Separation of Zolmitriptan and its Organic Impurities per USP Monograph

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Overview

Zolmitriptan is a selective serotonin receptor agonist of the 1B and 1D subtypes and its action on 5-HT 1B/1D receptors causes vasoconstriction in intracranial blood vessels. The development of a quick and efficient analysis of Zolmitriptan and its related organic impurities is of interest for generic drug manufacturers. In this application note, we report on the separation of Zolmitriptan and its related organic impurities using three batches of Luna Omega 5 µm C18 columns according to the USP monograph for Zolmitriptan.

The use of the 150 mm length Luna Omega 5 µm C18 column is an allowable adjustment per USP <621> since the L/dp ratio (150/5 = 30,000) is within the allowable range of -25 to +50 % of the L/dp ratio (125/5 = 25,000) for the original 125 mm length, 5 µm column used to elucidate the assay method.

System suitability per USP Monograph for the Zolmitriptan Assay requires resolution no less than (NLT) 5.0 between Zolmitriptan and Zolmitriptan Related Compound E, a percent relative standard deviation (%RSD) of no more than (NMT) 0.73 % for Zolmitriptan, and a symmetry factor NMT 2.0 for Zolmitriptan. All system suitability requirements for Zolmitriptan Assay were met with all three batches of Luna Omega C18 columns (**Figure 2**).

System suitability per USP Monograph for the Zolmitriptan Organic Impurities requires resolution NLT 5.0 between Zolmitriptan and Zolmitriptan Related Compound E and a symmetry factor NMT 3.0 for Zolmitriptan. These requirements for system suitability for Organic Impurities were met with all three batches of Luna Omega C18 columns (**Figure 3**).

Across the three batches of Luna Omega C18 columns tested, the retention time reproducibility for Assay was 1.33 % and 1.79 % for Zolmitriptan and Related Compound E, respectively (**Table 2**).

All solutions were prepared as indicated in the USP Monograph for Zolmitriptan. USP Zolmitriptan RS (Catalog No. 1727009) and USP Zolmitriptan Related Compound E RS (Catalog No. 1727064) were purchased from USP.

LC-UV Conditions

Column: Luna™ Omega 5 µm C18
Dimensions: 150 X 4.6 mm
Part No.: 00F-4785-E0
Mobile Phase: Mobile Phase (**Table 1**)
Flow Rate: 1.3 mL/min
Injection Volume: 20 µL
Temperature: Ambient
Detector: UV @ 225 nm
System: Waters® Arc HPLC

Table 1. Preparation of Solutions

Solution	Composition
Mobile Phase	Acetonitrile / Water / Trifluoroacetic Acid / Triethylamine (135:865:1:0.25, v/v/v/v)
Diluent	Mobile Phase
Standard Solution – Assay	0.025 mg/mL of USP Zolmitriptan RS in Diluent
System Suitability Solution – Assay	0.12 µg/mL of USP Zolmitriptan Related Compound E RS and 25 µg/mL of USP Zolmitriptan RS in Diluent
System Suitability Solution – Organic Impurities	0.5 µg/mL of USP Zolmitriptan Related Compound E RS and 0.1 mg/mL of USP Zolmitriptan RS in Diluent

Figure 1. Zolmitriptan Structure

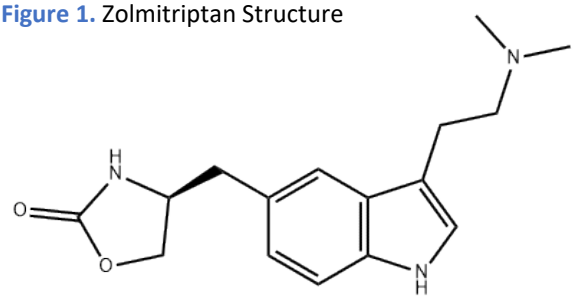
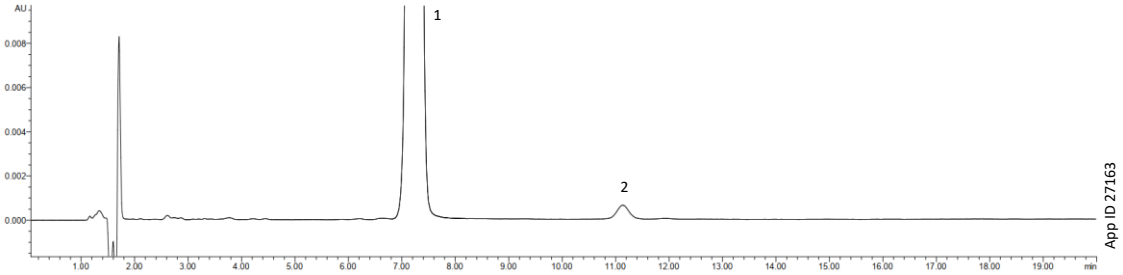


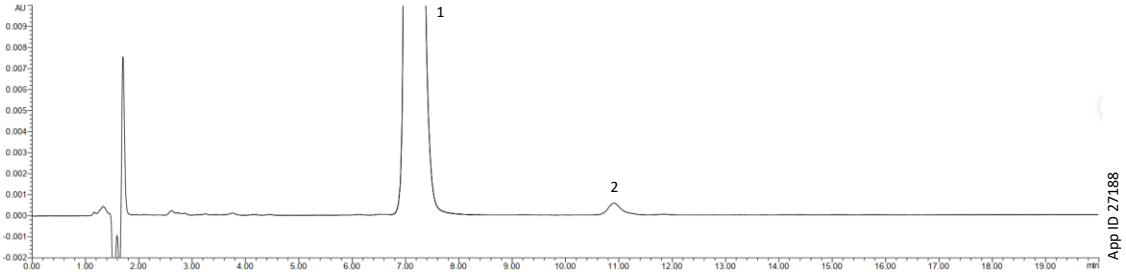
Figure 2. System Suitabiity Solution – Assay

Luna™ Omega 5 µm C18 – Batch 1



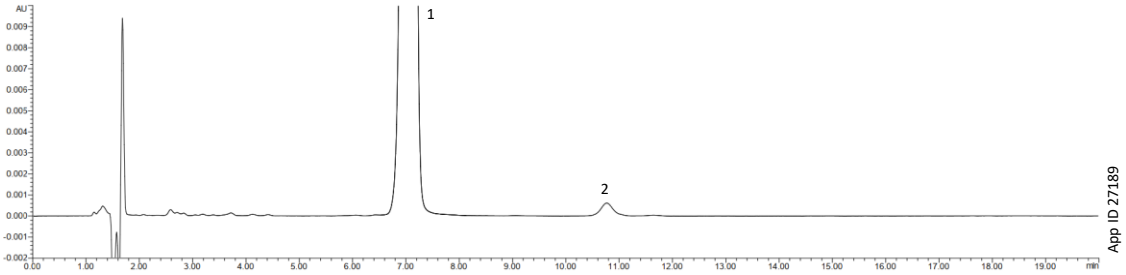
Peak No.	Analyte	Retention Time (min)	Resolution	Area %RSD	Symmetry Factor
1	Zolmitriptan	7.22	11.18	0.04	1.10
2	Zolmitriptan Related Compound E	11.14		-	-
N = 6 Injections					

Luna Omega 5 µm C18 – Batch 2



Peak No.	Analyte	Retention Time (min)	Resolution	Area %RSD	Symmetry Factor
1	Zolmitriptan	7.12	10.14	0.16	1.30
2	Zolmitriptan Related Compound E	10.91		-	-
N = 6 Injections					

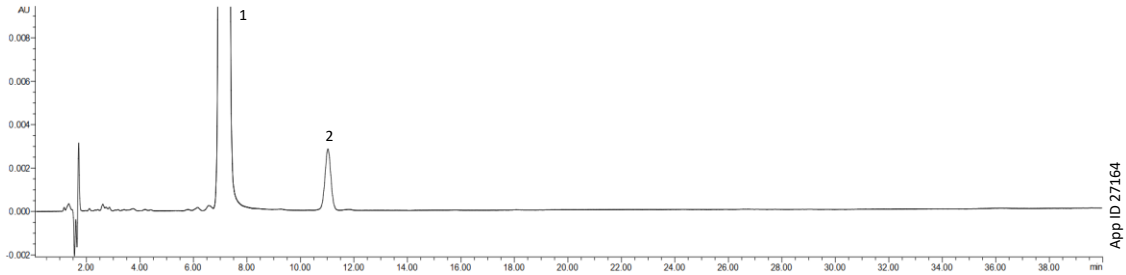
Luna Omega 5 µm C18 – Batch 3



Peak No.	Analyte	Retention Time (min)	Resolution	Area %RSD	Symmetry Factor
1	Zolmitriptan	7.03	10.65	0.27	1.06
2	Zolmitriptan Related Compound E	10.75		-	-
N = 6 Injections					

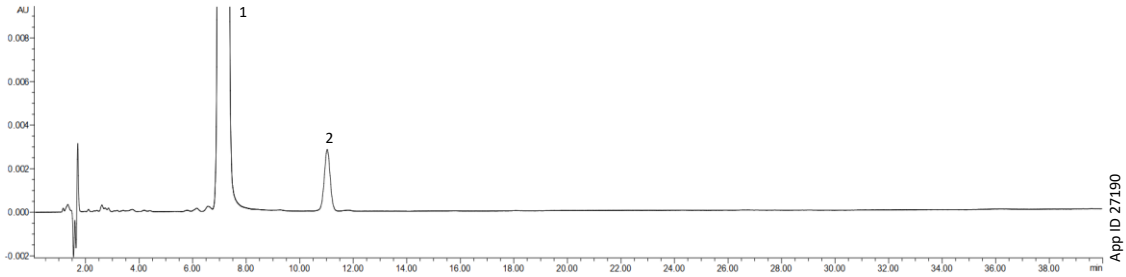
Figure 3. System Suitability Solution – Organic Impurities

Luna™ Omega 5 µm C18 – Batch 1



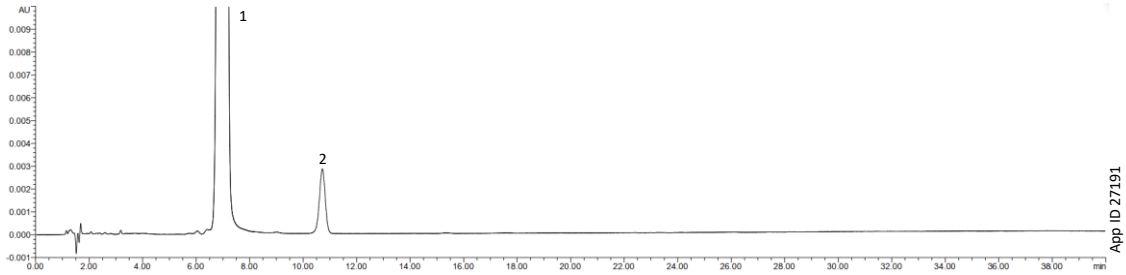
Peak No.	Analyte	Retention Time (min)	Resolution	Symmetry Factor
1	Zolmitriptan	7.08	11.0	1.48
2	Zolmitriptan Related Compound E	11.03		-

Luna Omega 5 µm C18 – Batch 2



Peak No.	Analyte	Retention Time (min)	Resolution	Symmetry Factor
1	Zolmitriptan	7.01	9.86	1.61
2	Zolmitriptan Related Compound E	10.87		-
N = 6 Injections				

Luna Omega 5 µm C18 – Batch 3



Peak No.	Analyte	Retention Time (min)	Resolution	Symmetry Factor
1	Zolmitriptan	6.90	10.64	1.41
2	Zolmitriptan Related Compound E	10.68		-
N = 6 Injections				

Table 2. Batch-to-Batch Retention Time Reproducilbilty of Luna™ Omega 5 µm C18 Columns for Assay

Batch No.	Zolmitriptan	Zolmitriptan Related Compound E
1	7.22	11.14
2	7.12	10.91
3	7.03	10.75
Mean	**7.12**	**10.93**
STD	**0.10**	**0.20**
%RSD	**1.33**	**1.79**

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