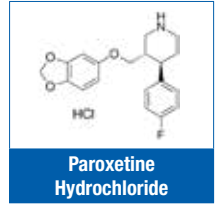


APPLICATION

Paroxetine Hydrochloride and Related Substances

Ph. Eur. monograph 2283



Overview

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.

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	<p>(a) Dilute 5.0 mL of the test solution to 50.0 mL with the solvent mixture</p> <p>(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</p> <p>(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</p> <p>(g) Dissolve 5 mg of Paroxetine Impurity A CRS* in the solvent mixture and dilute to 50 mL with the solvent mixture</p>

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: Trifluoroacetic acid R, tetrahydrofuran R, water R (5:100:900 V/V/V) B: Trifluoroacetic acid R, tetrahydrofuran R, acetonitrile R (5:100:900 V/V/V)												
Gradient	<table border="0"> <thead> <tr> <th>Time (min)</th> <th>%B</th> </tr> </thead> <tbody> <tr> <td>0 – 30 min</td> <td>20</td> </tr> <tr> <td>30 – 50 min</td> <td>20 → 80</td> </tr> <tr> <td>50 – 55 min</td> <td>80</td> </tr> <tr> <td>55 – 60 min</td> <td>80 → 20</td> </tr> <tr> <td>60 – 65 min</td> <td>20</td> </tr> </tbody> </table>	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
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
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* 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 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.

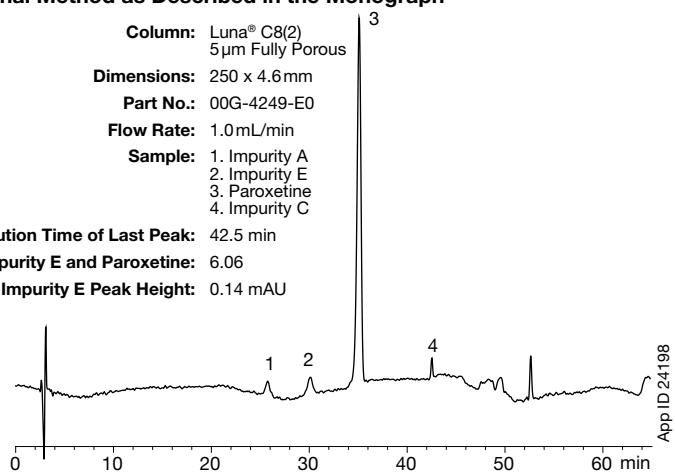


Method 1

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

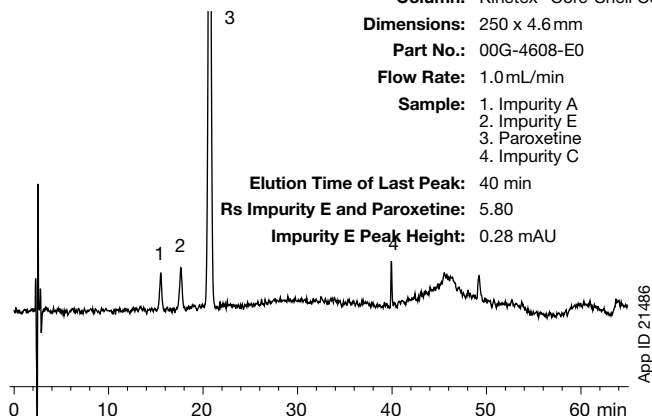


Method 2

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

Kinetex® Ordering Information

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
C8	—	00B-4608-AN	00D-4608-AN	—	AJO-8784 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
C8	00B-4608-Y0	00D-4608-Y0	—	AJO-8777 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
C8	00B-4608-E0	00D-4608-E0	00F-4608-E0	00G-4608-E0	AJO-8770 for 4.6 mm ID

[‡]SecurityGuard™ ULTRA Cartridges require holder, Part No.: AJO-9000

Luna® Ordering Information

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*	
C8(2)	—	00F-4249-A0	—	00A-4249-B0	00B-4249-B0	00F-4249-B0	00G-4249-B0	/10pk AJO-4289	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*
C8(2)	00A-4249-Y0	00B-4249-Y0	00F-4249-Y0	00G-4249-Y0	00A-4249-E0	00B-4249-E0	00C-4249-E0	/10pk AJO-4289	/10pk AJO-4290 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 [‡]
C8(2)	00D-4249-E0	00F-4249-E0	00G-4249-E0	00G-4249-N0	/10pk AJO-4290 for ID: 3.2-8.0 mm	/3pk AJO-7222 9-16 mm

*SecurityGuard™ Analytical Cartridges require holder, Part No.: KJO-4282
[‡]SemiPrep SecurityGuard Cartridges require holder, Part No.: AJO-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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