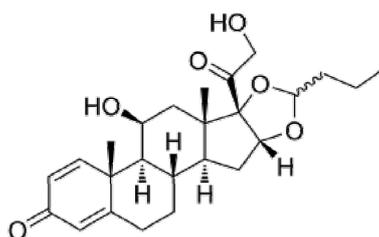


Budesonide and Related Substances (EP)



Budesonide

Budesonide is a glucocorticoid steroid for the treatment of asthma, COPD and non-infectious rhinitis (including hay fever and other allergies), and for treatment and prevention of nasal polyposis. In addition, it is used for Crohn's disease (inflammatory bowel disease).

A new extended-release formulation of budesonide called "Uceris" has been recently approved (2013) by the United States FDA for ulcerative colitis.

The current EP monograph method for Budesonide and related substances specifies the use of a 150x4.6 mm column with and end-capped octadecylsilyl (ODS or RP-18) silica gel for chromatography R (3 μm). The relative retention with reference to budesonide epimer B (retention time = about 17 min); impurity A = about 0.1; epimers of impurity D = about 0.63 and 0.67; impurity L = about 0.95; epimers of impurity G = about 1.2 and 1.3; epimers of impurity K = about 2.9 and 3.0. The system suitability criteria also specify a minimum resolution of 1.5 between the 2 principal peaks (budesonide epimers A and B) in the chromatogram.

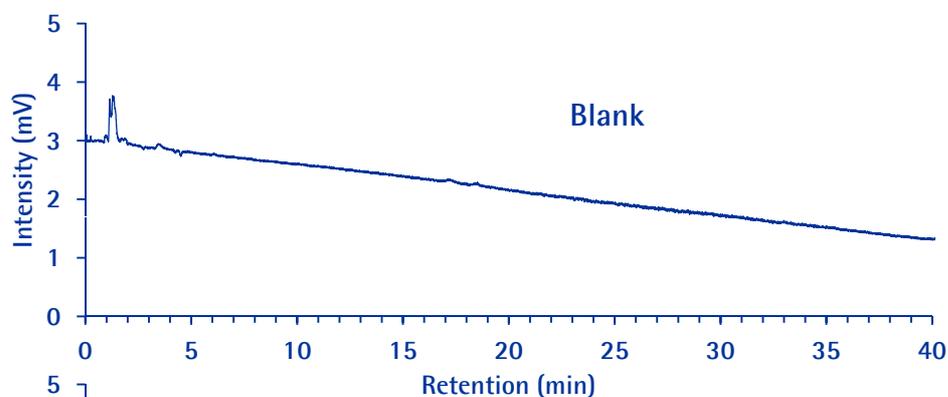
The following pages illustrate that the acceptance criteras are being met despite Impurity A and epimers of impurity K are not identified in the given chromatogram (not present in tested sample). Thus using a Purospher® STAR RP-18 endcapped (3 μm), Hibar® RT 150x4.6 mm column it is possible to comply with the given requirement for the analysis of Budesonide and related substances.

Budesonide and Related Substances (EP)

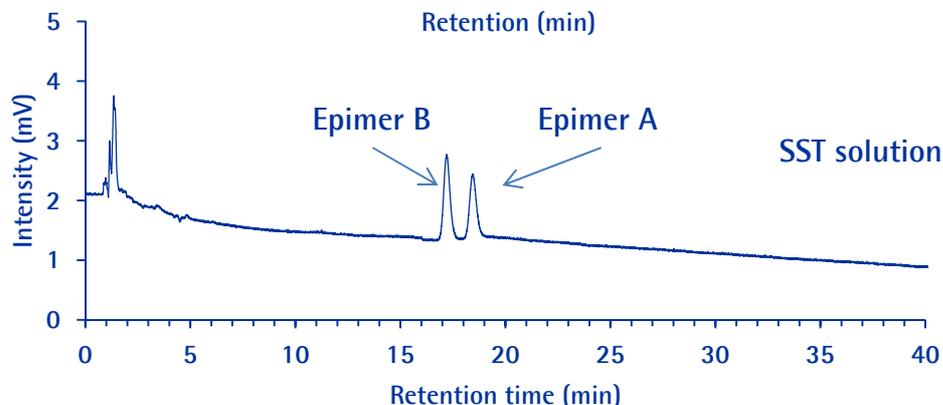
Purospher® STAR RP-18 endcapped

Chromatographic Conditions

Column: Purospher® STAR RP-18 endcapped (3 µm) Hibar®150x4.6 mm 1.50470.0001
 Injection: 20 µL
 Detection: UV, 240 nm
 Cell: 10 µL
 Flow Rate: 1.0 mL/min
 Buffer: to 900 mL of a 4 g/L solution of sodium dihydrogen phosphate , add 100 mL of a 2.5 g/L solution of phosphoric acid . Adjust the pH if necessary.
 Mobile Phase: A: Anhydrous ethanol , acetonitrile, phosphate buffer solution pH 3.2; 2:32:68 (v/v/v)
 B: Acetonitrile, phosphate buffer solution pH 3.2 R; 50:50 (v/v)
 Gradient: See table
 Temperature: 50°C
 Diluent: Acetonitrile R, phosphate buffer solution pH 3.2; 32:68 (v/v)
 Test Solution: 50 mg of the substance to be examined in 15 mL of acetonitrile and dilute to final volume (50 mL) with phosphate buffer solution pH 3.2.
 Resolution Solution: Dilute 1.0 mL of test solution (a) to 10.0 mL with the solvent mixture.
 Dilute 1.0 mL of this solution to 100.0 mL with the solvent mixture.
 Pressure Drop: 182 – 162 Bar (2639 – 2349 psi)

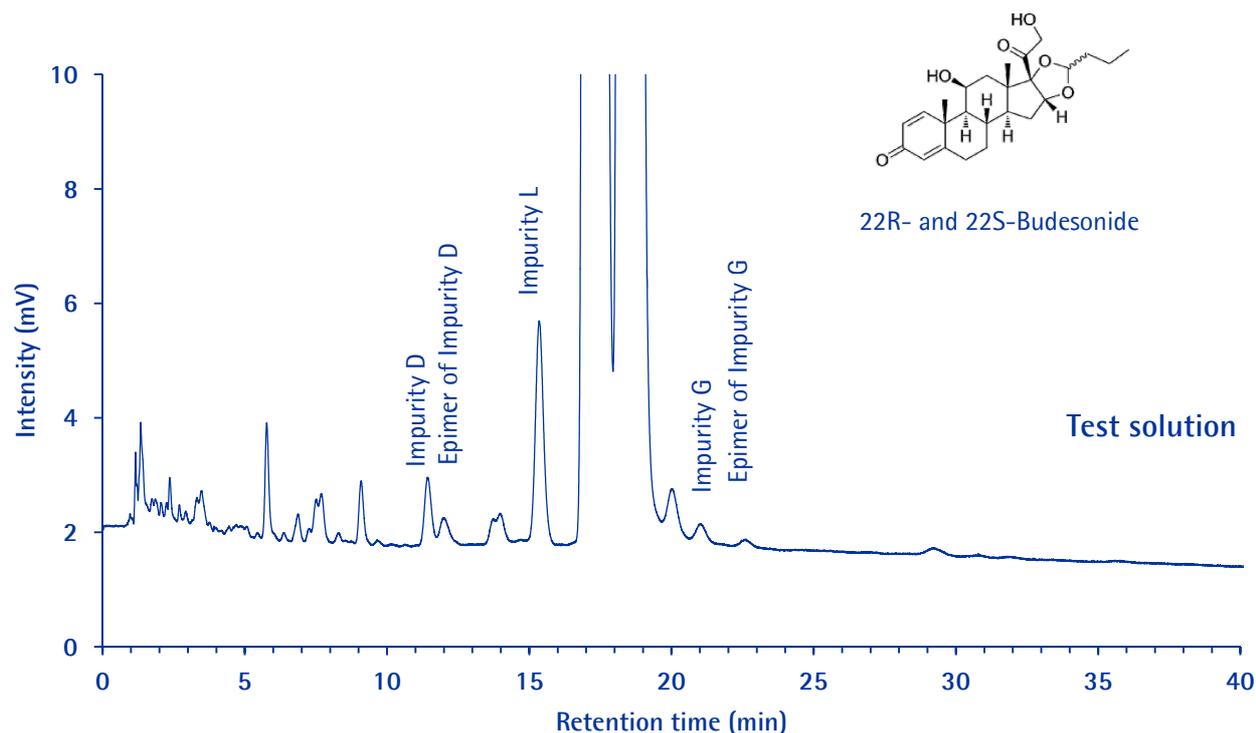


Time (min)	A (%)	B (%)
0.0	100	0
38.0	100	0
50.0	0	100
60.0	0	100
65.0	100	0
70.0	100	0



Budesonide and Related Substances (EP)

Purospher® STAR RP-18 endcapped



In this sample neither impurity A, nor the epimers of impurity K could be found!

Suitability requirement: NLT 1.5



Chromatographic Data:

No.	Compound	Retention Time (min)	Resolution	RRT
1	Impurity D	11.4		0.66
2	Epimer of Impurity D	12.0		0.69
3	Impurity L	15.4		0.90
4	Budesonide Epimer B	17.2		1.00
5	Budesonide Epimer A	18.4	2.2	1.07
6	Impurity G	21.0		1.22
7	Epimer of Impurity G	22.6		1.31