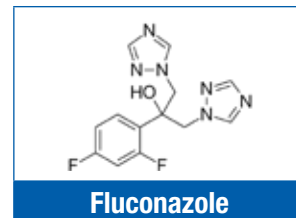


APPLICATION

Fluconazole and Related Substances

Ph. Eur. monograph 2287



Overview

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.

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
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* 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).

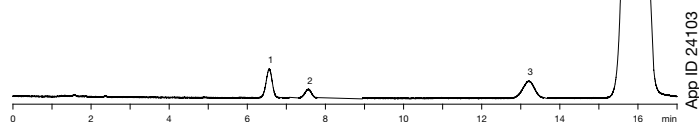
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

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

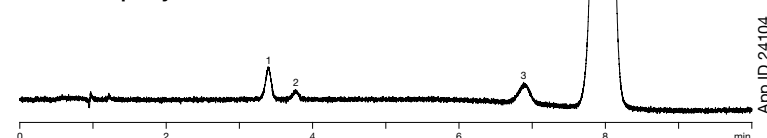


Method 2

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 %)

Luna® Ordering Information

3 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 C18(2)	00B-4251-AC	00F-4251-AC	00B-4251-AF	00F-4251-AF	—	03M-4251-AC	03M-4251-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*
C18(2)	00B-4251-A0	00F-4251-A0	00A-4251-B0	00B-4251-B0	00D-4251-B0	00F-4251-B0	AJ0-4286
							/10pk
							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*
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
									/10pk	/10pk
									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*	
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	
								/10pk	
								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*
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
								/10pk	/10pk
								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 ²
C18(2)	00D-4252-E0	00F-4252-E0	00G-4252-E0	00G-4252-N0	AJ0-4287	AJ0-7221
					/10pk	/3pk
					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



If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to a competing product of the same particle size, similar phase and dimensions, return the product with comparative data within 45 days for a FULL REFUND.



APPLICATION

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