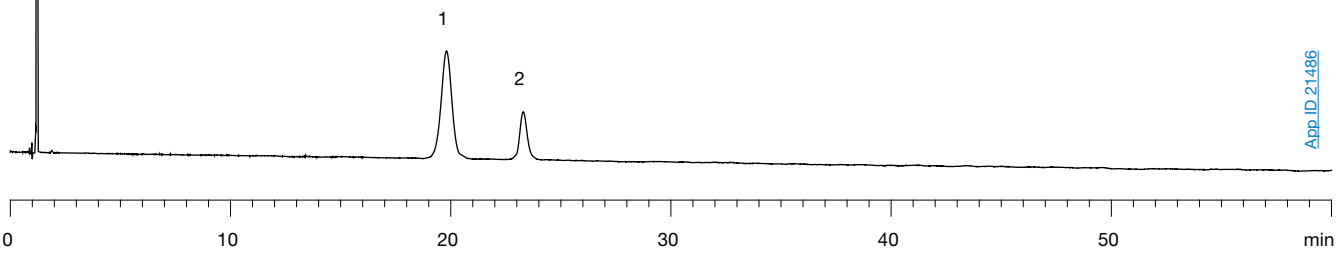
Original Method as Described in the Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.5 mL/min
Sample: 1. Oxycodone
2. Impurity B
Elution Time of Last Peak: 34.51 min
Rs Oxycodone and Impurity D: 3.79



Method 2
Faster Method Utilizing Core-Shell Technology

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.5 mL/min
Sample: 1. Oxycodone
2. Impurity B
Elution Time of Last Peak: 23.30 min
Rs Oxycodone and Impurity D: 4.75



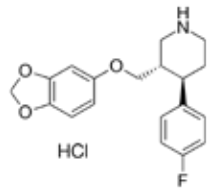
Adjustments for Meeting System Suitability
(European Pharmacopoeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2
Mobile Phase pH	No adjustment permitted	2 (as specified)	As specified
Concentration of Salts in Buffer	No adjustment permitted	As specified in Monograph 1793 Details Table	As specified
Composition of the Mobile Phase	Minor adjustments of the composition of the mobile phase and the gradient are acceptable, if the system suitability requirements are met, the principle peak(s) elute(s) within ± 15 % of the indicated retention time(s) and the final elution power of the mobile phase is not weaker in elution power than the prescribed composition	As specified in Monograph 1793 Details Table	As specified
Wavelength of Detector	No deviations permitted	230 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 5 °C	40 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	May be decreased, ± 70 %	150 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	No adjustment permitted	5 µm (as specified)	As specified
Flow Rate	Acceptable when changing the column dimensions	1.5 mL/min (as specified)	As specified

Paroxetine Hydrochloride and Related Substances

Ph. Eur. monograph 2283

The Ph. Eur. Monograph 2283 outlines the separation of Paroxetine Hydrochloride from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Paroxetine Hydrochloride

Ph. Eur. Monograph 2283 Details

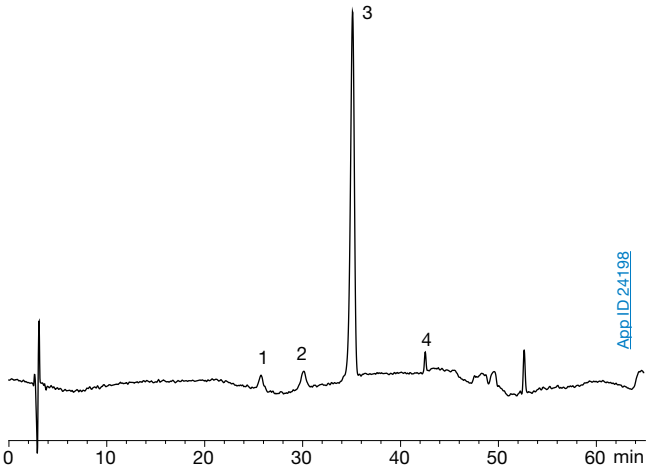
Solvent Mixture	Tetrahydrofuran R, water R (10:90 V/V)
Test Solution	Dissolve 50.0 mg of Paroxetine Hydrochloride (anhydrous) CRS* in the solvent mixture and dilute to 50.0 mL with the solvent mixture
Reference Solution	**(a)** Dilute 5.0 mL of the test solution to 50.0 mL with the solvent mixture **(c)** Dissolve 5.0 mg of anhydrous Paroxetine Hydrochloride Impurity C CRS* in 25 mL of tetrahydrofuran R and dilute to 50.0 mL with water R **(f)** Dissolve 2.5 mg of Paroxetine Impurity E CRS* in the solvent mixture, add 2.5 mL of the test solution and dilute to 100.0 mL with the solvent mixture **(g)** Dissolve 5 mg of Paroxetine Impurity A CRS* in the solvent mixture and dilute to 50 mL with the solvent mixture
Column	
Size	250 x 4.6 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	40 °C
Mobile Phase	A: Trifuoroacetic acid R, tetrahydrofuran R, water R (5:100:900 V/V/V) B: Trifuoroacetic acid R, tetrahydrofuran R, acetonitrile R (5:100:900 V/V/V)
Gradient	**Time (min) %B** 0 – 30 min 20 30 – 50 min 20 → 80 50 – 55 min 80 55 – 60 min 80 → 20 60 – 65 min 20
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 295 nm
Injection	20 µL of the test solution and reference solutions
Relative Retention with Reference to Paroxetine (about 28 min)**	
Impurity A	about 0.8
Impurity E	about 0.9
Impurity C	about 1.02
System Suitability	
Reference Solution (b)	Minimum resolution of 3.5 between peaks due to Impurity E and Paroxetine

* Paroxetine hydrochloride (anhydrous) CRS (Y0000578), Anhydrous Paroxetine Hydrochloride Impurity C CRS (Y0000579), Paroxetine Impurity E CRS (Y0000580) and Paroxetine Impurity A CRS (Y0000233) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

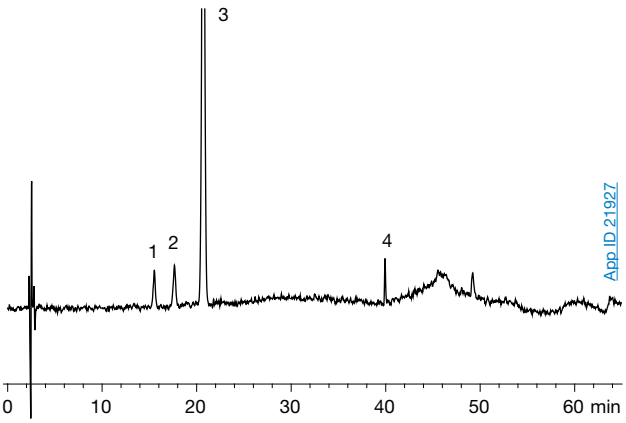
Method 1
Original Method as Described in the Monograph

Column: Luna® C8(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4249-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Impurity E
3. Paroxetine
4. Impurity C
Elution Time of Last Peak: 42.5 min
Rs Impurity E and Paroxetine: 6.06
Impurity E Peak Height: 0.14 mAU



Method 2
Faster Method Utilizing Core-Shell Technology

Column: Kinetex® Core-Shell C8 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4608-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Impurity E
3. Paroxetine
4. Impurity C
Elution Time of Last Peak: 40 min
Rs Impurity E and Paroxetine: 5.80
Impurity E Peak Height: 0.28 mAU



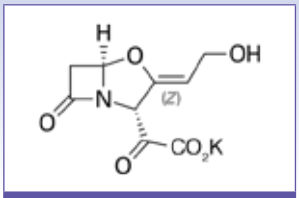
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2
Mobile Phase pH	No adjustment permitted	As specified	As specified
Concentration of Salts in Buffer	No adjustment permitted	As specified in Monograph 2283 Details Table	As specified
Composition of the Mobile Phase	Minor adjustments of the composition of the mobile phase and the gradient are acceptable, if the system suitability requirements are met, the principle peak(s) elute(s) within ± 15 % of the indicated retention time(s) and the final elution power of the mobile phase is not weaker in elution power than the prescribed composition	As specified in Monograph 2283 Details Table	As specified
Wavelength of Detector	No deviations permitted	295 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 5 °C	40° C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	End-capped octylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	250 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	No adjustment permitted	5 µm (as specified)	As specified
Flow Rate	Adjustment is acceptable when changing the column dimensions	1.0 mL/min (as specified)	As specified

Potassium Clavulanate and Related Substances

Ph. Eur. monograph 1140

The Ph. Eur. Monograph 1140 outlines the separation of Potassium Clavulanate from Amoxicillin. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Potassium Clavulanate

Ph. Eur. Monograph 1140 Details

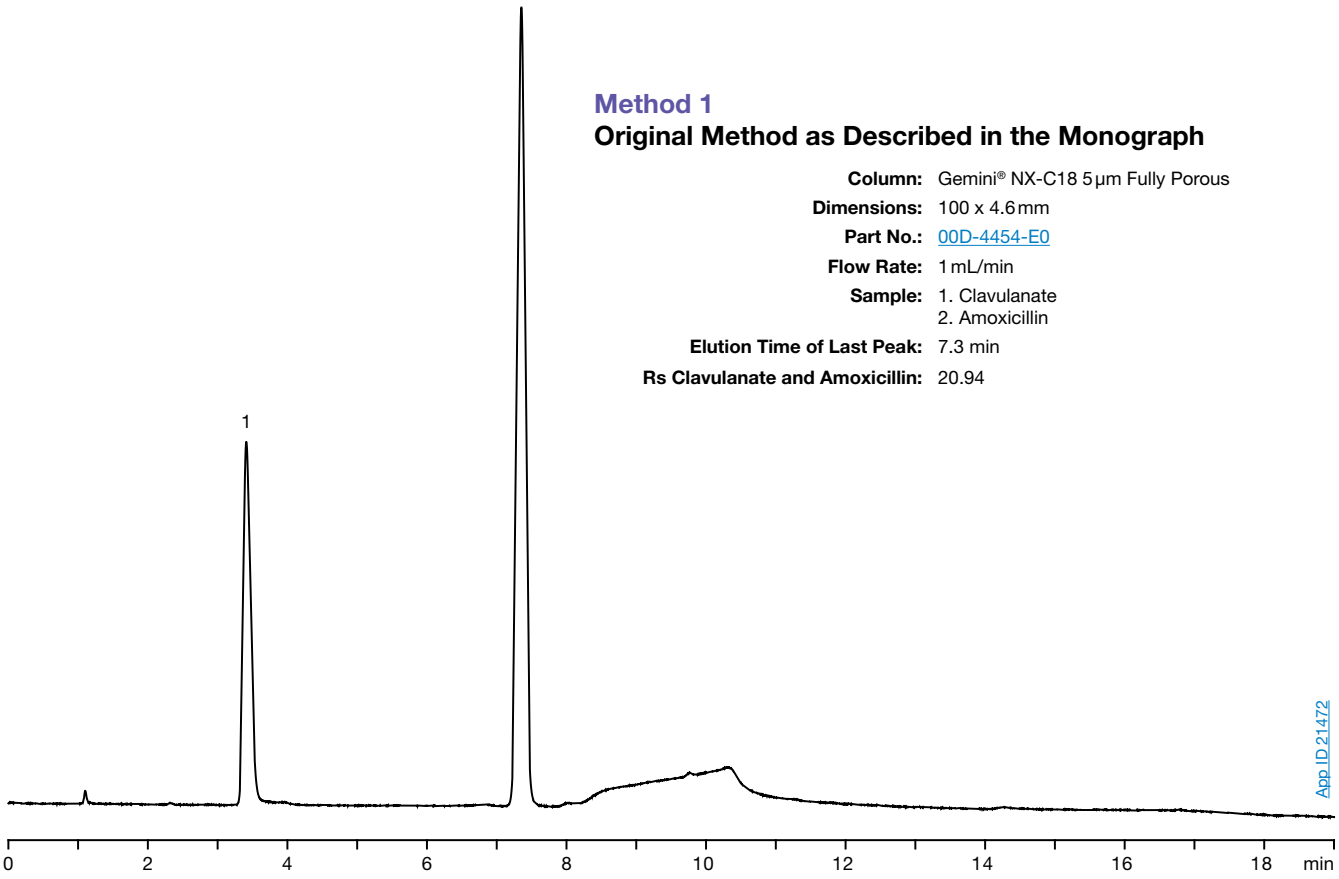
Reference Solution (b)	Dissolve 10 mg of Lithium Clavulanate CRS* and 10 mg of Amoxicillin Trihydrate CRS* in mobile phase A and dilute to 100 mL with mobile phase A
Column	
Size	100 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	40 °C
Mobile Phase	A: 7.8 g/L solution of sodium hydrogen phosphate R adjusted to pH 4.0 with phosphoric acid R B: Mixture of equal volumes of methanol R and mobile phase A
Gradient	**Time (min) %B** 0 – 4 0 4 – 15 0 → 50 15 – 18 50
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 230 nm
Injection	20 µL
System Suitability	
Reference Solution (b)	Minimum resolution of 13 between peaks due to Clavulanate (1st peak) and Amoxicillin (2nd peak)

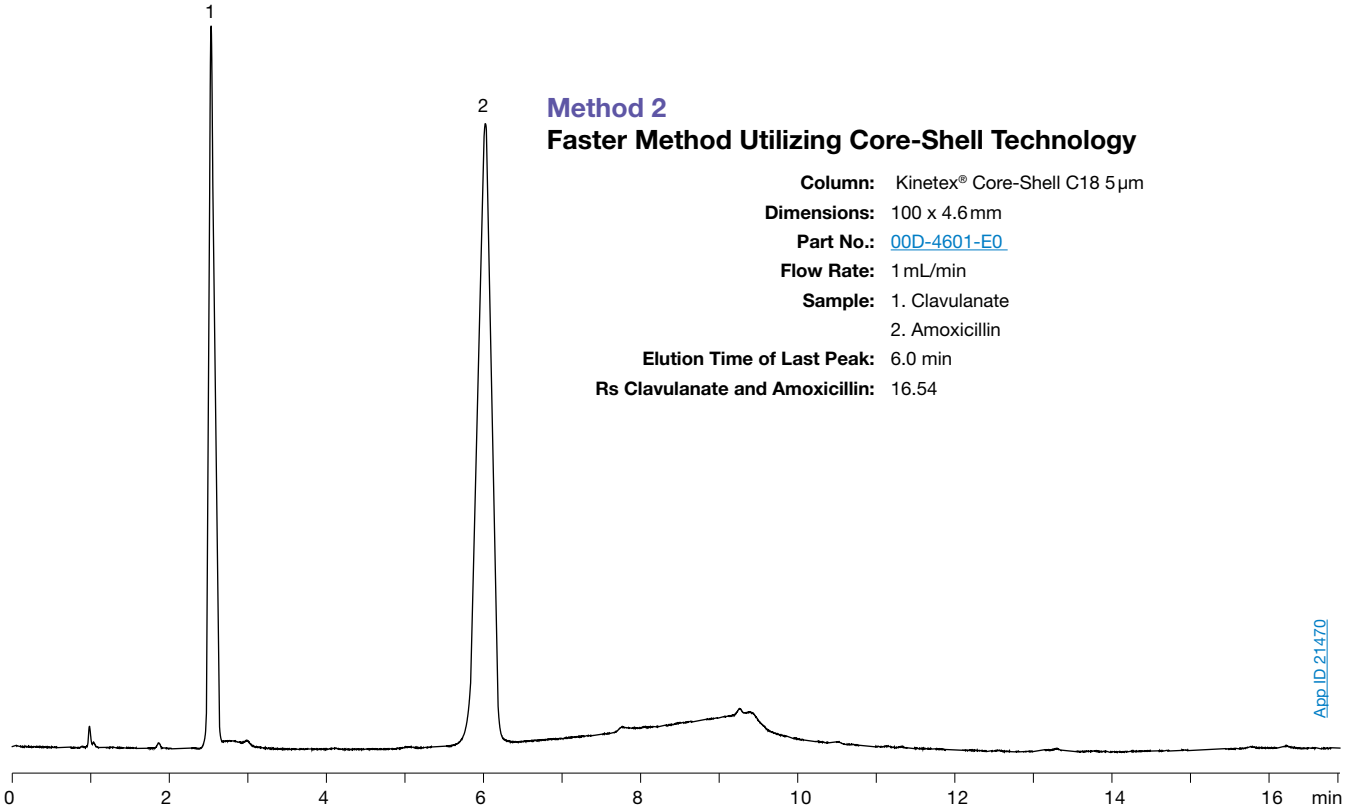
* Amoxicillin Trihydrate CRS (A0800000) and Lithium Clavulanate CRS (L0720000) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1

Original Method as Described in the Monograph

Column: Gemini® NX-C18 5 µm Fully Porous
Dimensions: 100 x 4.6 mm
Part No.: 00D-4454-E0
Flow Rate: 1 mL/min
Sample: 1. Clavulanate
2. Amoxicillin
Elution Time of Last Peak: 7.3 min
Rs Clavulanate and Amoxicillin: 20.94





Method 2
Faster Method Utilizing Core-Shell Technology

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4601-E0
Flow Rate: 1 mL/min
Sample: 1. Clavulanate
2. Amoxicillin
Elution Time of Last Peak: 6.0 min
Rs Clavulanate and Amoxicillin: 16.54

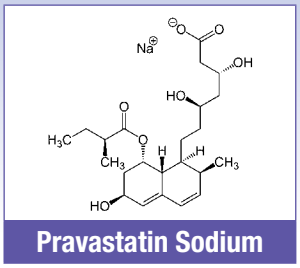
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2
Mobile Phase pH	No adjustment permitted	4 (as specified)	As specified
Concentration of Salts in Buffer	No adjustment permitted	As specified in Monograph 1140 Details Table	As specified
Composition of the Mobile Phase	Minor adjustments of the composition of the mobile phase and the gradient are acceptable, if the system suitability requirements are met, the principle peak(s) elute(s) within ± 15 % of the indicated retention time(s) and the final elution power of the mobile phase is not weaker in elution power than the prescribed composition	As specified in Monograph 1140 Details Table	As specified
Wavelength of Detector	No deviations permitted	230 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 5 °C	40 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	May be decreased, ± 70 %	100 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	No adjustment permitted	5 µm (as specified)	As specified
Flow Rate	Acceptable when changing the column dimensions	1 mL/min (as specified)	As specified

Pravastatin Sodium and Related Substances

Ph. Eur. monograph 2059

The Ph. Eur. Monograph 2059 outlines the separation of Pravastatin from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Pravastatin Sodium

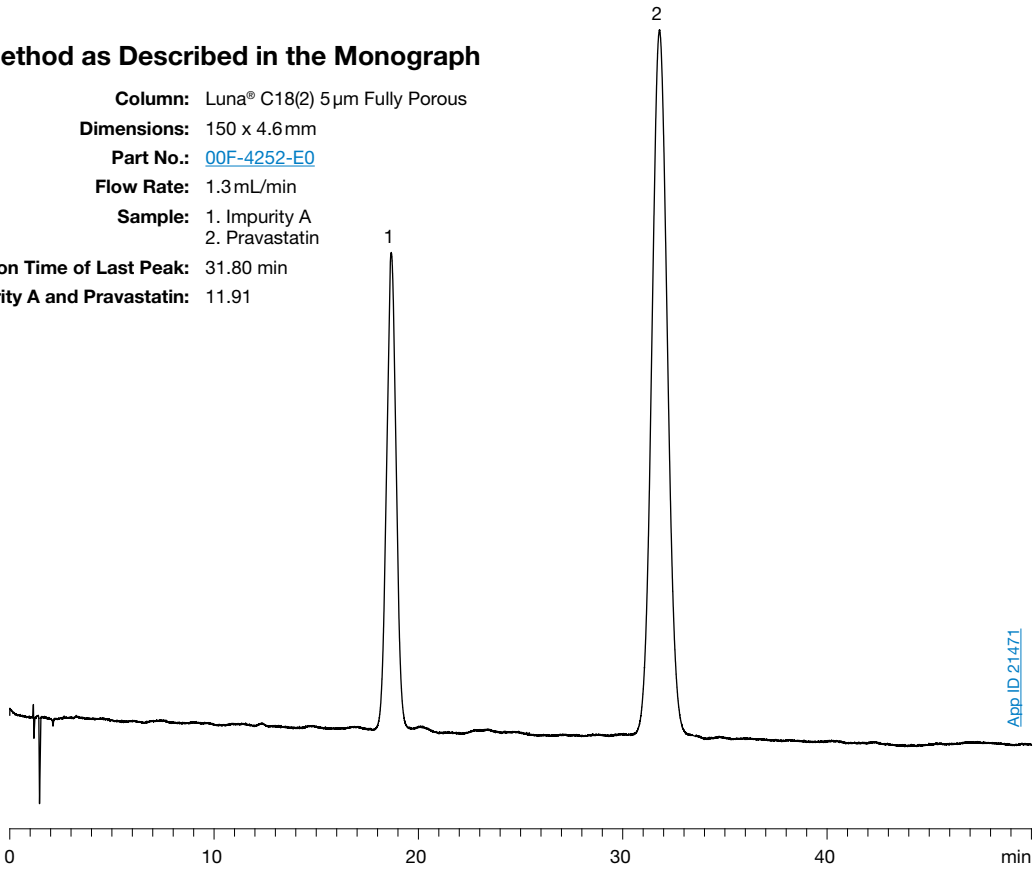
Ph. Eur. Monograph 2059 Details	
Solvent Mixture	Methanol R, water R (9:11 V/V)
Test Solution	**(a)** Dissolve 0.1000 g of Pravastatin 1,1,3,3-tetramethylbutylamine CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture **(b)** Dilute 10.0 mL of the test solution (a) to 100.0 mL with the solvent mixture
Reference Solution (a)	Dissolve the contents of a vial of Pravastatin Impurity A CRS* in 1.0 mL of test solution (b)
Column	
Size	150 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	25 °C
Mobile Phase	Glacial acetic acid R, trimethylamine R, methanol R, water R (1:1:450:550 V/V/V/V)
Flow Rate	1.3 mL/min
Detection	Spectrophotometer @ 238 nm
Injection	10 µL
Run Time	2.5 times the retention time of Pravastatin
Elution Order	1. Impurity A 2. Pravastatin
System Suitability	
Minimum resolution of 7.0 between peaks due to Impurity A and Pravastatin	

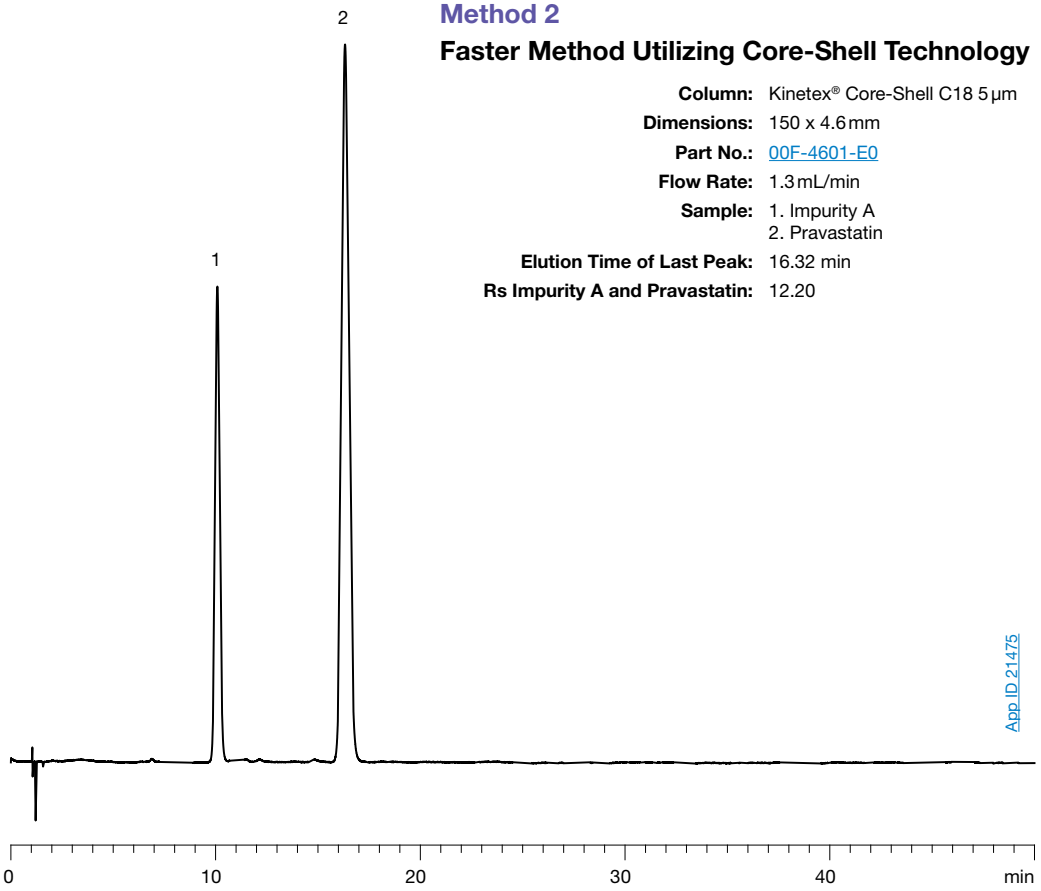
* Pravastatin 1,1,3,3-tetramethylbutylamine CRS (Y0000204) and Pravastatin Impurity A CRS (Y0000223) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1

Original Method as Described in the Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.3 mL/min
Sample: 1. Impurity A
2. Pravastatin
Elution Time of Last Peak: 31.80 min
Rs Impurity A and Pravastatin: 11.91





Method 2

Faster Method Utilizing Core-Shell Technology

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.3 mL/min
Sample: 1. Impurity A
2. Pravastatin
Elution Time of Last Peak: 16.32 min
Rs Impurity A and Pravastatin: 12.20

Adjustments for Meeting System Suitability

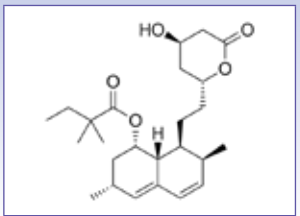
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 2059 Details Table	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 2059 Details Table	As specified
Wavelength of Detector	No deviations permitted	238 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)	As specified
Column Temperature	± 10 °C	25 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	150 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	-50 %	5 µm (as specified)	As specified
Flow Rate	± 50 %	1.3 mL/min (as specified)	As specified

Simvastatin and Related Substances

Ph. Eur. monograph 1563

The Ph. Eur. Monograph 1563 outlines the separation of Simvastatin from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Simvastatin

Ph. Eur. Monograph 1563 Details

Solvent Mixture	Mix 40 volumes of a 1.4 g/L solution of potassium dihydrogen phosphate R, adjusted to pH 4.0 with phosphoric acid R, and 60 volumes of acetonitrile R. Filter.
Reference Solution	**(a)** Dissolve 1.0 mg of Simvastatin CRS* and 1.0 mg of Lovastatin CRS* (Impurity E) in the solvent mixture and dilute to 50.0 mL with the solvent mixture **(d)** Dissolve 5 mg of Simvastatin for peak identification CRS* (containing Impurities A, B, C, D, E, F, and G) in 5 mL of the solvent mixture
Column	
Size	33 x 4.6 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (3 µm)
Temperature	25 °C
Mobile Phase	A: Mix 50 volumes of acetonitrile R and 50 volumes of a 0.1 % V/V solution of phosphoric acid R B: 0.1 % V/V solution of phosphoric acid R in acetonitrile R
Gradient	**Time (min)** — **%B** 0 – 4.5 — 0 4.5 – 4.6 — 0 → 5 4.6 – 8 — 5 → 95 8.0 – 11.5 — 75
Flow Rate	3 mL/min
Detection	Spectrophotometer @ 238 nm
Injection	5 µL
Relative Retention with Reference to Simvastatin (about 2.6 min)**	
Impurity A	about 0.5
Impurities E + F	about 0.6
Impurity G	about 0.8
Impurities B + C	about 2.4
Impurity D	about 3.8
System Suitability	
Minimum resolution of 4.0 between peaks due to Impurity E and Simvastatin	

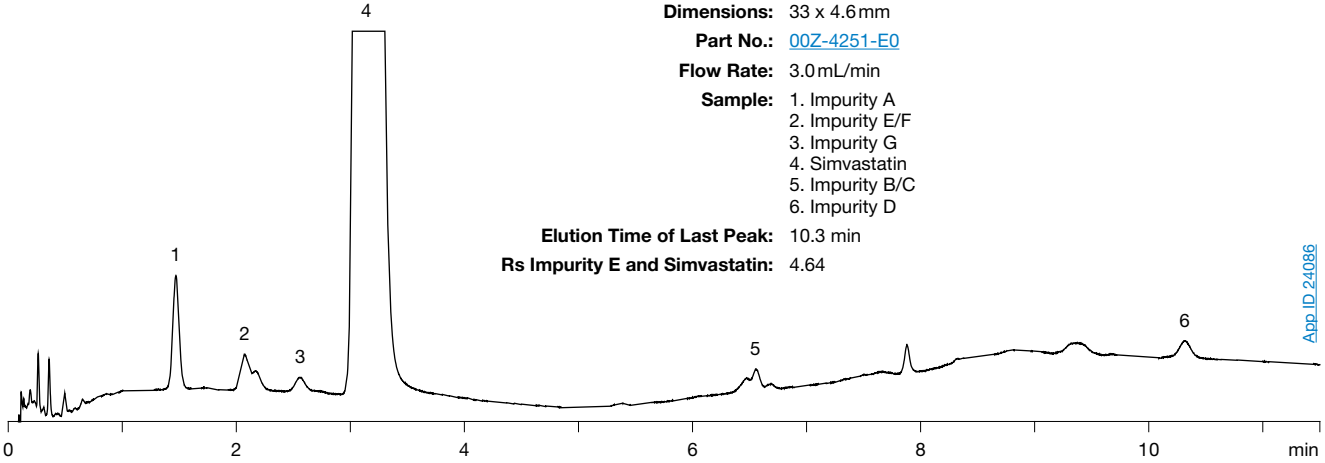
* Simvastatin CRS (S0650000), Lovastatin CRS (impurity E) (L0790000) and Simvastatin for peak identification CRS* (containing Impurities A, B, C, D, E, F, and G) (Y0001066) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method as Described in the Monograph

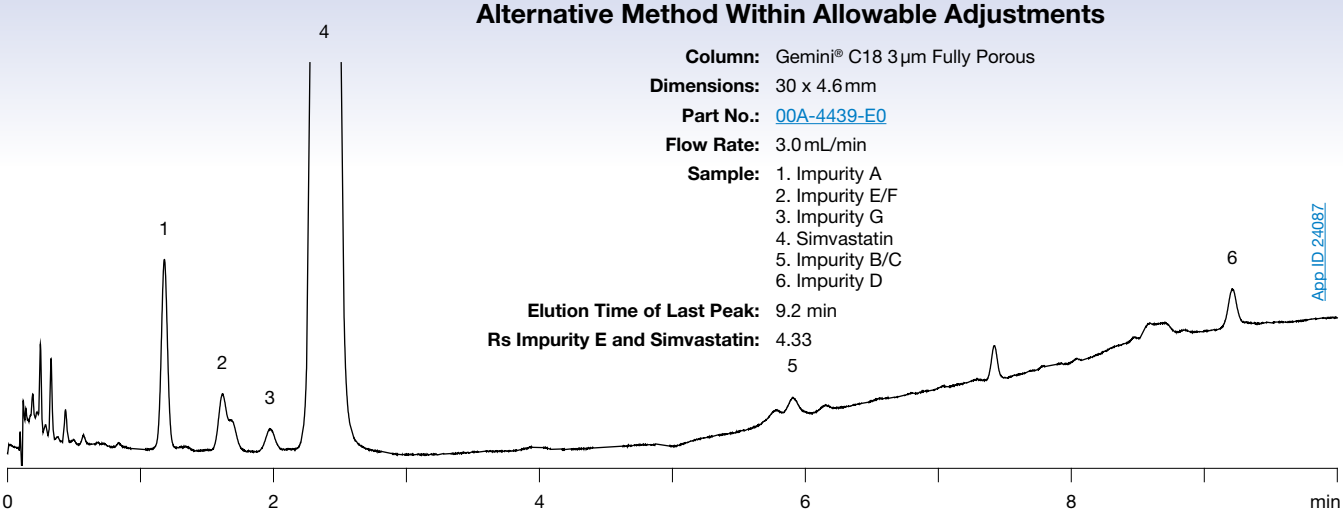
Column: Luna® C18(2) 3 µm Fully Porous
Dimensions: 33 x 4.6 mm
Part No.: 00Z-4251-E0
Flow Rate: 3.0 mL/min
Sample: 1. Impurity A
2. Impurity E/F
3. Impurity G
4. Simvastatin
5. Impurity B/C
6. Impurity D
Elution Time of Last Peak: 10.3 min
Rs Impurity E and Simvastatin: 4.64



Method 2
Alternative Method Within Allowable Adjustments

Column: Gemini® C18 3 µm Fully Porous
Dimensions: 30 x 4.6 mm
Part No.: 00A-4439-E0
Flow Rate: 3.0 mL/min
Sample: 1. Impurity A
2. Impurity E/F
3. Impurity G
4. Simvastatin
5. Impurity B/C
6. Impurity D
Elution Time of Last Peak: 9.2 min
Rs Impurity E and Simvastatin: 4.33

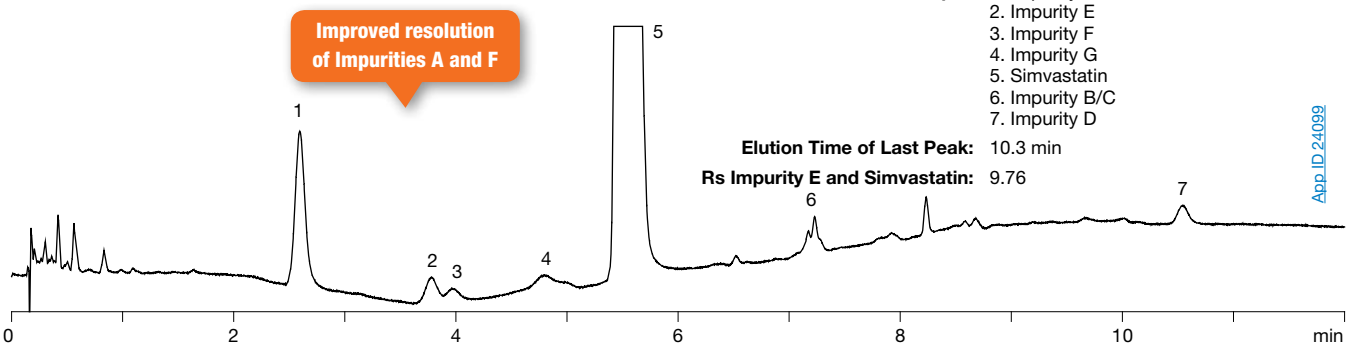
App ID 24087



Method 3
Faster Method Outside Allowable Adjustments

Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 50 x 4.6 mm
Part No.: 00B-4462-E0
Flow Rate: 3.0 mL/min
Sample: 1. Impurity A
2. Impurity E
3. Impurity F
4. Impurity G
5. Simvastatin
6. Impurity B/C
7. Impurity D
Elution Time of Last Peak: 10.3 min
Rs Impurity E and Simvastatin: 9.76

App ID 24099



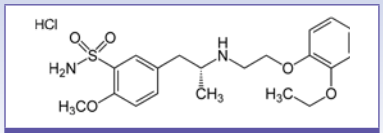
Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2	Method 3
Mobile Phase pH	No adjustment permitted	As specified	As specified	As specified
Concentration of Salts in Buffer	No adjustment permitted	As specified in Monograph 1563 Details Table	As specified	As specified
Composition of the Mobile Phase	Minor adjustments of the composition of the mobile phase and the gradient are acceptable, if the system suitability requirements are met, the principle peak(s) elute(s) within ± 15 % of the indicated retention time(s) and the final elution power of the mobile phase is not weaker in elution power than the prescribed composition	As specified in Monograph 1563 Details Table	As specified	As specified
Wavelength of Detector	No deviations permitted	238 nm (as specified)	As specified	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	5 µL (as specified)	As specified	As specified
Column Temperature	± 5 °C	Ambient (as specified)	As specified	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	End-capped octadcylsilyl silica gel for chromatography (as specified)	As specified	As specified
Column Length	± 70 %	33 mm (as specified)	30 mm (-9 %)	50 mm (+51 %)
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified	As specified
Particle Size	No adjustment permitted	3 µm (as specified)	As specified	2.6 µm (outside of allowed adjustments)
Flow Rate	Adjustment is acceptable when changing the column dimensions	3.0 mL/min (as specified)	As specified	As specified

Tamsulosin Hydrochloride and Related Substances

Ph. Eur. monograph 2131

The Ph. Eur. Monograph 2131 outlines the separation of Tamsulosin from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Tamsulosin

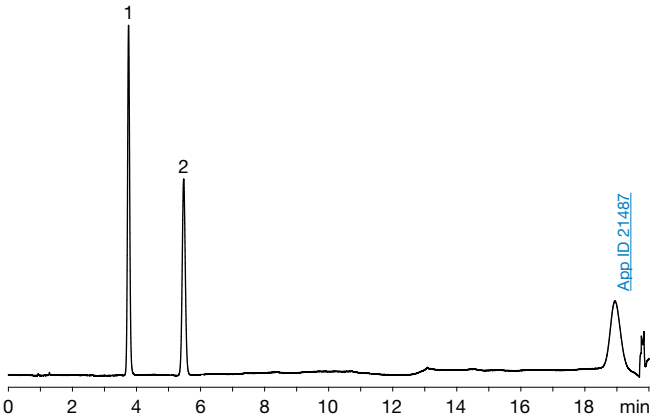
Ph. Eur. Monograph 2131 Details- Tamsulosin (A)	
Reference Solution	**(b)** Dissolve 4 mg of Tamsulosin Impurity D CRS* and 4 mg Tamsulosin Hydrochloride CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 20.0 mL with the mobile phase. **(c)** Dissolve 4 mg of Tamsulosin Impurity H CRS* and 4 mg Tamsulosin Hydrochloride CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 20.0 mL with the mobile phase.
Column	
Size	150 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm).
Temperature	40 °C
Mobile Phase	Dissolve 3.0 g of sodium hydroxide R in a mixture of 8.7 mL of perchloric acid R and 1.9 L of water R; adjust to pH 2.0 with 0.5 M sodium hydroxide and dilute to 2 L with water R; to 1.4 L of this solution, add 600 mL of acetonitrile R.
Flow Rate	1.3 mL/min
Detection	Spectrophotometer @ 225 nm
Injection	10 µL
Run Time	1.5 times the retention of Tamsulosin (about 6 min)
System Suitability	
Reference Solution (b)	Minimum resolution of 6.0 between peaks due to Impurity D and Tamsulosin

* Tamsulosin impurity D CRS* (Y0000651), Tamsulosin Impurity H CRS (Y0000652) and Tamsulosin Hydrochloride CRS (Y0000650) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1

Original Method as Described in the Monograph

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.3 mL/min
Sample: 1. Impurity B
2. Tamsulosin
Elution Time of Last Peak: 5.47 min
Rs Impurity D and Tamsulosin: 11.78



Adjustments for Meeting System Suitability

(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	2 (as specified)
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 2131 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 2131 Details Table
Wavelength of Detector	No deviations permitted	225 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)
Column Temperature	± 10 %	40 °C (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octadecylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	150 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.3 mL/min (as specified)

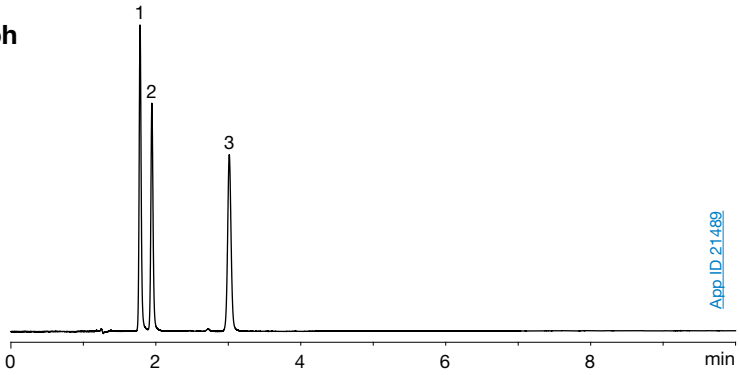
Ph. Eur. Monograph 2131 Details- Tamsulosin (B)

Reference Solution	**(c)** Dissolve 4 mg of Tamsulosin Impurity H CRS* and 4 mg Tamsulosin Hydrochloride CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 20.0 mL with the mobile phase.
Column	
Size	150 x 4.6 mm
Stationary Phase	Octadecylsilyl silica gel for chromatography R (5 µm).
Temperature	40 °C
Mobile Phase	Dissolve 3.0 g of sodium hydroxide R in a mixture of 8.7 mL of perchloric acid R and 1.9 L of water R; adjust to pH 2.0 with 0.5 M sodium hydroxide and dilute to 2 L with water R; add 2 L of acetonitrile R.
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 225 nm
Injection	10 µL
Run Time	5 times the retention of Tamsulosin (about 2.5 min)
System Suitability	
Reference Solution (c)	Minimum resolution of 2.0 between peaks due to Tamsulosin and Impurity H

* Tamsulosin Impurity D CRS* (Y0000651), Tamsulosin Impurity H CRS (Y0000652) and Tamsulosin Hydrochloride CRS (Y0000650) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1
Original Method as Described in the Monograph

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity D
2. Tamsulosin
3. Impurity H
Elution Time of Last Peak: 3.01 min
Rs Tamsulosin and Impurity H: 15.37



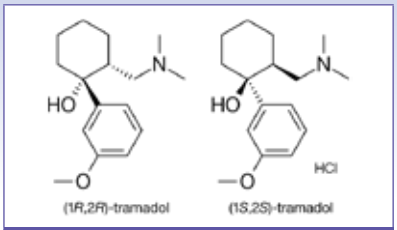
Adjustments for Meeting System Suitability
(European Pharmacopoeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	2 (as specified)
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 2131 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 2131 Details Table
Wavelength of Detector	No deviations permitted	225 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)
Column Temperature	± 10 °C	40 °C (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography
Column Length	± 70 %	150 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.0 mL/min (as specified)

Tramadol Hydrochloride and Related Substances

Ph. Eur. monograph 1681

The Ph. Eur. Monograph 1681 outlines the separation of Tramadol from impurities. This method was studied and recommendations have been made to conform with the Ph. Eur. Monograph 1681 requirements.



Tramadol Hydrochloride

Ph. Eur. Monograph 1681 Details	
Test Solution	Dissolve 0.15 g of Tramadol Hydrochloride CRS* in the mobile phase and dilute to 100 mL with the mobile phase.
Reference Solution (b)	Dissolve 5 mg of Tramadol Impurity A CRS* in 4.0 mL of the test solution and dilute to 100 mL with the mobile phase.
Column	
Size	250 x 4.0 mm
Stationary Phase	End-capped base-deactivated octylsilyl silica gel for chromatography R (5 µm)
Temperature	25 °C
Mobile Phase	295 volumes of acetonitrile R and 705 volumes of a mixture of 0.2 mL of trifluoroacetic acid R and 100 mL of water R
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 270 nm
Injection	20 µL
Run Time	4 times the retention time of Tramadol
Relative Retention with Reference to Tramadol (about 5 min)**	
Impurity A	about 0.85 min
System Suitability	
Reference Solution (b)	Minimum resolution of 2.0 between peaks due to Impurity A and Tramadol

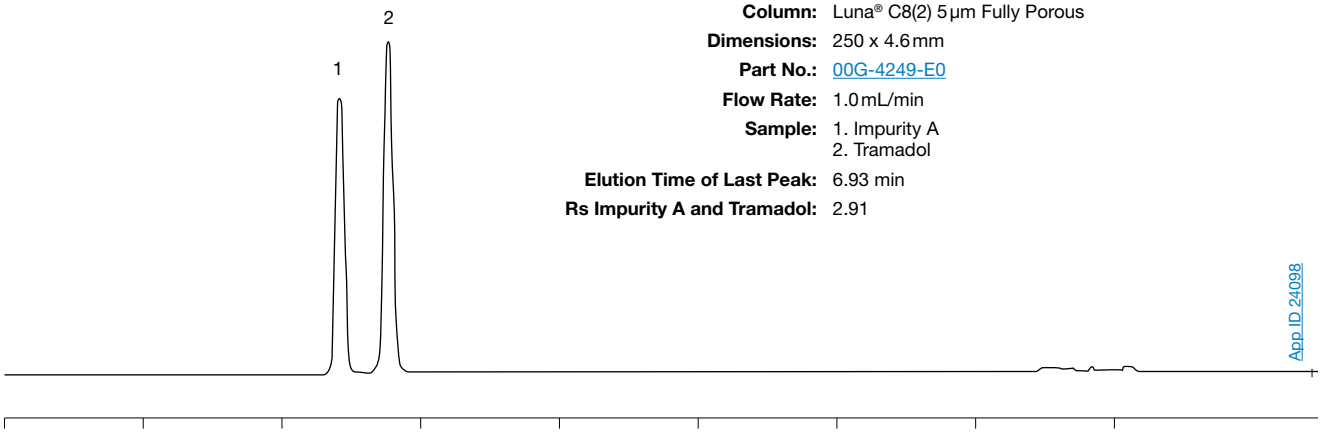
* Tramadol Hydrochloride CRS (Y0000155) and Tramadol Impurity A CRS (Y0000156) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Improved Resolution Within Allowable Adjustments

Column: Luna® C8(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4249-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Tramadol
Elution Time of Last Peak: 6.93 min
Rs Impurity A and Tramadol: 2.91



Adjustments for Meeting System Suitability

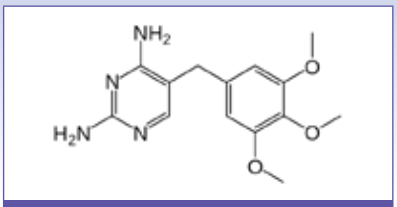
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1681 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1681 Details Table
Wavelength of Detector	No deviations permitted	270 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)
Column Temperature	± 10 °C	Ambient (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	250 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.0 ml/min (as specified)

Trimethoprim and Related Substances

Ph. Eur. monograph 0060

The Ph. Eur. Monograph 0060 outlines the separation of Trimethoprim from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.



Trimethoprim

Ph. Eur. Monograph 0060 Details

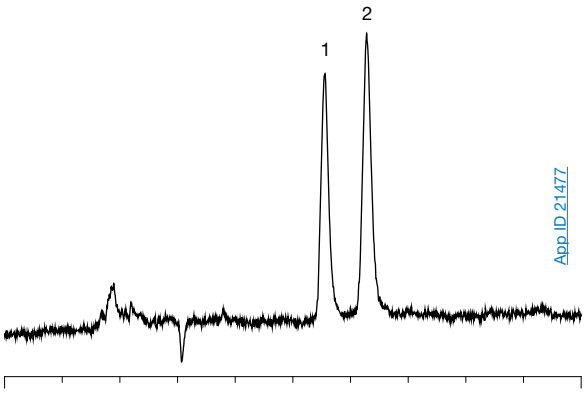
Reference Solution (b)	Dissolve the contents of a vial of Trimethoprim for system suitability CRS* (containing Impurity E) in 1 mL of mobile phase.
Column	
Size	250 x 4.0 mm
Stationary Phase	Base-deactivated octadecylsilyl silica gel for chromatography R (5 µm)
Temperature	25 °C
Mobile Phase	Mix 30 volumes of methanol R and 70 volumes of a 1.4 g/L solution of sodium perchlorate R adjusted to pH 3.6 with phosphoric acid R.
Flow Rate	1.3 mL/min
Detection	Spectrophotometer @ 280 nm
Injection	20 µL loop injector
Run Time	11 times the retention time of Trimethoprim
System Suitability	
Reference Solution (b)	Minimum resolution of 2.5 between peaks due to Impurity E and Trimethoprim

* Trimethoprim for system suitability CRS (containing Impurity E) (Y0000684) was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Method 1

Original Method as Described in the Monograph

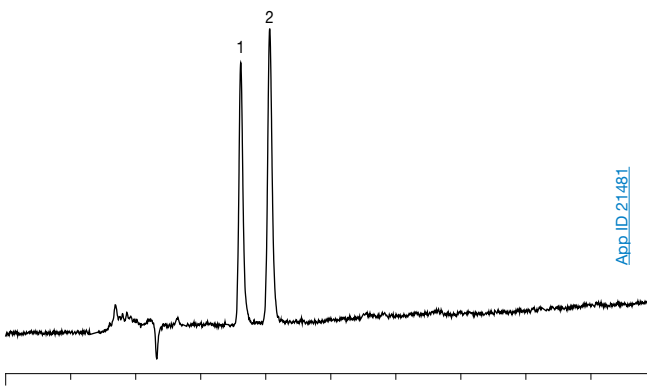
Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4252-E0
Flow Rate: 1.3 mL/min
Sample: 1. Impurity E
2. Trimethoprim
Elution Time of Last Peak: 6.28 min
Rs Impurity E and Trimethoprim: 2.92



Method 2

Faster Method Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 1.3 mL/min
Sample: 1. Impurity E
2. Trimethoprim
Elution Time of Last Peak: 4.06 min
Rs Impurity E and Trimethoprim: 3.85



Adjustments for Meeting System Suitability

(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	3.6 (as specified)	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 0060 Details Table	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 0060 Details Table	As specified
Wavelength of Detector	No deviations permitted	280 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	Octadecylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	250 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)	As specified
Flow Rate	± 50 %	1.3 mL/min (as specified)	As specified

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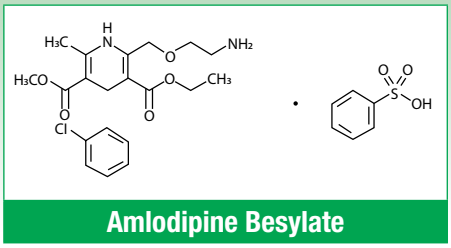
United States Pharmacopeia (USP) Monographs for Generic Drugs

Amlodipine Besylate

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Amlodipine Besylate. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Amlodipine Besylate

USP Monograph: Amlodipine Besylate Details

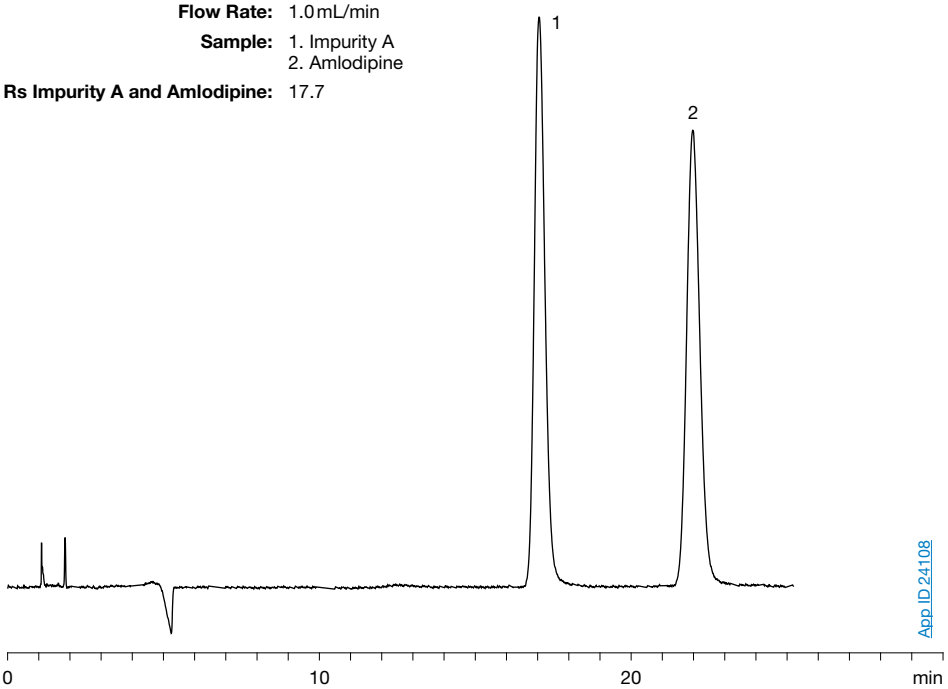
pH 3.0 Buffer	Dissolve 7.0 of triethylamine in 800 mL of water. Adjust with phosphoric acid to a pH of 3.0± 0.1, and dilute with water to 1 L.
System Suitability Solution	Dissolve about 5 mg of Amlodipine Besylate in 5 mL of hydrogen peroxide, and heat at 70° C for 45 minutes
Standard Preparation	Dissolve USP Amlodipine Besylate RS in mobile phase to obtain a concentration of 0.003 mg/mL
Test Solution	Dissolve 50 mg of Amlodipine Besylate in a 50 mL volumetric flask and dilute to volume with mobile phase
Column	
Size	150 x 3.9 mm
Stationary Phase	L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod
Mobile Phase	pH 3.0 Buffer, Methanol and acetonitrile (50:35:15)
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 237 nm
Injection	10 µL
Relative Retention with Reference to Amlodipine*	
Benzene Sulfonate	about 0.2
Impurity A	about 0.5
System Suitability	
Minimum resolution of 4.5 between Amlodipine and Impurity A	

* Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

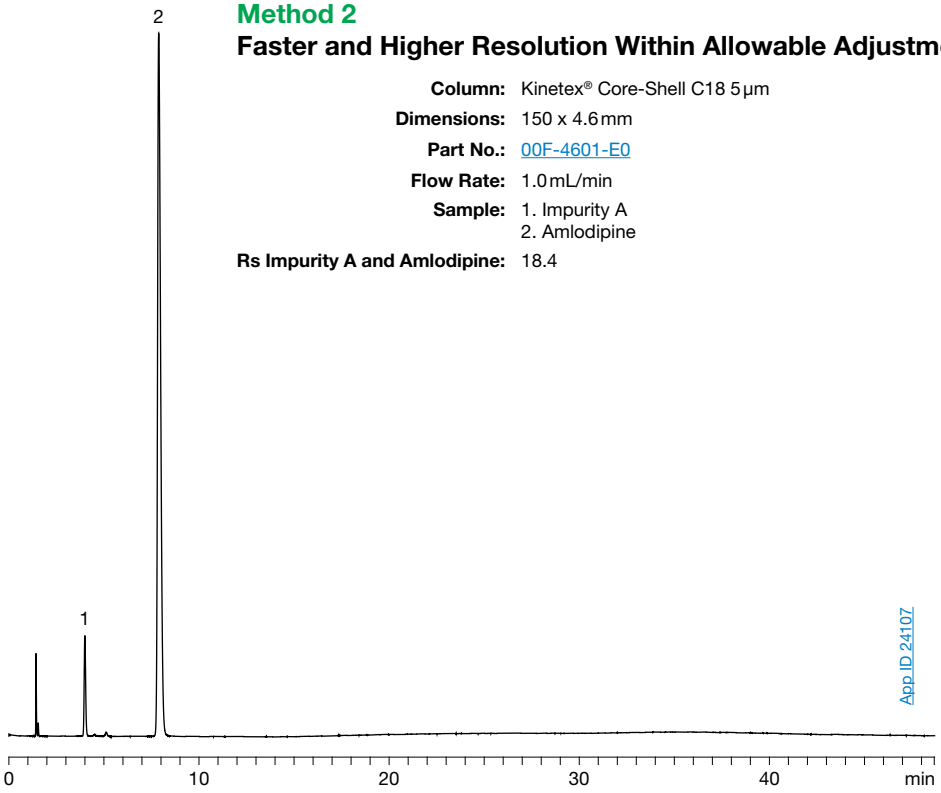
Method 1

Standard Method Within Allowable Adjustments

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Amlodipine
Rs Impurity A and Amlodipine: 17.7



Reduce run times by >50% with Kinetex Core-Shell Columns



Method 2

Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Amlodipine
Rs Impurity A and Amlodipine: 18.4

Adjustments for Meeting System Suitability

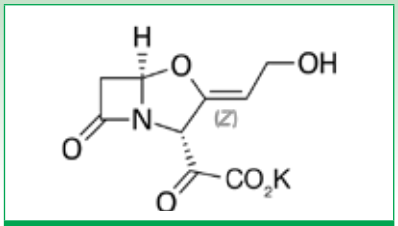
Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	237 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	10 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	150 mm (as specified)	As specified
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (+18 %)	4.6 mm (+18 %)
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	5 µm (as specified)	As specified
Flow Rate	± 50 % (at given ID)	1.0 mL/min (as specified)	As specified

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Clavulanate Potassium and Related Substances

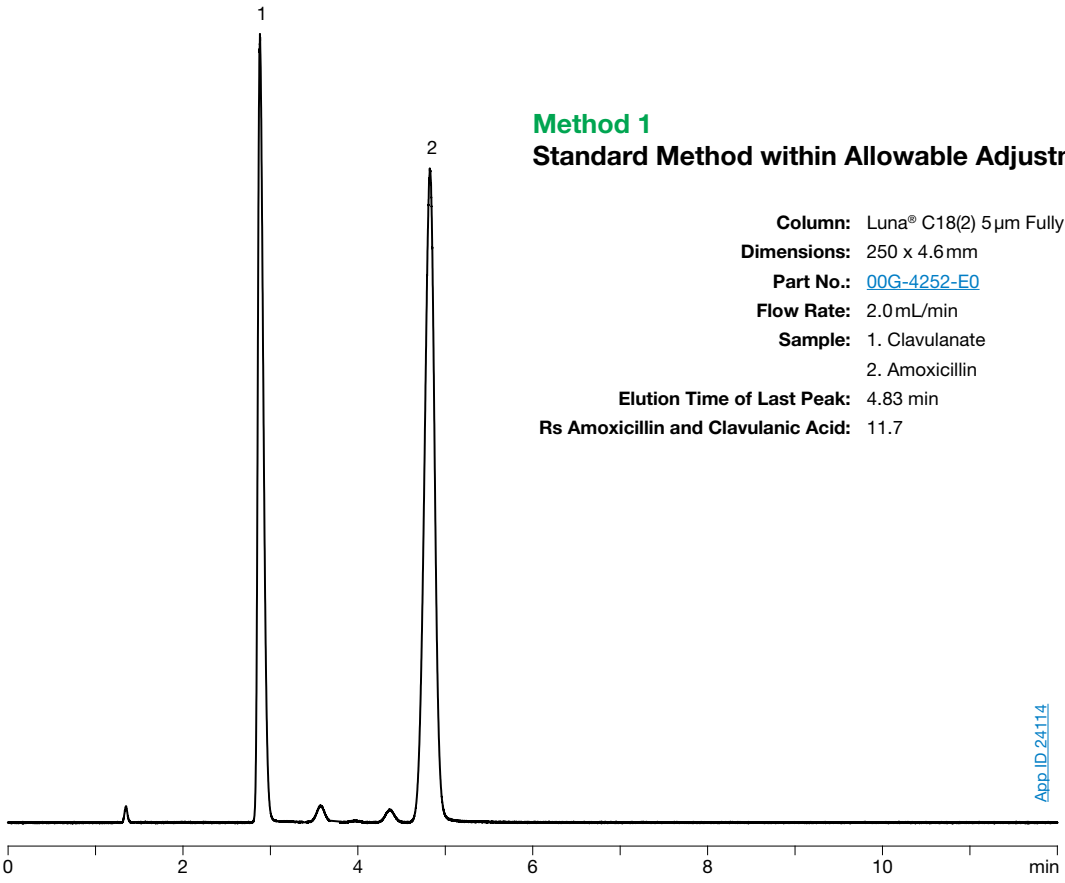
USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Clavulanate Potassium. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Clavulanate Potassium

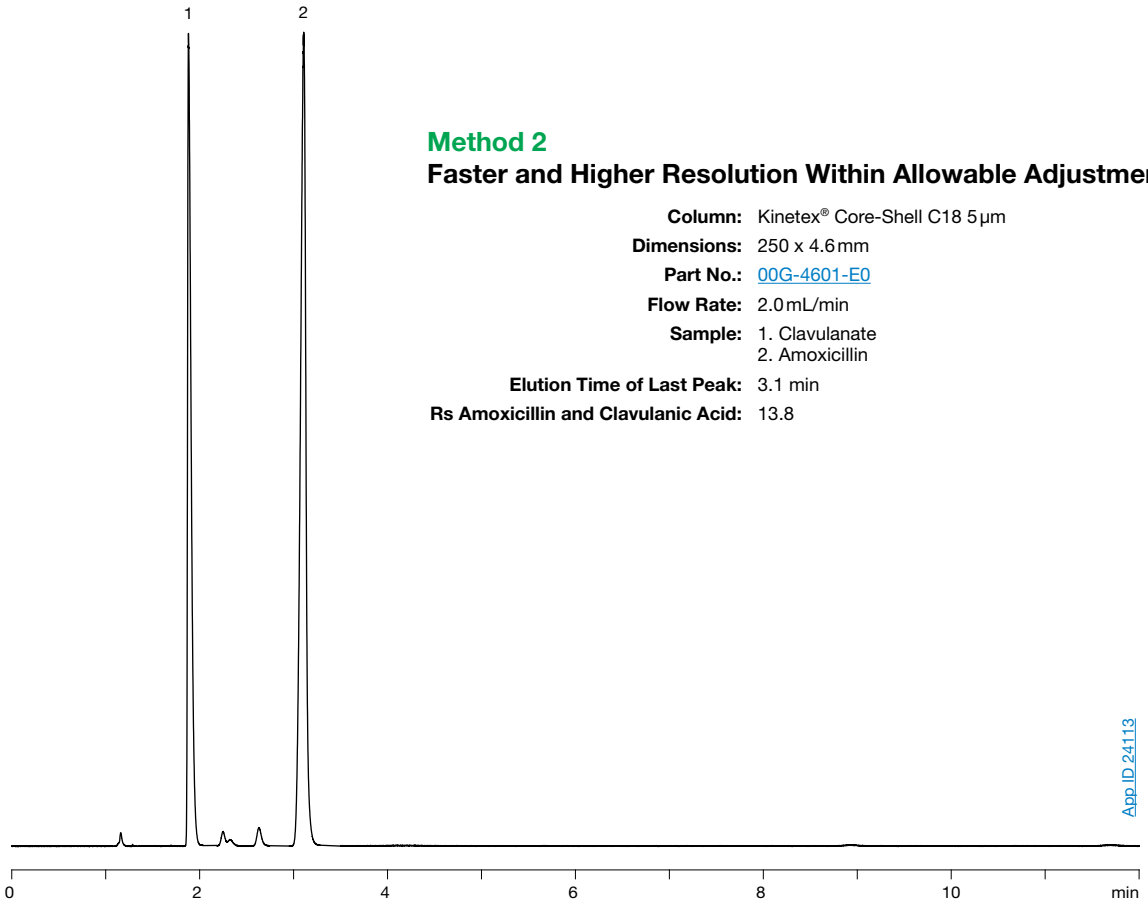
USP Monograph: Clavulanate Potassium Details	
Solution A	7.8 mg/mL of monobasic sodium phosphate in water. Adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 4.4 ± 0.1 before final dilution.
Standard Solution	0.25 mg/mL of USP Clavulanate Lithium RS in water
System Suitability Solution	0.5 mg/ml of Amoxicillin dissolved in Standard Solution
Sample Solution	0.25 mg/mL of Clavulanate Potassium in water
Column	
Size	30 x 4.0 mm
Stationary Phase	L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod
Mobile Phase	Methanol and Solution A (1:19)
Flow Rate	2.0 mL/min
Detection	Spectrophotometer @ 220 nm
Injection	20 µL
System Suitability	
Minimum resolution of 3.5 between Amoxicillin and Clavulanic Acid	



Method 1

Standard Method within Allowable Adjustments

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4252-E0
Flow Rate: 2.0 mL/min
Sample: 1. Clavulanate
2. Amoxicillin
Elution Time of Last Peak: 4.83 min
Rs Amoxicillin and Clavulanic Acid: 11.7



Method 2

Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 2.0 mL/min
Sample: 1. Clavulanate
2. Amoxicillin
Elution Time of Last Peak: 3.1 min
Rs Amoxicillin and Clavulanic Acid: 13.8

Adjustments for Meeting System Suitability

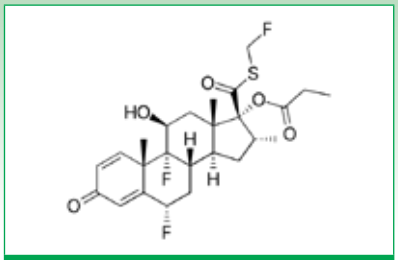
Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	220 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	20 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	250 mm (-17 %)	250 mm (-17 %)
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	5 µm (as specified)	As specified
Flow Rate	± 50 % (at given ID)	2.0 mL/min (as specified)	As specified

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Fluticasone Propionate and Related Substances

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Fluticasone Propionate. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Fluticasone Propionate

USP Monograph: Fluticasone Propionate Details

System Suitability Solution	Dissolve 2.0 mg of USP Fluticasone Propionate
System Suitability Mixture	RS in 5 mL of Solution A using sonication. Add 5 mL of Solution C.
Sample Solution	Dissolve 2.0 mg of Fluticasone Propionate in 5 mL of Solution A using sonication. Add 5 mL of Solution C.
Column	
Size	250 x 4.6 mm
Stationary Phase	5 µm, L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod
Mobile Phase	**A:** 0.5 mL of phosphoric acid in 1000 mL of acetonitrile **B:** 0.5 mL of phosphoric acid in 1000 mL of methanol **C:** 0.5 mL of phosphoric acid in 1000 mL of water
Gradient	**Time (min): % (A/B/C)** 0 42/3/55 40 53/3/44 60 87/3/10 70 87/3/10 75 42/3/55
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 239 nm
Injection	50 µL
Relative Retention with Reference to Fluticasone Propionate*	
Related Compound A	about 0.5
Related Compound B	about 0.75
Related Compound C	about 0.8
Related Compound D	about 0.95
Related Compound E	about 1.3
System Suitability	
Minimum resolution of 0.6 between Related Compound B and Related Compound C. Minimum resolution of 1.5 between Related Compound D and Fluticasone Propionate.	

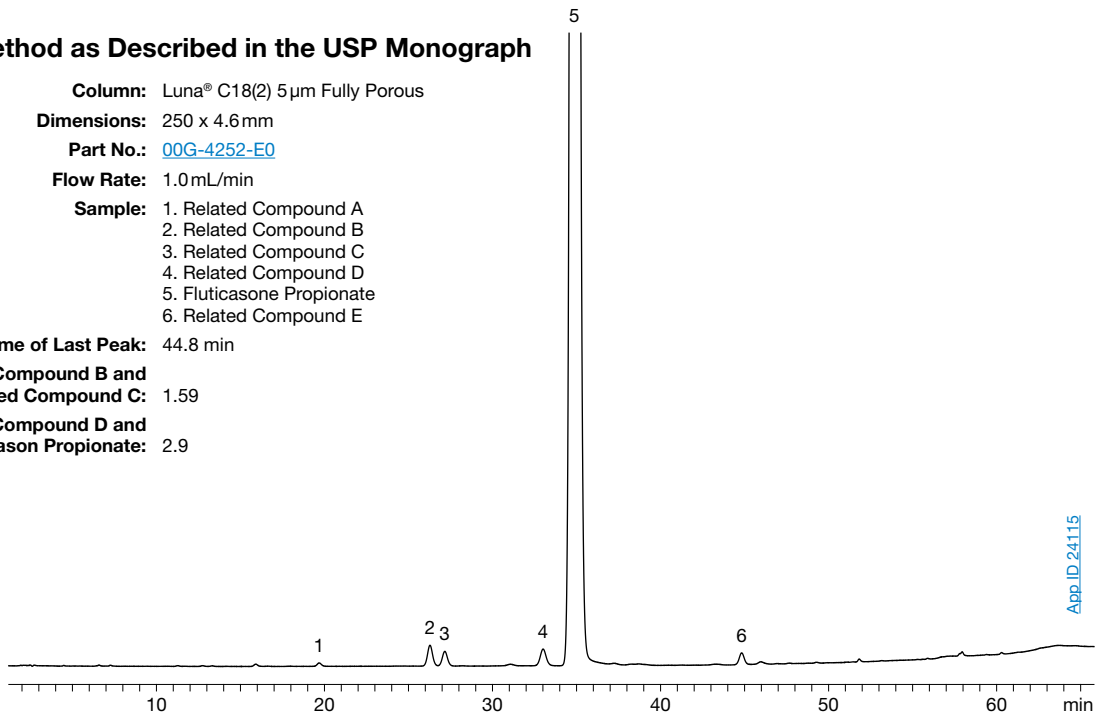
* Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

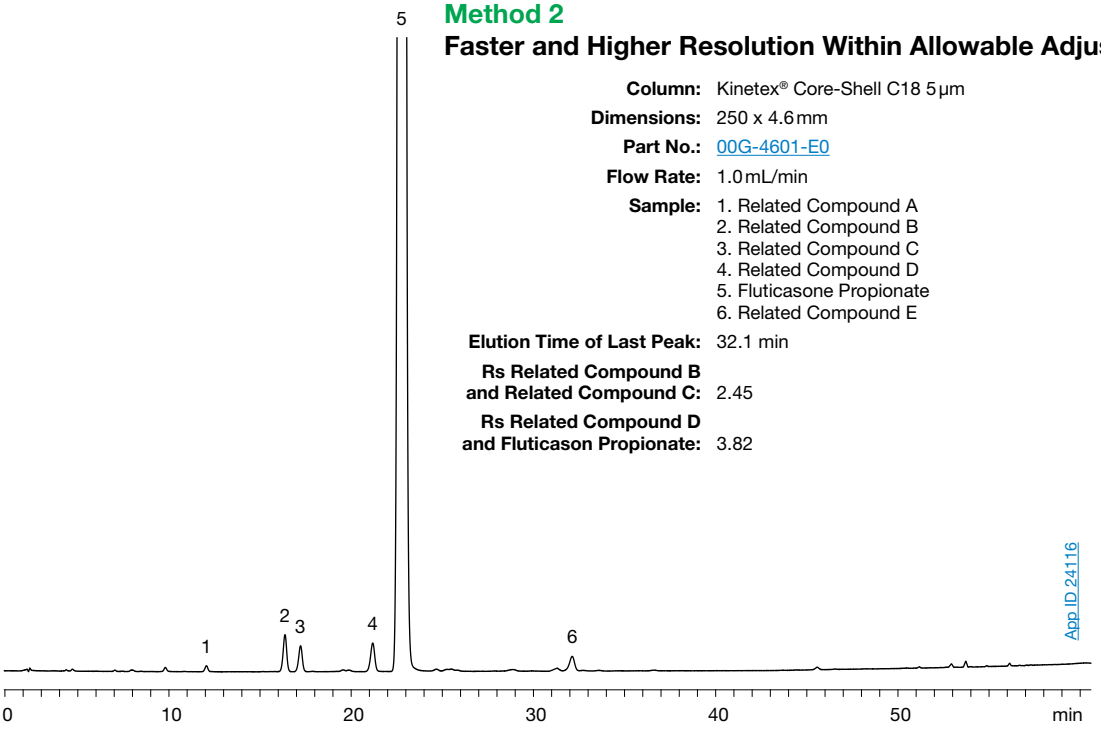
Method 1

Original Method as Described in the USP Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4252-E0
Flow Rate: 1.0 mL/min
Sample:
1. Related Compound A
2. Related Compound B
3. Related Compound C
4. Related Compound D
5. Fluticasone Propionate
6. Related Compound E

Elution Time of Last Peak: 44.8 min
Rs Related Compound B and Related Compound C: 1.59
Rs Related Compound D and Fluticason Propionate: 2.9





Method 2

Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 1.0 mL/min
Sample:
1. Related Compound A
2. Related Compound B
3. Related Compound C
4. Related Compound D
5. Fluticasone Propionate
6. Related Compound E

Elution Time of Last Peak: 32.1 min
Rs Related Compound B and Related Compound C: 2.45
Rs Related Compound D and Fluticason Propionate: 3.82

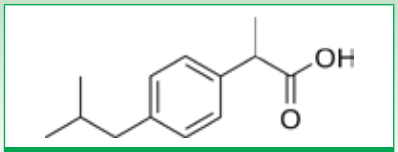
Adjustments for Meeting System Suitability

Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	Changes to gradient composition are not recommended	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	239 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	50 µL (as specified)	As specified
Column Temperature	± 10 °C	40 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	No deviations permitted	250 mm (as specified)	As specified
Column Internal Diameter	No deviations permitted	4.6 mm (as specified)	As specified
Particle Size	No deviations permitted	5 µm (as specified)	As specified
Flow Rate	No deviations permitted	1.0 mL/min (as specified)	As specified

Ibuprofen

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Ibuprofen. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Ibuprofen

USP Monograph: Ibuprofen Details

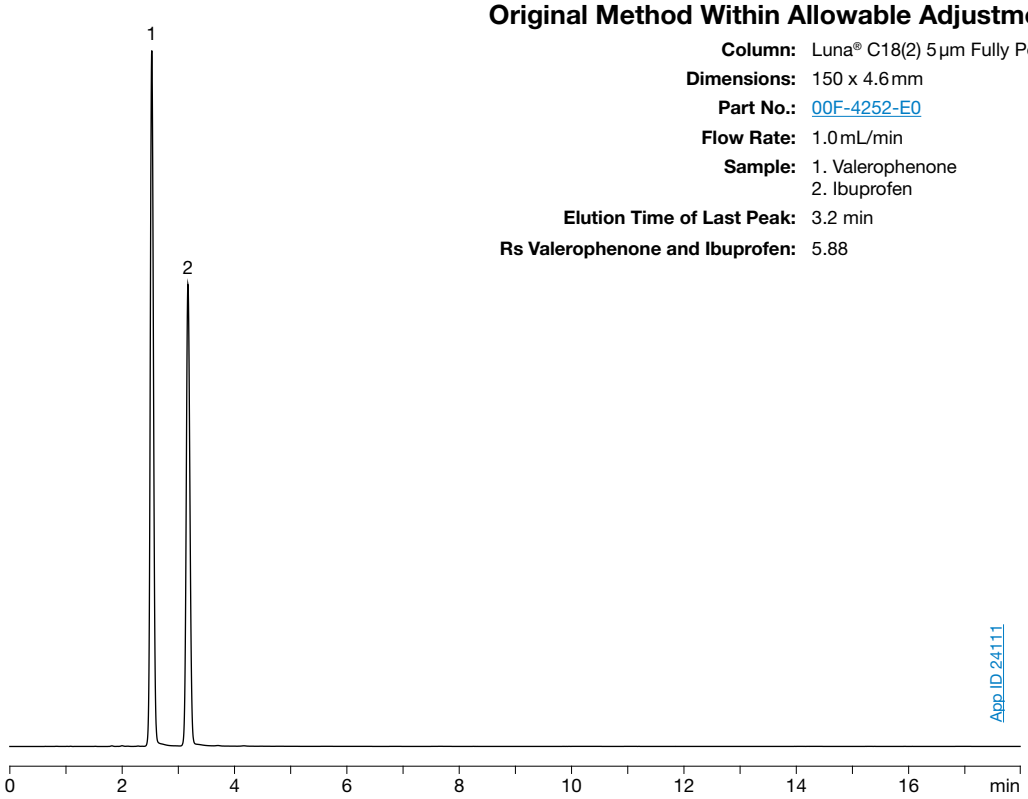
Resolution Solution	Prepare a solution in acetonitrile containing in each mL about 5 mg of Ibuprofen and 5 mg of Valerophenone
Test Preparation	Prepare a solution of Ibuprofen in acetonitrile containing about 5 mg per mL
Column	
Size	150 x 4.0 mm
Stationary Phase	5 µm, L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod
Temperature	30 °C ± 0.5 °C
Mobile Phase	Prepare a suitable filtered mixture of water, previously adjusted with phosphoric acid to pH 2.5 and acetonitrile (1340:680).
Flow Rate	2.0 mL/min
Detection	Spectrophotometer @ 214 nm
Injection	5 µL
Relative Retention with Reference to Ibuprofen*	
Valerophenone	about 0.8
System Suitability	
Minimum resolution of 2.0 between Valerophenone and Ibuprofen	

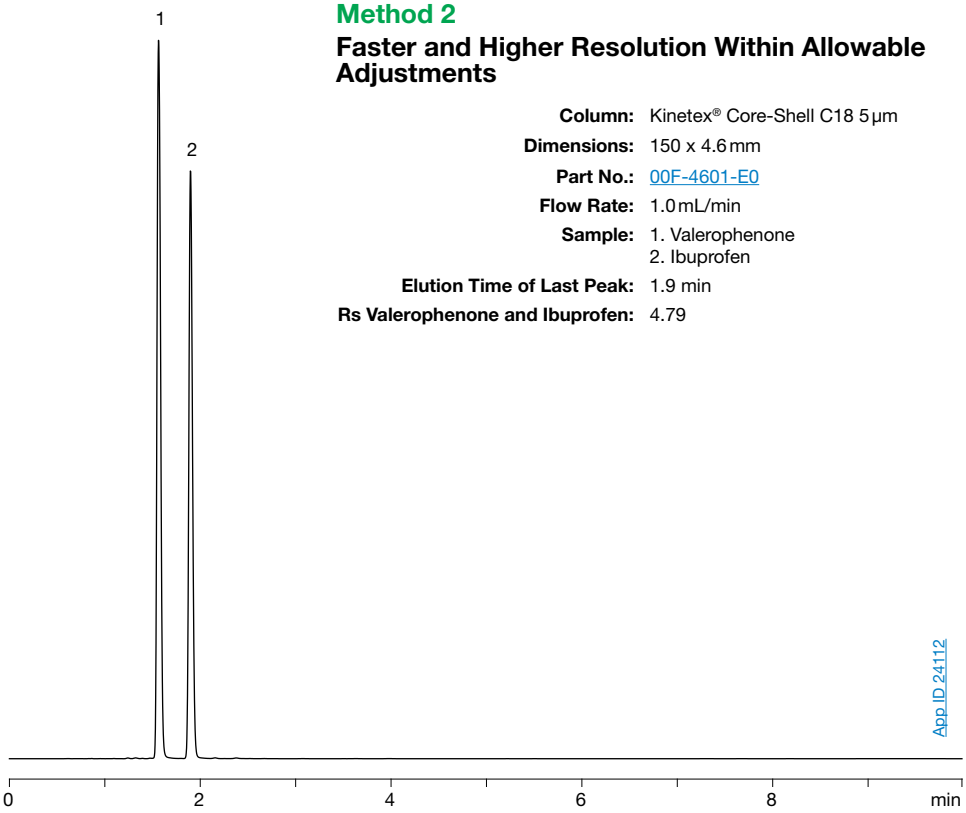
* Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method Within Allowable Adjustments

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4252-E0
Flow Rate: 1.0 mL/min
Sample: 1. Valerophenone
2. Ibuprofen
Elution Time of Last Peak: 3.2 min
Rs Valerophenone and Ibuprofen: 5.88





Method 2

Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Flow Rate: 1.0 mL/min
Sample: 1. Valerophenone
2. Ibuprofen
Elution Time of Last Peak: 1.9 min
Rs Valerophenone and Ibuprofen: 4.79

Adjustments for Meeting System Suitability

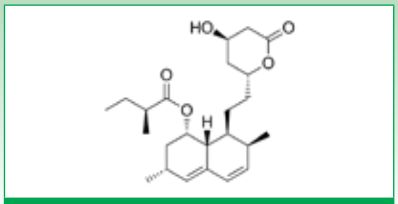
Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	214 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	5 µL (as specified)	As specified
Column Temperature	± 10 °C	30 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	150 mm (as specified)	As specified
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	5 µm (as specified)	As specified
Flow Rate	± 50 % (at given ID)	1.0 mL/min (-50 %)	1.0 mL/min (-50 %)

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Lovastatin

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Lovastatin. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Lovastatin

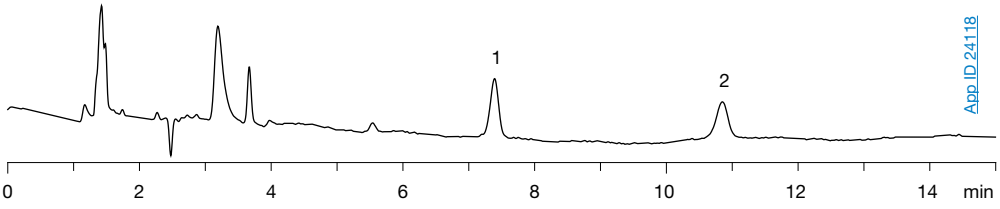
USP Monograph: Lovastatin Details	
System Suitability Solution	Dissolve USP Lovastatin RS and USP Lovastatin Related Compound A RS in acetonitrile to obtain a concentration of 2.0 µg/mL of each
Standard Solution	Dissolve USP Lovastatin RS in acetonitrile to obtain a concentration of about 2.0 µg/mL
Test Solution	Dissolve 25 mg of Lovastatin in a 25 mL volumetric flask and dilute to volume with acetonitrile, mix
Column	
Size	250 x 4.6 mm
Stationary Phase	5 µm, L7: Octyl silane chemically bonded to totally or superficially porous silica particles, 1.5 to 10 µm in diameter, or a monolithic silica rod
Temperature	40 °C
Mobile Phase	Acetonitrile and 0.01 M Phosphoric acid (13:7)
Flow Rate	1.5 mL/min
Detection	Spectrophotometer @ 200 nm
Injection	10 µL
Relative Retention with Reference to Lovastatin*	
Related Compound A	about 1.3
System Suitability	
Minimum resolution of 6.0 between Lovastatin and Related Compound A	

* Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method within as Described in the USP Monograph

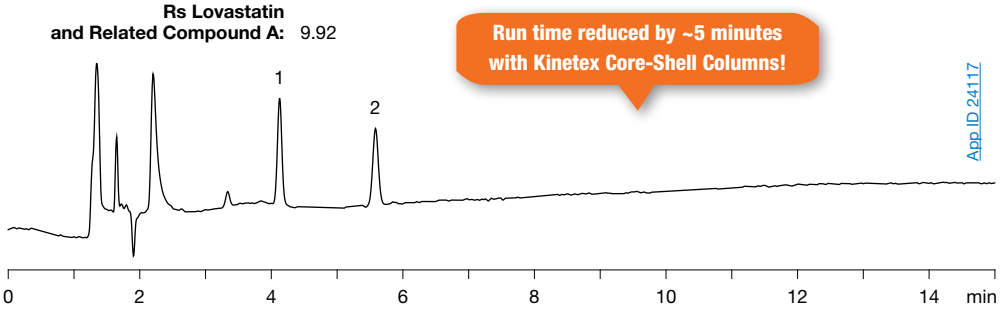
Column: Luna® C8(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4249-E0
Flow Rate: 1.5 mL/min
Sample: 1. Lovastatin
2. Related Compound A
Elution Time of Last Peak: 10.9 min
Rs Lovastatin and Related Compound A: 12.33



Method 2

Faster and Higher Resolution Within Allowable Adjustments

Column: Kinetex® Core-Shell C8 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4608-E0
Flow Rate: 1.5 mL/min
Sample: 1. Lovastatin
2. Related Compound A
Elution Time of Last Peak: 5.6 min
Rs Lovastatin and Related Compound A: 9.92



Adjustments for Meeting System Suitability

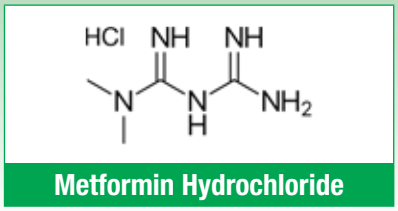
Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	200 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	10 µL (as specified)	As specified
Column Temperature	± 10 °C	40 °C (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	L7 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	250 mm (as specified)	As specified
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (as specified)	As specified
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	5 µm (as specified)	As specified
Flow Rate	± 50 % (at given ID)	1.5 mL/min (as specified	As specified

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Metformin Hydrochloride

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Metformin Hydrochloride. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



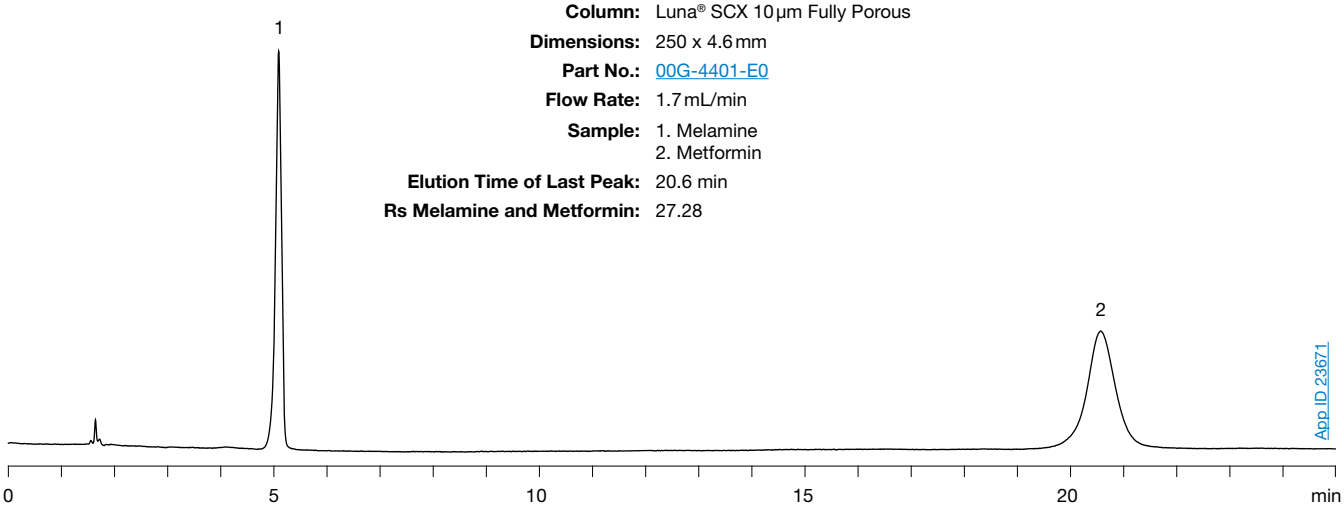
Metformin Hydrochloride

USP Monograph: Metformin Hydrochloride Details	
System Suitability Stock Solution	0.25 mg/mL of Metformin Hydrochloride and 0.1 mg/mL of Melamine in water
System Suitability Solution	Transfer 1.0 mL of system suitability stock solution to a 50 mL volumetric flask, dilute with mobile phase to volume
Standard Stock Solution	0.2 mg/mL of USP Metformin Related Compound A RS in water
Standard Solution	0.001 mg/mL of USP Metformin Related Compound A RS in Mobile Phase from Standard stock solution
Sample Solution	5 mg/mL of Metformin Hydrochloride in mobile phase
Diluted Sample Solution	0.005 mg/mL of Metformin Hydrochloride in Mobile Phase from the Sample solution
Column	
Size	250 x 4.6 mm
Stationary Phase	L9: Irregular or spherical, totally porous silica gel having a chemically bonded, strongly acidic cation-exchange coating, 3 to 10 µm in diameter
Mobile Phase	17 g/L of monobasic ammonium phosphate in water, adjusted with phosphoric acid to a pH 3.0
Flow Rate	1.0 - 1.7 mL/min
Detection	Spectrophotometer @ 218 nm
Injection	20 µL
Run Time	Not less than twice the retention time of Metformin
System Suitability	
Minimum resolution of 10 between Melamine and Metformin	

Method 1

Original Method as Described in the USP Monograph

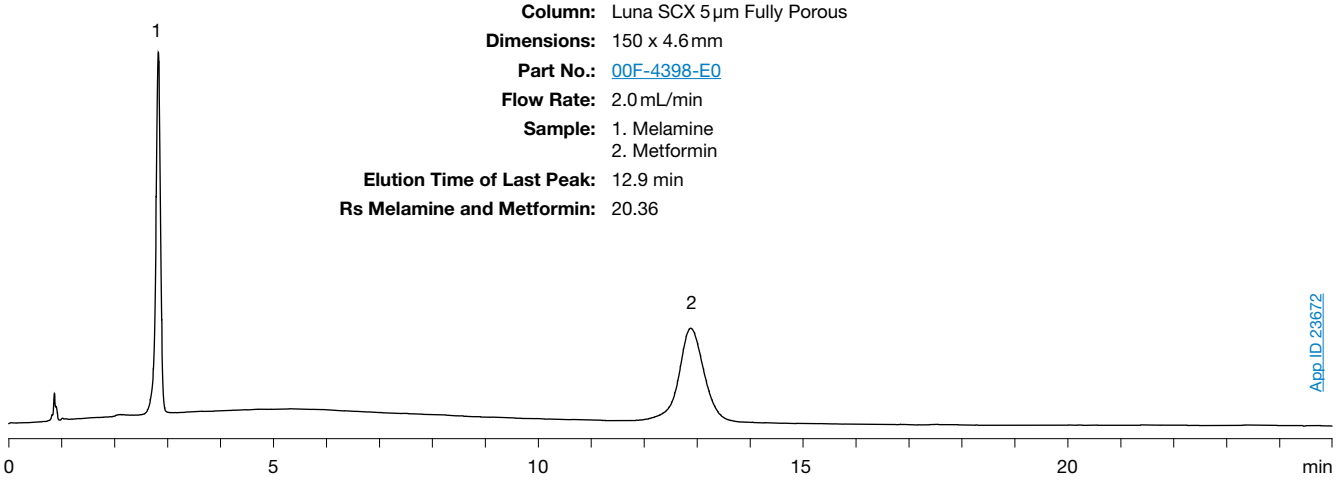
Column: Luna® SCX 10 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4401-E0
Flow Rate: 1.7 mL/min
Sample: 1. Melamine
2. Metformin
Elution Time of Last Peak: 20.6 min
Rs Melamine and Metformin: 27.28



Method 2

Faster Method Within Allowable Adjustments

Column: Luna SCX 5 µm Fully Porous
Dimensions: 150 x 4.6 mm
Part No.: 00F-4398-E0
Flow Rate: 2.0 mL/min
Sample: 1. Melamine
2. Metformin
Elution Time of Last Peak: 12.9 min
Rs Melamine and Metformin: 20.36



Adjustments for Meeting System Suitability

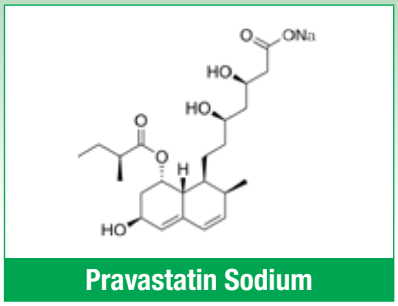
Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	218 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	20 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L9 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	250 mm (as specified)	150 mm (-40 %)
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (as specified)	As specified
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	10 µm (as specified)	5 µm (as specified)
Flow Rate	± 50 % (at given ID)	1.7 mL/min (as specified)	2.0 mL/min (+18)

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Pravastatin Sodium

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Pravastatin Sodium. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Pravastatin Sodium

USP Monograph: Pravastatin Sodium Details

Diluent	Prepare a mixture of methanol and water (1:1)	
Buffer pH 7.0	Prepare a 0.08 M phosphoric acid solution, adjust with triethylamine to pH 7.0, mix	
Standard Solution*	Dissolve an accurately weighed quantity of USP Pravastatin 1,1,3,3-Tetramethylbutylamine RS in Diluent, and dilute quantitatively with Diluent to obtain a solution having a known concentration of about 1.25 µg of pravastatin 1,1,3,3-tetramethylbutylamine per mL	
System Suitability Solution	Dissolve accurately weighed quantities of USP Pravastatin 1,1,3,3-Tetramethylbutylamine Rs and USP Pravastatin Related Compound A RS in Diluent to obtain a solution containing about 0.6 mg of USP Pravastatin 1,1,3,3 tetramethylbutylamine RS and 0.001 mg of USP Pravastatin Related Compound A RS per mL. (Note-USP Pravastatin Related Compound A RS is a sodium salt of 3α-hydroxisocompactin acid)	
Test Solution*	Transfer about 50 mg of Pravastatin Sodium to a 100 mL volumetric flask, dissolve in and dilute with Diluent to volume, and mix	
Column		
Size	100 x 4.0 mm	
Stationary Phase	3 µm, L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod	
Mobile Phase	Use variable mixtures of Solution A and Solution B as directed for: **A.** Prepare a filtered and degassed mixture of water, Buffer pH 7.0, and acetonitrile (52:30:10) **B.** Prepare a filtered and degassed mixture of acetonitrile, Buffer pH 7.0, and water (60:30:10)	
Gradient	**Time** 0 – 3.0 min 3.0 – 26.5 min 26.5 – 26.6 min 26.6 – 30.0 min	**%B** 0 0 → 100 100 → 0 0
Flow Rate	1.0 mL/min	
Detection	Spectrophotometer @ 238 nm	
Injection	10 µL	
Relative Retention with Reference to Pravastatin**		
Related Compound A	about 1.1	
System Suitability		
Minimum resolution of 2.0 between Pravastatin and Pravastatin Related Compound A		

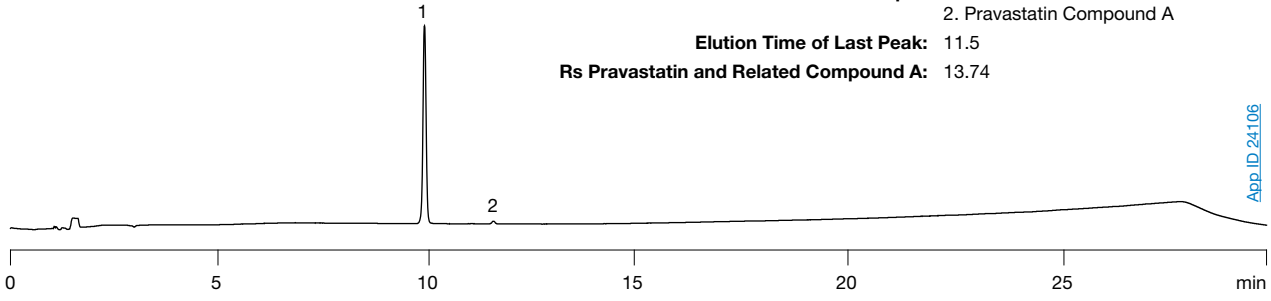
*The Standard solution and the Test solution are maintained at 15° C until injected into the chromatograph

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method Outside Allowable Adjustments

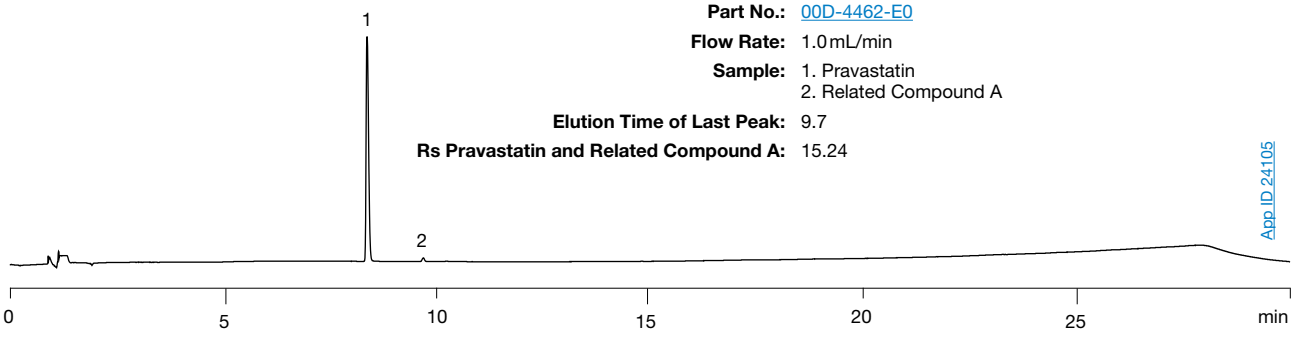
Column: Luna® C18(2) 3 µm Fully Porous
Dimensions: 100 x 4.6 mm
Part No.: 00D-4251-E0
Flow Rate: 1.0 mL/min
Sample: 1. Pravastatin
2. Pravastatin Compound A
Elution Time of Last Peak: 11.5
Rs Pravastatin and Related Compound A: 13.74



Method 2

Faster and Higher Resolution Outside Allowable Adjustments

Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 1.0 mL/min
Sample: 1. Pravastatin
2. Related Compound A
Elution Time of Last Peak: 9.7
Rs Pravastatin and Related Compound A: 15.24



Adjustments for Meeting System Suitability

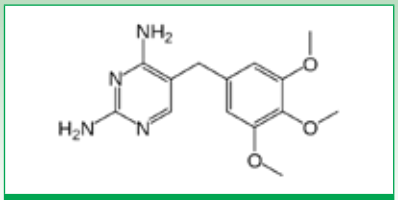
Method Parameter	Allowed Adjustments (gradient elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified	As specified
Composition of the Mobile Phase	Changes to gradient composition are not recommended	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	238 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	10 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	No deviations permitted	100 mm (as specified)	As specified
Column Internal Diameter	No deviations permitted	4.6 mm (+15 %)	4.6 mm (+15)
Particle Size	No deviations permitted	3 µm (as specified)	2.6 µm (-13 %)
Flow Rate	No deviations permitted	1.0 mL/min (as specified)	As specified

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Trimethoprim

USP

The related substances test of the USP monograph outlines the separation of all relevant impurities from Trimethoprim. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.



Trimethoprim

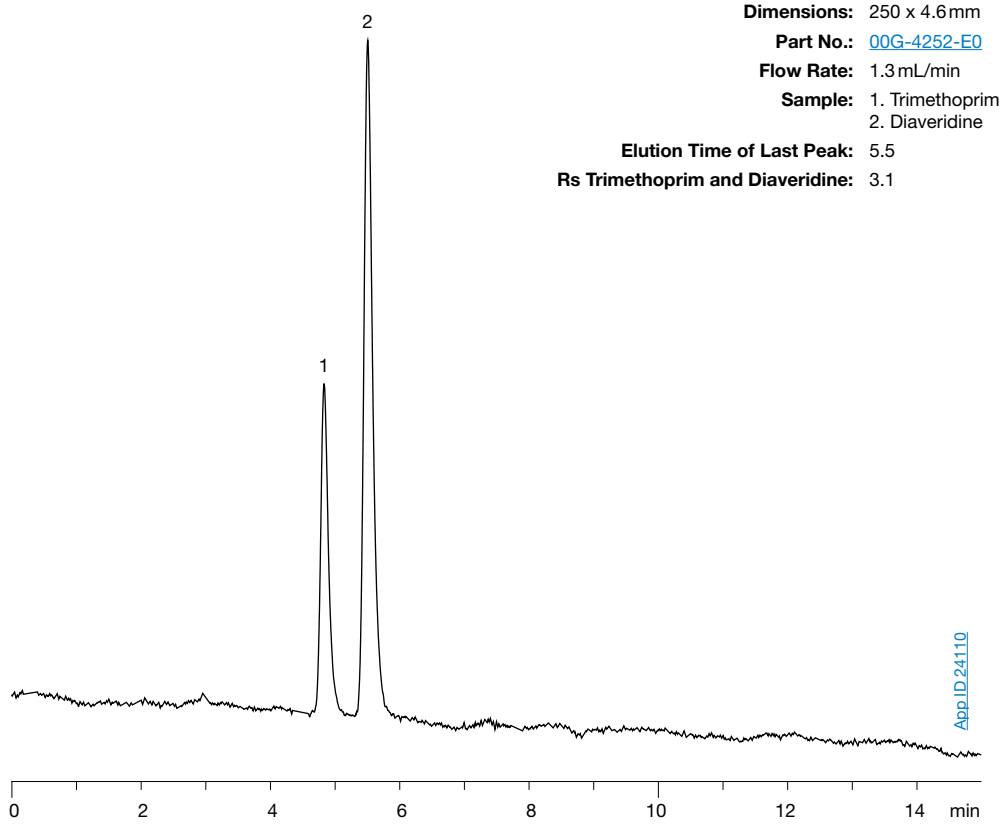
USP Monograph: Trimethoprim Details

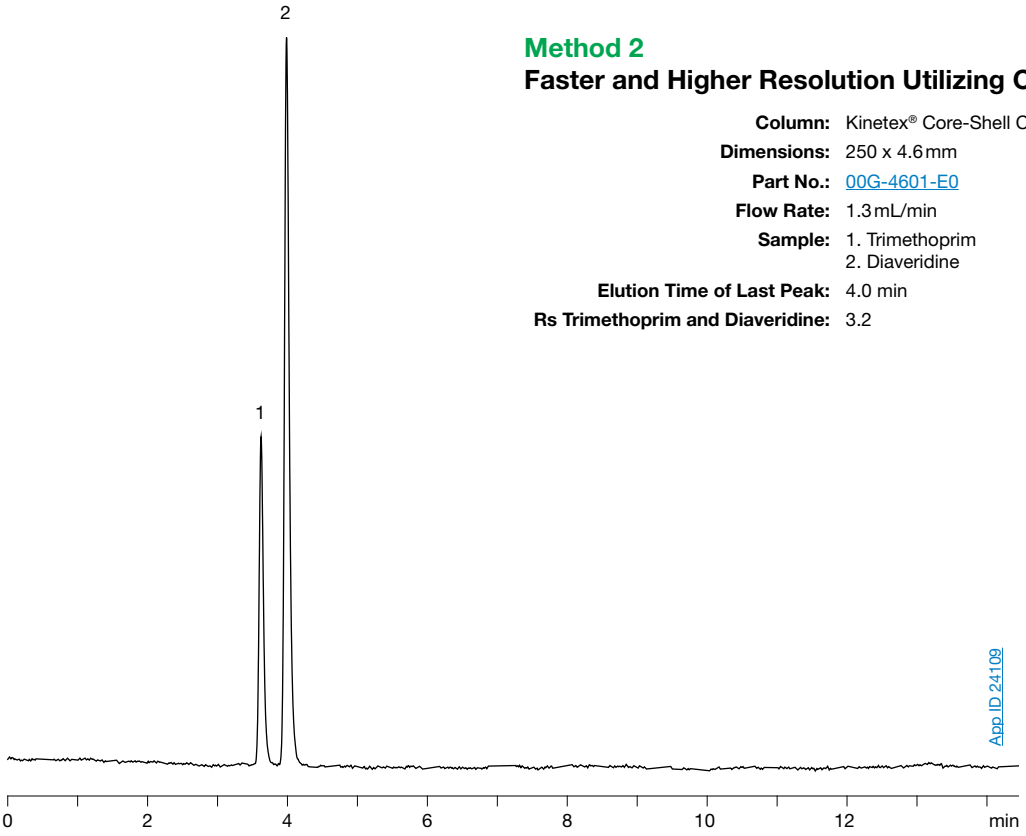
Buffer Solution	Prepare a 10 mM sodium perchlorate solution in water, adjust with phosphoric acid to pH 3.6, and mix
Resolution Solution	Dissolve accurately weighed quantities of USP Trimethoprim RS and Diaveridine; and dilute quantitatively with mobile phase to obtain a solution having known concentrations of about 10 µg per mL and 5 µg per mL, respectively
Test Solution	Transfer about 25.0 mg of Trimethoprim to a 25 mL volumetric flask, dissolve in and dilute with mobile phase to volume, and mix
Column	
Size	250 x 4.6 mm
Stationary Phase	L1: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic microparticles, 1.5 to 10 µm in diameter, or a monolithic rod
Mobile Phase	Prepare a filtered and degassed mixture of Buffer Solution and methanol (7:3)
Flow Rate	1.3 mL/min
Detection	Spectrophotometer @ 280 nm
Injection	20 µL
System Suitability	
Minimum resolution of 2.5 between Trimethoprim and Diaveridine Relative standard deviation for replicate injections is not more than 2.0 %	

Method 1

Original Method as Described in the USP Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 250 x 4.6 mm
Part No.: 00G-4252-E0
Flow Rate: 1.3 mL/min
Sample: 1. Trimethoprim
2. Diaveridine
Elution Time of Last Peak: 5.5
Rs Trimethoprim and Diaveridine: 3.1





Method 2

Faster and Higher Resolution Utilizing Core-Shell Technology

Column: Kinetex® Core-Shell C18 5 µm
Dimensions: 250 x 4.6 mm
Part No.: 00G-4601-E0
Flow Rate: 1.3 mL/min
Sample: 1. Trimethoprim
2. Diaveridine
Elution Time of Last Peak: 4.0 min
Rs Trimethoprim and Diaveridine: 3.2

Adjustments for Meeting System Suitability

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph Details Table	As specified
Composition of the Mobile Phase	± 30 % Relative; cannot exceed ± 10 % Absolute change; cannot be reduced to zero	As specified in Monograph Details Table	As specified
Wavelength of Detector	No deviations permitted	280 nm (as specified)	As specified
Injection Volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	20 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	L1 (as specified)	As specified
Column Length	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	250 mm (as specified)	As specified
Column Internal Diameter	Can be adjusted so long as linear velocity if maintained	4.6 mm (as specified)	As specified
Particle Size	Column length (L) to particle size diameter (dp) ratio can be adjusted between -25 % and +50 %*	5 µm (as specified)	As specified
Flow Rate	± 50 % (at given ID)	1.3 mL/min (as specified)	As specified

*Alternatively (as for the application of particle size adjustment to superficially porous particles), other L/dp combinations can be used provided that the number of theoretical plates (N) is within -25 % to +50 %

Kinetex Ordering Information

KINETEX® Core-Shell Technology™

5 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges‡
Phases	30 x 2.1	50 x 2.1	100 x 2.1	150 x 2.1	3/pk
EVO C18	00A-4633-AN	00B-4633-AN	00D-4633-AN	00F-4633-AN	AJ0-9298
F5	00A-4724-AN	00B-4724-AN	00D-4724-AN	00F-4724-AN	AJ0-9322
Biphenyl	00A-4627-AN	00B-4627-AN	00D-4627-AN	—	AJ0-9209
XB-C18	00A-4605-AN	00B-4605-AN	00D-4605-AN	—	AJ0-8782
C18	00A-4601-AN	00B-4601-AN	00D-4601-AN	00F-4601-AN	AJ0-8782
C8	—	00B-4608-AN	00D-4608-AN	—	AJ0-8784
Phenyl-Hexyl	—	00B-4603-AN	—	—	AJ0-8788

for 2.1 mm ID

5 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges‡
Phases	50 x 3.0	100 x 3.0	150 x 3.0	3/pk
EVO C18	00B-4633-Y0	00D-4633-Y0	00F-4633-Y0	AJ0-9297
F5	00B-4724-Y0	00D-4724-Y0	00F-4724-Y0	AJ0-9321
Biphenyl	00B-4627-Y0	00D-4627-Y0	00F-4627-Y0	AJ0-9208
XB-C18	00B-4605-Y0	00D-4605-Y0	00F-4605-Y0	AJ0-8775
C18	00B-4601-Y0	00D-4601-Y0	00F-4601-Y0	AJ0-8775
C8	00B-4608-Y0	00D-4608-Y0	—	AJ0-8777
Phenyl-Hexyl	00B-4603-Y0	00D-4603-Y0	—	AJ0-8781

for 3.0 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges‡
Phases	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	3/pk
EVO C18	00B-4633-E0	00D-4633-E0	00F-4633-E0	00G-4633-E0	AJ0-9296
F5	00B-4724-E0	00D-4724-E0	00F-4724-E0	00G-4724-E0	AJ0-9320
Biphenyl	00B-4627-E0	00D-4627-E0	00F-4627-E0	00G-4627-E0	AJ0-9207
XB-C18	00B-4605-E0	00D-4605-E0	00F-4605-E0	00G-4605-E0	AJ0-8768
C18	00B-4601-E0	00D-4601-E0	00F-4601-E0	00G-4601-E0	AJ0-8768
C8	00B-4608-E0	00D-4608-E0	00F-4608-E0	00G-4608-E0	AJ0-8770
Phenyl-Hexyl	00B-4603-E0	00D-4603-E0	00F-4603-E0	00G-4603-E0	AJ0-8774

for 4.6 mm ID

5 µm Semi-Preparative Columns (mm)			SecurityGuard SemiPrep Cartridges***
Phases	150 x 10	250 x 10	3/pk
EVO C18	00F-4633-N0	00G-4633-N0	AJ0-9306
F5	—	00G-4724-N0	AJ0-9323
C18	00F-4601-N0	00G-4601-N0	AJ0-9278
Biphenyl	00F-4627-N0	00G-4627-N0	AJ0-9280

for 9-16 mm ID

3.5 µm Analytical Columns (mm)			SecurityGuard ULTRA Cartridges‡
Phases	100 x 4.6	150 x 4.6	3/pk
XB-C18	00D-4744-E0	00F-4744-E0	AJ0-8768

for 4.6 mm ID

2.6 µm Microbore Columns (mm)			
Phases	50 x 1.0	100 x 1.0	150 x 1.0
XB-C18	00B-4496-A0	00D-4496-A0	00F-4496-A0

‡SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

***SemiPrep SecurityGuard Cartridges require holder, Part No.: AJ0-9281

Kinetex Ordering Information (cont'd)

KINETEX® Core-Shell Technology™

2.6 µm Minibore Columns (mm)						SecurityGuard™ ULTRA Cartridges‡
Phases	30 x 2.1	50 x 2.1	75 x 2.1	100 x 2.1	150 x 2.1	3/pk
EVO C18	00A-4725-AN	00B-4725-AN	—	00D-4725-AN	00F-4725-AN	AJ0-9298
Polar C18	00A-4759-AN	00B-4759-AN	—	00D-4759-AN	00F-4759-AN	AJ0-9530
F5	00A-4723-AN	00B-4723-AN	—	00D-4723-AN	00F-4723-AN	AJ0-9322
Biphenyl	00A-4622-AN	00B-4622-AN	—	00D-4622-AN	00F-4622-AN	AJ0-9209
XB-C18	00A-4496-AN	00B-4496-AN	00C-4496-AN	00D-4496-AN	00F-4496-AN	AJ0-8782
C18	00A-4462-AN	00B-4462-AN	00C-4462-AN	00D-4462-AN	00F-4462-AN	AJ0-8782
C8	00A-4497-AN	00B-4497-AN	00C-4497-AN	00D-4497-AN	00F-4497-AN	AJ0-8784
HILIC	00A-4461-AN	00B-4461-AN	00C-4461-AN	00D-4461-AN	00F-4461-AN	AJ0-8786
Phenyl-Hexyl	00A-4495-AN	00B-4495-AN	00C-4495-AN	00D-4495-AN	00F-4495-AN	AJ0-8788

for 2.1 mm ID

2.6 µm MidBore™ Columns (mm)						SecurityGuard ULTRA Cartridges‡
Phases	30 x 3.0	50 x 3.0	75 x 3.0	100 x 3.0	150 x 3.0	3/pk
EVO C18	—	00B-4725-Y0	—	00D-4725-Y0	00F-4725-Y0	AJ0-9297
Polar C18	—	00B-4759-Y0	—	00D-4759-Y0	00F-4759-Y0	AJ0-9531
F5	—	00B-4723-Y0	—	00D-4723-Y0	00F-4723-Y0	AJ0-9321
Biphenyl	—	00B-4622-Y0	—	00D-4622-Y0	00F-4622-Y0	AJ0-9208
XB-C18	00A-4496-Y0	00B-4496-Y0	00C-4496-Y0	00D-4496-Y0	00F-4496-Y0	AJ0-8775
C18	00A-4462-Y0	00B-4462-Y0	00C-4462-Y0	00D-4462-Y0	00F-4462-Y0	AJ0-8775
C8	00A-4497-Y0	00B-4497-Y0	00C-4497-Y0	00D-4497-Y0	00F-4497-Y0	AJ0-8777
HILIC	00A-4461-Y0	—	—	—	00F-4461-Y0	AJ0-8779
Phenyl-Hexyl	—	00B-4495-Y0	—	00D-4495-Y0	00F-4495-Y0	AJ0-8781

for 3.0 mm ID

2.6 µm Analytical Columns (mm)						SecurityGuard ULTRA Cartridges‡
Phases	30 x 4.6	50 x 4.6	75 x 4.6	100 x 4.6	150 x 4.6	3/pk
EVO C18	—	00B-4725-E0	—	00D-4725-E0	00F-4725-E0	AJ0-9296
Polar C18	—	00B-4759-E0	—	00D-4759-E0	00F-4759-E0	AJ0-9532
F5	—	00B-4723-E0	—	00D-4723-E0	00F-4723-E0	AJ0-9320
Biphenyl	—	00B-4622-E0	—	00D-4622-E0	00F-4622-E0	AJ0-9207
XB-C18	—	00B-4496-E0	00C-4496-E0	00D-4496-E0	00F-4496-E0	AJ0-8768
C18	00A-4462-E0	00B-4462-E0	00C-4462-E0	00D-4462-E0	00F-4462-E0	AJ0-8768
C8	—	00B-4497-E0	00C-4497-E0	00D-4497-E0	00F-4497-E0	AJ0-8770
HILIC	—	00B-4461-E0	00C-4461-E0	00D-4461-E0	00F-4461-E0	AJ0-8772
Phenyl-Hexyl	—	00B-4495-E0	00C-4495-E0	00D-4495-E0	00F-4495-E0	AJ0-8774

for 4.6 mm ID

1.7 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges‡
Phases	30 x 2.1	50 x 2.1	100 x 2.1	150 x 2.1	3/pk
EVO C18	—	00B-4726-AN	00D-4726-AN	00F-4726-AN	AJ0-9298
Biphenyl	—	00B-4628-AN	00D-4628-AN	00F-4628-AN	AJ0-9209
XB-C18	00A-4498-AN	00B-4498-AN	00D-4498-AN	00F-4498-AN	AJ0-8782
C18	00A-4475-AN	00B-4475-AN	00D-4475-AN	00F-4475-AN	AJ0-8782
C8	00A-4499-AN	00B-4499-AN	00D-4499-AN	00F-4499-AN	AJ0-8784
HILIC	00A-4474-AN	00B-4474-AN	00D-4474-AN	—	AJ0-8786
Phenyl-Hexyl	—	00B-4500-AN	00D-4500-AN	00F-4500-AN	AJ0-8788
F5	—	00B-4722-AN	00D-4722-AN	00F-4722-AN	AJ0-9322

for 2.1 mm ID

1.7 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges‡
Phases	30 x 3.0	50 x 3.0	100 x 3.0	3/pk
XB-C18	00A-4498-Y0	00B-4498-Y0	00D-4498-Y0	AJ0-8775
C18	—	00B-4475-Y0	00D-4475-Y0	AJ0-8775
C8	00A-4499-Y0	00B-4499-Y0	00D-4499-Y0	AJ0-8777
HILIC	—	00B-4474-Y0	—	AJ0-8779

for 3.0 mm ID

1.7 µm Microbore Columns (mm)			
Phases	50 x 1.0	100 x 1.0	150 x 1.0
C18	00B-4726-AN	00D-4726-AN	00F-4726-AN

1.3 µm Minibore Columns (mm)		
Phases	30 x 2.1	50 x 2.1
C18	00A-4515-AN	00B-4515-AN

‡SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

Luna Ordering Information

explore LUNA®

2.5 µm High Speed Technology (HST) Columns (mm)					
Phase	**30 x 2.0**	**50 x 2.0**	**100 x 2.0**	**50 x 3.0**	**100 x 3.0**
Luna 2.5 µm C18(2)-HST	00A-4446-B0	00B-4446-B0	00D-4446-B0	00B-4446-Y0	00D-4446-Y0

3 µm and 5 µm Capillary Columns (mm)						Guard Columns (mm)	
Phases	**50 x 0.30**	**150 x 0.30**	**50 x 0.50**	**150 x 0.50**	**250 x 0.50**	**20 x 0.30**	**20 x 0.50**
3 µm C8(2)	—	—	00B-4248-AF	00F-4248-AF	—	—	—
3 µm C18(2)	00B-4251-AC	00F-4251-AC	00B-4251-AF	00F-4251-AF	—	03M-4251-AC	03M-4251-AF
5 µm C8(2)	—	00F-4249-AC	—	—	—	—	—
5 µm C18(2)	00B-4252-AC	00F-4252-AC	—	00F-4252-AF	00G-4252-AF	—	—
5 µm Phenyl-Hexyl	00B-4257-AC	—	00B-4257-AF	00F-4257-AF	—	—	—

3 µm Microbore and Minibore Columns (mm)							SecurityGuard Cartridges (mm)
Phases	**50 x 1.0**	**150 x 1.0**	**30 x 2.0**	**50 x 2.0**	**100 x 2.0**	**150 x 2.0**	**4 x 2.0***
							/10pk
Silica(2)	—	00F-4162-A0	00A-4162-B0	00B-4162-B0	00D-4162-B0	00F-4162-B0	AJ0-4347
C8(2)	00B-4248-A0	00F-4248-A0	00A-4248-B0	00B-4248-B0	00D-4248-B0	00F-4248-B0	AJ0-4289
C18(2)	00B-4251-A0	00F-4251-A0	00A-4251-B0	00B-4251-B0	00D-4251-B0	00F-4251-B0	AJ0-4286
CN	—	—	00A-4254-B0	00B-4254-B0	00D-4254-B0	00F-4254-B0	AJ0-4304
Phenyl-Hexyl	00B-4256-A0	—	00A-4256-B0	00B-4256-B0	00D-4256-B0	00F-4256-B0	AJ0-4350
NH_2	—	00F-4377-A0	00A-4377-B0	00B-4377-B0	00D-4377-B0	00F-4377-B0	AJ0-4301
HILIC	—	—	00A-4449-B0	00B-4449-B0	00D-4449-B0	00F-4449-B0	AJ0-8328
PFP(2)	—	00F-4447-A0	00A-4447-B0	00B-4447-B0	00D-4447-B0	00F-4447-B0	AJ0-8326
							for ID: 2.0-3.0 mm

3 µm MidBore™ and Analytical Columns (mm)									SecurityGuard™ Cartridges (mm)	
Phases	**30 x 3.0**	**50 x 3.0**	**150 x 3.0**	**30 x 4.6**	**50 x 4.6**	**75 x 4.6**	**100 x 4.6**	**150 x 4.6**	**4 x 2.0***	**4 x 3.0***
									/10pk	/10pk
Silica(2)	—	00B-4162-Y0	00F-4162-Y0	00A-4162-E0	00B-4162-E0	00C-4162-E0	00D-4162-E0	00F-4162-E0	AJ0-4347	AJ0-4348
C8(2)	00A-4248-Y0	00B-4248-Y0	00F-4248-Y0	00A-4248-E0	00B-4248-E0	00C-4248-E0	00D-4248-E0	00F-4248-E0	AJ0-4289	AJ0-4290
C18(2)	00A-4251-Y0	00B-4251-Y0	00F-4251-Y0	00A-4251-E0	00B-4251-E0	00C-4251-E0	00D-4251-E0	00F-4251-E0	AJ0-4286	AJ0-4287
CN	—	00B-4254-Y0	00F-4254-Y0	00A-4254-E0	00B-4254-E0	—	00D-4254-E0	00F-4254-E0	AJ0-4304	AJ0-4305
Phenyl-Hexyl	—	00B-4256-Y0	00F-4256-Y0	—	00B-4256-E0	00C-4256-E0	00D-4256-E0	00F-4256-E0	AJ0-4350	AJ0-4351
NH_2	—	00B-4377-Y0	00F-4377-Y0	—	00B-4377-E0	—	00D-4377-E0	00F-4377-E0	AJ0-4301	AJ0-4302
HILIC	—	00B-4449-Y0	00F-4449-Y0	—	—	—	00D-4449-E0	00F-4449-E0	AJ0-8328	AJ0-8329
PFP(2)	—	00B-4447-Y0	00F-4447-Y0	—	00B-4447-E0	—	00D-4447-E0	00F-4447-E0	AJ0-8326	AJ0-8327
									for ID: 2.0-3.0 mm	3.2-8.0 mm

5 µm Microbore and Minibore Columns (mm)								SecurityGuard™ Cartridges (mm)
Phases	**50 x 1.0**	**150 x 1.0**	**250 x 1.0**	**30 x 2.0**	**50 x 2.0**	**150 x 2.0**	**250 x 2.0**	**4 x 2.0***
								/10pk
Silica(2)	—	—	—	00A-4274-B0	00B-4274-B0	00F-4274-B0	00G-4274-B0	AJ0-4347
C5	—	—	—	00A-4043-B0	00B-4043-B0	00F-4043-B0	—	AJ0-4292
C8(2)	—	00F-4249-A0	—	00A-4249-B0	00B-4249-B0	00F-4249-B0	00G-4249-B0	AJ0-4289
C18(2)	00B-4252-A0	00F-4252-A0	00G-4252-A0	00A-4252-B0	00B-4252-B0	00F-4252-B0	00G-4252-B0	AJ0-4286
CN	—	—	—	—	00B-4255-B0	00F-4255-B0	—	AJ0-4304
Phenyl-Hexyl	00B-4257-A0	—	—	00A-4257-B0	00B-4257-B0	00F-4257-B0	00G-4257-B0	AJ0-4350
NH_2	00B-4378-A0	00F-4378-A0	—	00A-4378-B0	00B-4378-B0	00F-4378-B0	00G-4378-B0	AJ0-4301
PFP(2)	—	—	—	00A-4448-B0	00B-4448-B0	00F-4448-B0	—	AJ0-8326
								for ID: 2.0-3.0 mm

5 µm MidBore and Analytical Columns (mm)								SecurityGuard™ Cartridges (mm)	
Phases	**30 x 3.0**	**50 x 3.0**	**150 x 3.0**	**250 x 3.0**	**30 x 4.6**	**50 x 4.6**	**75 x 4.6**	**4 x 2.0***	**4 x 3.0***
								/10pk	/10pk
Silica(2)	—	00B-4274-Y0	00F-4274-Y0	—	—	00B-4274-E0	—	AJ0-4347	AJ0-4348
C5	—	—	00F-4043-Y0	—	—	00B-4043-E0	—	AJ0-4292	AJ0-4293
C8(2)	00A-4249-Y0	00B-4249-Y0	00F-4249-Y0	00G-4249-Y0	00A-4249-E0	00B-4249-E0	00C-4249-E0	AJ0-4289	AJ0-4290
C18(2)	00A-4252-Y0	00B-4252-Y0	00F-4252-Y0	00G-4252-Y0	00A-4252-E0	00B-4252-E0	00C-4252-E0	AJ0-4286	AJ0-4287
CN	—	00B-4255-Y0	00F-4255-Y0	00G-4255-Y0	00A-4255-E0	00B-4255-E0	00C-4255-E0	AJ0-4304	AJ0-4305
Phenyl-Hexyl	—	00B-4257-Y0	00F-4257-Y0	00G-4257-Y0	00A-4257-E0	00B-4257-E0	—	AJ0-4350	AJ0-4351
NH_2	—	00B-4378-Y0	00F-4378-Y0	00G-4378-Y0	—	00B-4378-E0	—	AJ0-4301	AJ0-4302
SCX	—	—	00F-4398-Y0	—	—	00B-4398-E0	—	AJ0-4307	AJ0-4308
HILIC	—	—	00F-4450-Y0	—	—	—	—	AJ0-8328	AJ0-8329
PFP(2)	—	00B-4448-Y0	00F-4448-Y0	—	—	00B-4448-E0	—	AJ0-8326	AJ0-8327
								for ID: 2.0-3.0 mm	3.2-8.0 mm

5 µm Analytical and Semi-Prep Columns (mm)					SecurityGuard™ Cartridges (mm)	
Phases	**100 x 4.6**	**150 x 4.6**	**250 x 4.6**	**250 x 10**	**4 x 3.0***	**10 x 10‡**
					/10pk	/3pk
Silica(2)	00D-4274-E0	00F-4274-E0	00G-4274-E0	00G-4274-N0	AJ0-4348	AJ0-7223
C5	00D-4043-E0	00F-4043-E0	00G-4043-E0	00G-4043-N0	AJ0-4293	AJ0-7372
C8(2)	00D-4249-E0	00F-4249-E0	00G-4249-E0	00G-4249-N0	AJ0-4290	AJ0-7222
C18(2)	00D-4252-E0	00F-4252-E0	00G-4252-E0	00G-4252-N0	AJ0-4287	AJ0-7221
CN	00D-4255-E0	00F-4255-E0	00G-4255-E0	00G-4255-N0	AJ0-4305	AJ0-7313
Phenyl-Hexyl	00D-4257-E0	00F-4257-E0	00G-4257-E0	00G-4257-N0	AJ0-4351	AJ0-7314
NH_2	00D-4378-E0	00F-4378-E0	00G-4378-E0	00G-4378-N0	AJ0-4302	AJ0-7364
SCX	00D-4398-E0	00F-4398-E0	00G-4398-E0	00G-4398-N0	AJ0-4308	AJ0-7369
HILIC	00D-4450-E0	00F-4450-E0	00G-4450-E0	00G-4450-N0	AJ0-8329	AJ0-8902
PFP(2)	00D-4448-E0	00F-4448-E0	00G-4448-E0	00G-4448-N0	AJ0-8327	AJ0-8376
					for ID: 3.2-8.0 mm	9-16 mm

Luna Ordering Information (cont'd)

5 µm Axia™ Packed Preparative Columns (mm)								SecurityGuard™ Cartridges (mm)	
Phases	**50 x 21.2**	**100 x 21.2**	**150 x 21.2**	**250 x 21.2**	**50 x 30**	**100 x 30**	**250 x 30**	**15 x 21.2****	**15 x 30 ◆**
								/ea	/ea
Silica(2)	—	00D-4274-P0-AX	00F-4274-P0-AX	00G-4274-P0-AX	—	—	00G-4274-U0-AX	AJ0-7229	AJ0-8312
C5	—	—	—	00G-4043-P0-AX	—	—	—	—	—
C8(2)	—	—	00F-4249-P0-AX	00G-4249-P0-AX	—	00D-4249-U0-AX	—	AJ0-7840	AJ0-8302
C18(2)	00B-4252-P0-AX	00D-4252-P0-AX	00F-4252-P0-AX	00G-4252-P0-AX	00B-4252-U0-AX	00D-4252-U0-AX	00G-4252-U0-AX	AJ0-7839	AJ0-8301
CN	—	—	—	00G-4255-P0-AX	—	—	00G-4255-U0-AX	AJ0-8220	AJ0-8311
Phenyl-Hexyl	—	—	00F-4257-P0-AX	00G-4257-P0-AX	—	—	00G-4257-U0-AX	AJ0-7841	AJ0-8303
NH_2	—	—	00F-4378-P0-AX	00G-4378-P0-AX	—	—	—	AJ0-8162	AJ0-8309
PFP(2)	—	00D-4448-P0-AX	00F-4448-P0-AX	00G-4448-P0-AX	—	00D-4448-U0-AX	—	AJ0-8377	AJ0-8378
HILIC	—	00D-4450-P0-AX	00F-4450-P0-AX	00G-4450-P0-AX	—	—	00G-4450-U0-AX	AJ0-8829	AJ0-8830
								for ID: 18-29 mm	30-49 mm

10 µm Axia™ Packed Preparative Columns (mm) (continued)						SecurityGuard Cartridges (mm)	
Phases	**50 x 21.2**	**100 x 21.2**	**250 x 21.2**	**250 x 30**	**250 x 50**	**15 x 21.2****	**15 x 30 ◆**
						/ea	/ea
Silica(2)	—	—	00G-4091-P0-AX	00G-4091-U0-AX	00G-4091-V0-AX	AJ0-7229	AJ0-8312
C5	—	00D-4092-P0-AX	00G-4092-P0-AX	—	00G-4092-V0-AX	—	—
C8(2)	—	—	00G-4250-P0-AX	—	00G-4250-V0-AX	AJ0-7840	AJ0-8302
C18(2)	00B-4253-P0-AX	00D-4253-P0-AX	00G-4253-P0-AX	00G-4253-U0-AX	00G-4253-V0-AX	AJ0-7839	AJ0-8301
CN	—	—	00G-4300-P0-AX	—	—	AJ0-8220	AJ0-8311
Phenyl-Hexyl	—	—	00G-4285-P0-AX	00G-4285-U0-AX	—	AJ0-7841	AJ0-8303
NH_2	—	—	00G-4379-P0-AX	—	—	AJ0-8162	AJ0-8309
						for ID: 18-29 mm	30-49 mm

10 µm Analytical and Semi-Prep Columns (mm)			SecurityGuard Cartridges (mm)	
Phases	**250 x 4.6**	**250 x 10**	**4 x 3.0***	**10 x 10‡**
			/10 pk	/3 pk
Silica(2)	00G-4091-E0	00G-4091-N0	AJ0-4348	AJ0-7223
C8(2)	00G-4250-E0	00G-4250-N0	AJ0-4290	AJ0-7222
C18(2)	00G-4253-E0	00G-4253-N0	AJ0-4287	AJ0-7221
CN	00G-4300-E0	—	AJ0-4305	AJ0-7313
Phenyl-Hexyl	00G-4285-E0	00G-4285-N0	AJ0-4351	AJ0-7314
NH_2	00G-4379-E0	00G-4379-N0	AJ0-4302	AJ0-7364
SCX	00G-4401-E0	00G-4401-N0	AJ0-4308	AJ0-7369
			for ID: 3.2-8.0 mm	9-16 mm

*SecurityGuard™ Analytical Cartridges require holder, Part No.: KJ0-4282
‡SemiPrep SecurityGuard Cartridges require holder, Part No.: AJ0-9281
**PREP SecurityGuard Cartridges require holder, Part No.: AJ0-8223
◆PREP SecurityGuard Cartridges require holder, Part No.: AJ0-8277

15 µm Pilot Scale Columns (mm)	
Phases	**250 x 4.6**
C18(2)	00G-4273-E0
Phenyl-Hexyl	00G-4286-E0

Gemini Ordering Information

3µm Microbore, Minibore and MidBore™ Columns (mm)										SecurityGuard™ Cartridges (mm)
Phases	**50 x 1.0**	**20 x 2.0**	**30 x 2.0**	**50 x 2.0**	**100 x 2.0**	**150 x 2.0**	**50 x 3.0**	**100 x 3.0**	**150 x 3.0**	**4 x 2.0***
										/10pk
C18	00B-4439-A0	00M-4439-B0	00A-4439-B0	00B-4439-B0	00D-4439-B0	00F-4439-B0	00B-4439-Y0	00D-4439-Y0	00F-4439-Y0	AJ0-7596
C6-Phenyl	00B-4443-A0	—	00A-4443-B0	00B-4443-B0	00D-4443-B0	00F-4443-B0	00B-4443-Y0	00D-4443-Y0	00F-4443-Y0	AJ0-7914
										/10pk
NX-C18	00B-4453-A0	00M-4453-B0	00A-4453-B0	00B-4453-B0	00D-4453-B0	00F-4453-B0	00B-4453-Y0	00D-4453-Y0	00F-4453-Y0	AJ0-8367

for ID: 2.0-3.0 mm

3µm Analytical Columns (mm)						SecurityGuard™ Cartridges (mm)
Phases	**30 x 4.6**	**50 x 4.6**	**100 x 4.6**	**150 x 4.6**	**250 x 4.6**	**4 x 3.0***
						/10pk
C18	00A-4439-E0	00B-4439-E0	00D-4439-E0	00F-4439-E0	00G-4439-E0	AJ0-7597
C6-Phenyl	00A-4443-E0	00B-4443-E0	00D-4443-E0	00F-4443-E0	00G-4443-E0	AJ0-7915
						/10pk
NX-C18	—	00B-4453-E0	00D-4453-E0	00F-4453-E0	00G-4453-E0	AJ0-8368

for ID: 3.2-8.0 mm

5µm Minibore and MidBore Columns (mm)									SecurityGuard™ Cartridges (mm)
Phases	**30 x 2.0**	**50 x 2.0**	**150 x 2.0**	**250 x 2.0**	**50 x 3.0**	**100 x 3.0**	**150 x 3.0**	**250 x 3.0**	**4 x 2.0***
									/10pk
C18	00A-4435-B0	00B-4435-B0	00F-4435-B0	00G-4435-B0	00B-4435-Y0	00D-4435-Y0	00F-4435-Y0	00G-4435-Y0	AJ0-7596
C6-Phenyl	—	00B-4444-B0	00F-4444-B0	—	00B-4444-Y0	—	00F-4444-Y0	00G-4444-Y0	AJ0-7914
									/10pk
NX-C18	00A-4454-B0	00B-4454-B0	00F-4454-B0	—	00B-4454-Y0	00D-4454-Y0	00F-4454-Y0	00G-4454-Y0	AJ0-8367

for ID: 2.0-3.0 mm

5µm Analytical Columns (mm)						SecurityGuard™ Cartridges (mm)
Phases	**30 x 4.6**	**50 x 4.6**	**100 x 4.6**	**150 x 4.6**	**250 x 4.6**	**4 x 3.0***
						/10pk
C18	00A-4435-E0	00B-4435-E0	00D-4435-E0	00F-4435-E0	00G-4435-E0	AJ0-7597
C6-Phenyl	—	00B-4444-E0	00D-4444-E0	00F-4444-E0	00G-4444-E0	AJ0-7915
						/10pk
NX-C18	—	00B-4454-E0	00D-4454-E0	00F-4454-E0	00G-4454-E0	AJ0-8368

for ID: 3.2-8.0 mm

5µm Semi-Prep Columns (mm)			SecurityGuard™ Cartridges (mm)
Phases	**150 x 10**	**250 x 10**	**10 x 10‡**
			/3pk
C18	00F-4435-N0	00G-4435-N0	AJ0-7598
C6-Phenyl	—	00G-4444-N0	AJ0-9156
			/3pk
NX-C18	00F-4454-N0	00G-4454-N0	AJ0-8369

for ID: 9-16 mm

*SecurityGuard™ Analytical Cartridges require holder, Part No.: KJ0-4282
‡SemiPrep SecurityGuard™ Cartridges require holder, Part No.: AJ0-9281
**PREP SecurityGuard™ Cartridges require holder, Part No.: AJ0-8223
◆PREP SecurityGuard™ Cartridges require holder, Part No.: AJ0-8277

Axia™ Packed Preparative Columns (mm)							SecurityGuard™ Cartridges (mm)	
Phases	**50 x 21.2**	**100 x 21.2**	**150 x 21.2**	**250 x 21.2**	**50 x 30**	**75 x 30**	**15 x 21.2****	**15 x 30.0◆**
5µm							/ea	/ea
C18	00B-4435-P0-AX	00D-4435-P0-AX	00F-4435-P0-AX	00G-4435-P0-AX	00B-4435-U0-AX	—	AJ0-7846	AJ0-8308
C6-Phenyl	—	00D-4444-P0-AX	00F-4444-P0-AX	00G-4444-P0-AX	—	—	AJ0-9157	AJ0-9158
5µm							/ea	/ea
NX-C18	00B-4454-P0-AX	00D-4454-P0-AX	00F-4454-P0-AX	00G-4454-P0-AX	00B-4454-U0-AX	00C-4454-U0-AX	AJ0-8370	AJ0-8371
10µm							/ea	/ea
C18	—	00D-4436-P0-AX	00F-4436-P0-AX	00G-4436-P0-AX	—	—	AJ0-7846	AJ0-8308
10µm							/ea	/ea
NX-C18	00B-4455-P0-AX	00D-4455-P0-AX	00F-4455-P0-AX	00G-4455-P0-AX	—	—	AJ0-8370	AJ0-8371

for ID: 18-29 mm | 30-49 mm

Axia™ Packed Preparative Columns (mm) continued							SecurityGuard™ Cartridges (mm)
Phases	**100 x 30**	**150 x 30**	**250 x 30**	**100 x 50**	**150 x 50**	**250 x 50**	**15 x 30.0◆**
5µm							/ea
C18	00D-4435-U0-AX	00F-4435-U0-AX	00G-4435-U0-AX	—	—	—	AJ0-8308
5µm							/ea
NX-C18	00D-4454-U0-AX	00F-4454-U0-AX	00G-4454-U0-AX	—	—	—	AJ0-8371
10µm							/ea
C18	00D-4436-U0-AX	00F-4436-U0-AX	00G-4436-U0-AX	—	00F-4436-V0-AX	00G-4436-V0-AX	AJ0-8308
10µm							/ea
NX-C18	00D-4455-U0-AX	00F-4455-U0-AX	00G-4455-U0-AX	00D-4455-V0-AX	00F-4455-V0-AX	00G-4455-V0-AX	AJ0-8371

for ID: 30-49 mm


guarantee
If Phenomenex analytical columns do not provide at least an equivalent separation as compared to a competing column of same particle size, similar phase, and dimensions, return the column with comparative data within 45 days for a FULL REFUND.

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Australia
t: +61 (0)2-9428-6444
f: +61 (0)2-9428-6445
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Austria
t: +43 (0)1-319-1301
f: +43 (0)1-319-1300
anfrage@phenomenex.com

Belgium
t: +32 (0)2 503 4015 (French)
t: +32 (0)2 511 8666 (Dutch)
f: +31 (0)30-2383749
beinfo@phenomenex.com

Canada
t: +1 (800) 543-3681
f: +1 (310) 328-7768
info@phenomenex.com

China
t: +86 400-606-8099
f: +86 (0)22 2532-1033
phen@agela.com

Denmark
t: +45 4824 8048
f: +45 4810 6265
nordicinfo@phenomenex.com

Finland
t: +358 (0)9 4789 0063
f: +45 4810 6265
nordicinfo@phenomenex.com

France
t: +33 (0)1 30 09 21 10
f: +33 (0)1 30 09 21 11
franceinfo@phenomenex.com

Germany
t: +49 (0)6021-58830-0
f: +49 (0)6021-58830-11
anfrage@phenomenex.com

India
t: +91 (0)40-3012 2400
f: +91 (0)40-3012 2411
indiainfo@phenomenex.com

Ireland
t: +353 (0)1 247 5405
f: +44 1625-501796
eireinfo@phenomenex.com

Italy
t: +39 051 6327511
f: +39 051 6327555
italiainfo@phenomenex.com

Luxembourg
t: +31 (0)30-2418700
f: +31 (0)30-2383749
nlinfo@phenomenex.com

Mexico
t: 01-800-844-5226
f: 001-310-328-7768
tecnicomx@phenomenex.com

The Netherlands
t: +31 (0)30-2418700
f: +31 (0)30-2383749
nlinfo@phenomenex.com

New Zealand
t: +64 (0)9-4780951
f: +64 (0)9-4780952
nzinfo@phenomenex.com

Norway
t: +47 810 02 005
f: +45 4810 6265
nordicinfo@phenomenex.com

Puerto Rico
t: +1 (800) 541-HPLC
f: +1 (310) 328-7768
info@phenomenex.com

Spain
t: +34 91-413-8613
f: +34 91-413-2290
espinfo@phenomenex.com

Sweden
t: +46 (0)8 611 6950
f: +45 4810 6265
nordicinfo@phenomenex.com

United Kingdom
t: +44 (0)1625-501367
f: +44 (0)1625-501796
ukinfo@phenomenex.com

USA
t: +1 (310) 212-0555
f: +1 (310) 328-7768
info@phenomenex.com

All other countries
Corporate Office USA
t: +1 (310) 212-0555
f: +1 (310) 328-7768
info@phenomenex.com

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