

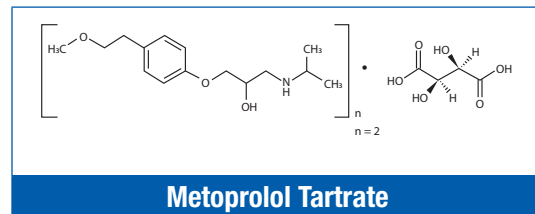
# APPLICATION

## Metoprolol Tartrate and Related Substances

Ph. Eur. monograph 1028

### Overview

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.



### 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

<b>Size</b>	150 x 3.9 mm
<b>Stationary Phase</b>	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
<b>Mobile Phase</b>	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
<b>Flow Rate</b>	1.0 mL/min
<b>Detection</b>	Spectrophotometer @ 280 nm
<b>Injection</b>	20 µL
<b>Run Time</b>	3 times the retention time of Metoprolol
<b>Elution Order</b>	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

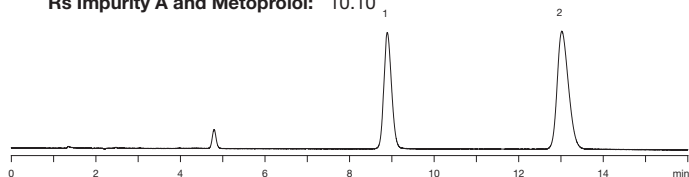
\* Metoprolol impurity A CRS (Y0000145) and Metoprolol Tartrate CRS (M1830000) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allée Kastner CS 30026F - 67081 STRASBOURG (France).

### Method 1

#### Original Method as Described in the Monograph within Allowable Adjustments

**Column:** Luna<sup>®</sup> 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

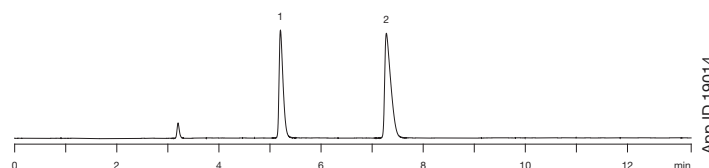


### Method 2

#### Faster Method Within Allowable Adjustments

**Column:** Kinetex<sup>®</sup> 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

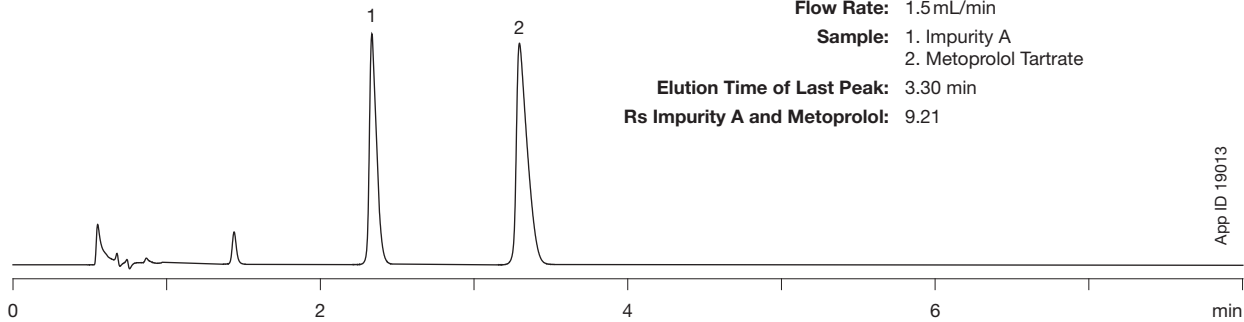


### Method 3

#### Even Faster Method within Allowable Adjustments

**Column:** Kinetex® Core-Shell C18 2.6µm  
**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 %)

## Kinetex® Ordering Information

5 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges <sup>‡</sup>
Phases	30 x 2.1	50 x 2.1	100 x 2.1	150 x 2.1	3/pk
C18	00A-4601-AN	00B-4601-AN	00D-4601-AN	00F-4601-AN	AJO-8782 for 2.1 mm ID

5 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges <sup>‡</sup>
Phases	50 x 3.0	100 x 3.0	150 x 3.0	3/pk
C18	00B-4601-YO	00D-4601-YO	00F-4601-YO	AJO-8775 for 3.0 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges <sup>‡</sup>
Phases	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	3/pk
C18	00B-4601-E0	00D-4601-E0	00F-4601-E0	00G-4601-E0	AJO-8768 for 4.6 mm ID

5 µm Semi-Preparative Columns (mm)			SecurityGuard SemiPrep Cartridges <sup>***</sup>
Phases	150 x 10	250 x 10	3/pk
C18	00F-4601-N0	00G-4601-N0	AJO-9278 for 9-16 mm ID

<sup>‡</sup>SecurityGuard ULTRA Cartridges require holder, Part No.: AJO-9000

<sup>\*\*\*</sup>SemiPrep SecurityGuard Cartridges require holder, Part No.: AJO-9281

## 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*
C18(2)	00B-4252-A0	00F-4252-A0	00G-4252-A0	00A-4252-B0	00B-4252-B0	00F-4252-B0	00G-4252-B0	/10pk AJO-4286 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	/10pk AJO-4286 for ID: 2.0-3.0 mm	/10pk AJO-4287 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 <sup>‡</sup>
C18(2)	00D-4252-E0	00F-4252-E0	00G-4252-E0	00G-4252-N0	/10pk AJO-4287 for ID: 3.2-8.0 mm	/3pk AJO-7221 9-16 mm

<sup>\*</sup>SecurityGuard™ Analytical Cartridges require holder, Part No.: KJO-4282

<sup>‡</sup>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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