



## CONFIDENTIAL REPORT

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### Testing of Fluticasone and Azelastine Nasal Spray

Thank you for contacting Avomeen Analytical Services for testing of Fluticasone and Azelastine Nasal Spray. Following are the results, methodology, and data associated with our analysis.

**Table 1:** Sample description

	Avomeen ID	Batch Number	Sample Description	Expire Day
Sample 1	053116ST1395	A16009SV	Boxes of AZEFLO N/S drug product, LUPIN	01/2018
Sample 2	053116ST1396	DND0214	Boxes of NASOMAC –AF drug product, MACLEODS	10/20/2017
Sample 3	053116ST1398	MS1476	Boxes of COMBINASE AQ drug product, CADILA	12/2017
Sample 4	053116ST1399	ASA16002	Boxes of FLORESP AZ Drug product, EMCURE	01/2018
Sample 5	053116ST1400	1601009	Boxes of EZICAS AZ Drug Product , INTAS	12/2017
Sample 6	053116ST1401	END0237	Boxes of NASOCOM AZ drug product, DR REDDY	11/2017

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**Figure 1:** Samples as received

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## Executive Summary

The testing results of Fluticasone and Azelastine Nasal Spray for particle size, pH Value, EDTA, Glycerin, Polysorbate 80, and MCC are shown in Table 2. The accuracy of each measurement will be within five relative percent per excipient. The information of APIs and the preservatives on the label is also included in Table 3.

**Table 2:** Testing results for particle size, PH Value, EDTA, Glycerin, Polysorbate 80, and MCC

	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Ethylenediaminetetraacetic Acid (EDTA) (wt %)	<0.0001	<0.0001	0.02	<0.0001	<0.0001	<0.0001
Glycerin (wt %)	2.1	2.4	2.0	3.0	2.4	2.5
Polysorbate 80 (wt %)	Detected	Detected	Detected	Detected	Detected	Detected
Micro Crystalline Cellulose with carboxymethyl cellulose (wt %)	2.8	2.7	2.9	2.9	2.9	2.9
Particle Size Mean Diameter(nm) by ZetaPALS	460.4	309.8	442.9	460.9	452.2	391.7
Particle Size Mean Diameter(μm) by light microscopy	1.14 ±0.32	0.84±0.38	0.98±0.40	0.98±0.42	1.02±0.41	0.84±0.28
pH Value	6.21	6.32	5.75	6.27	6.33	6.33

**Table 3:** Information on the label for APIs and preservatives

	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Azelastine Hydrochloride IP (W/v)	0.14	0.14	0.14	0.14	0.14	0.14
Fluticasone Propionate IP (W/v)	0.05	0.05	0.05	0.05	0.05	0.05
Benzalkonium Chloride Solution IP (W/v)	0.02	0.01	0.01	0.02	0.01	0.01
Phenylethyl Alcohol IP (W/v)	0.25	0.25	0.25	0.25	0.25	0.25

## Quality Statement

The work reported herein was conducted non- GMP and was not reviewed by Quality Assurance. All data in this report accurately reflects the raw data stored in the archives of Avomeen Analytical Services.

## Analytical Testing

### High Performance Liquid Chromatography (HPLC) Analysis for Ethylenediaminetetraacetic Acid (EDTA)

Instrument: Agilent 1100

Column: Supelco Lichrosphere RPC18, 250 mm × 4.6 mm, 5 μm

Column Temperature: 30°C

Flow rate: 1 mL/min

Injection Volume: 10 μL

Mobile phase: 25 mM sodium acetate buffer with 1 mM tetrabutylammonium bromide in 950 mL deionized water and 50 mL Methanol, pH 4.0, isocratic 20 min

Detector wavelength: 265 nm

EDTA standard preparation: EDTA standard was derivatized with a ferric chloride solution and analyzed by HPLC-UV. An EDTA standard (EDTA content 1.002 mg/mL) stock solution was prepared in D.I. water. 5 mL of the EDTA standard solution was derivatized by 3 mL of ferric chloride solution (3.2 mg/mL) in 50 mL volumetric flask. The mixture was shaken and kept in the oven at 70°C for 20 min, and finally the

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volume was made up with D.I. water. The derivatized EDTA solution was diluted and used for a calibration curve.

Sample preparation: ~500 mg of samples was mixed with 5 mL of ferric chloride solution (3.2 mg/mL) in 10 mL volumetric flask. The mixture was shaken well and kept in the oven at 70°C for 20 min, then cooled to room temperature, made with D.I. water and filtered for HPLC analysis. The amount of ferric chloride for standard and samples was assured to be in excess for the derivatization.

**High Performance Liquid Chromatography Analysis (HPLC-ELSD) for Polysorbate 80**

Apparatus: Agilent HPLC 1100 with Alltech 2000ES Evaporative Light Scattering detector (ELSD)

Column: Kinetex, particle size 2.6 µm, 150 × 4.6 mm, 100A

ELSD conditions: Impactor On mode, 60°C drift tube temperature, 2.0 L/min nitrogen flow rate

Injection volume: 10 µL

Column temperature: 30°C

Column flow rate: 0.6 mL/min

Run time: 50 min

Mobile phase A: D.I. water with 0.1% Formic Acid

Mobile phase B: Acetonitrile with 0.1% Formic Acid

Gradient Elution:

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0	70	30
30	0	100
45	0	100
45.1	70	30
50	70	30

Sample preparation: about 1 g of each sample was dissolved individually with 5 mL of methanol and sonicated for 10 min at room temperature. After thoroughly mixing, the sample solution was filtered prior to injection into the HPLC-ELSD. 57 mg of Polysorbate 80 standard was dissolved in 25 mL methanol and diluted to 1000 – 3000 µg/mL as calibration standards.

**HPLC-ELSD Analysis for Glycerin**

Instrument: Agilent 1100 equipped with Alltech 2000 evaporative light scattering detector (ELSD)

Column: Imstakt Unison UK-Amino, 250 mm × 4.6 mm, 3 µm

Column Temperature: 37°C

Injection Volume: 20 µL

Mobile phase: A: D.I. water; B: Acetonitrile

Gradient: Isocratic 80% A, 20% B

Run time: 30 min

Flow rate: 1.0 mL/min

ELSD parameters: Impactor ON mode

Tube temperature: 42°C

Gas flow rate: 1.5 L/min

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