



BDG SYNTHESIS

Certificate of Analysis

BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

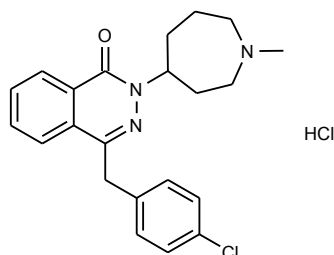
Barry Dent

Barry R. Dent, PhD, Director
17 December 2012

Name: Azelastine HCl

CAS Number: 79307-93-0

Structure:



Molecular Weight: $C_{22}H_{24}ClN_3O \cdot HCl = 418.36$

Lot Number: BDG 3925.1

Appearance: White, crystalline solid

Corrected Purity: 98.9 % (HPLC) - 0.9 % (ethanol) - 5.3 % (water) = 92.7 %

Re-test Date: 17 December 2017

Storage and Handling: Temperature: refrigerate for prolonged storage; may be handled and shipped at ambient temperature.

Humidity: may be hygroscopic; store desiccated; recommended to determine water content periodically.

Light: protect from strong sunlight.

Caution: only experienced laboratory personnel should handle the material.

Identity and Purity

Proton NMR Spectrum

Identity: The signals are consistent with the proposed structure and in accord with literature where available. The spectrum shows the presence of more than one conformer of the product as indicated by the broadening of some signals or the presence of some smaller sets of lesser intensity.

Residual Solvents: a small amount of ethanol (0.9 % w/w) is observed.

Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: The signals are consistent with the proposed structure and in accord with literature where available. All carbon peaks have an associated signal indicating the presence of more than one conformer of the product as seen in the proton spectrum.

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 382.1684. $C_{22}H_{25}ClN_3O$ $[M+H]^+$ (free base) requires m/z 382.1686. The deviation of 0.5 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A sharp, symmetrical peak is observed (98.9 %). Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis

	Found:	C 60.01, H 6.21, N 9.50 %
$C_{22}H_{24}ClN_3O \cdot HCl \cdot 1.2H_2O$	Requires:	C 60.06, H 6.28, N 9.55 %
$C_{22}H_{24}ClN_3O \cdot HCl$	Requires:	C 63.16, H 6.02, N 10.04 %

The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the "best-fit" hydrated molecular formula is given.

Karl-Fischer Analysis

	Found:	H ₂ O 5.3 %
$C_{22}H_{24}ClN_3O \cdot HCl \cdot 1.2H_2O$	Requires:	H ₂ O 4.9 %

Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

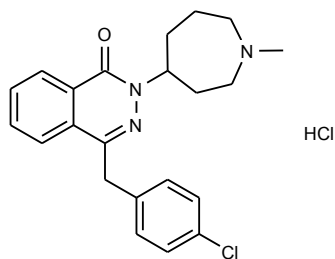
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.

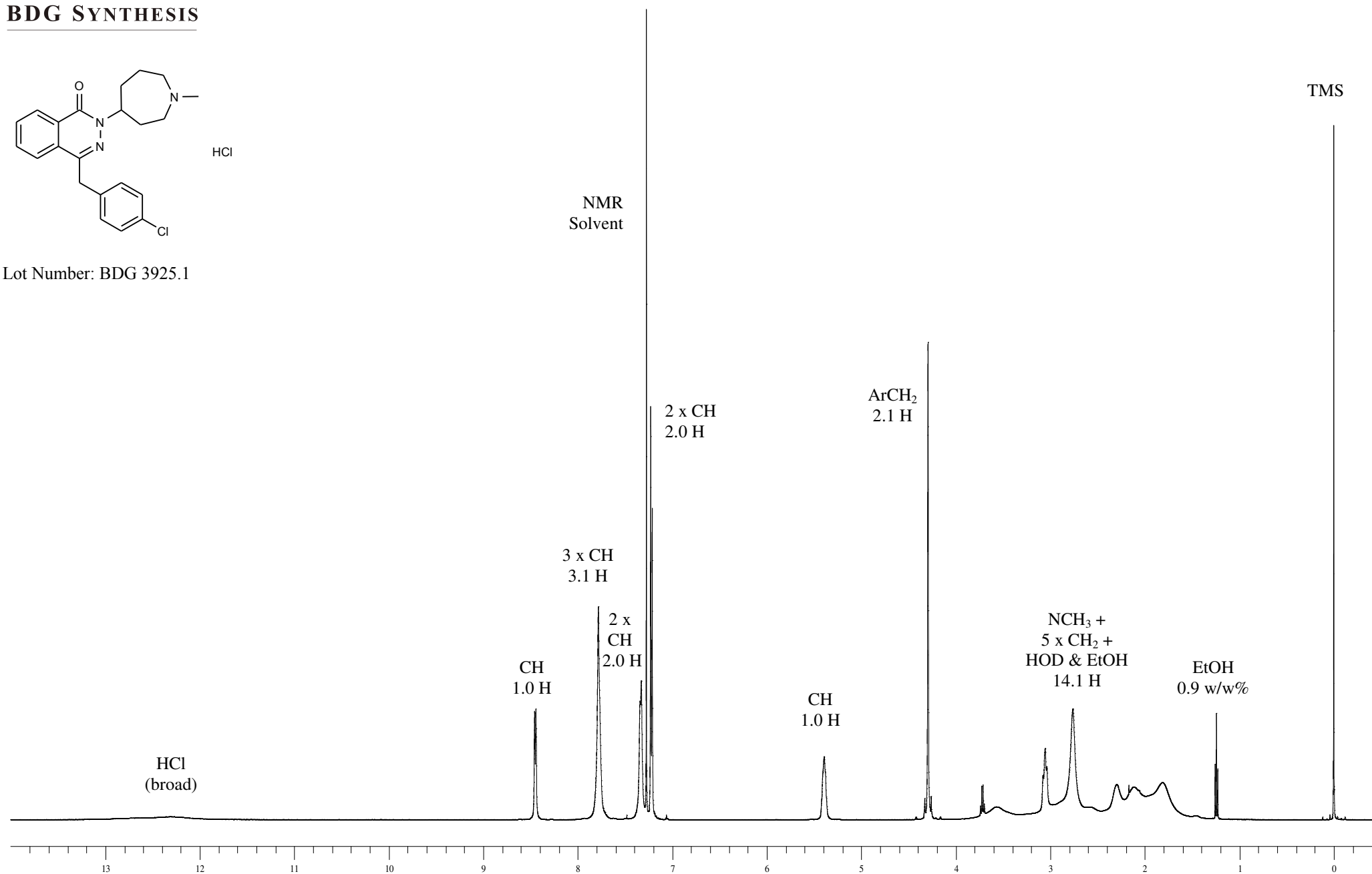


Proton NMR Spectrum of Azelastine HCl in CDCl₃

BDG SYNTHESIS



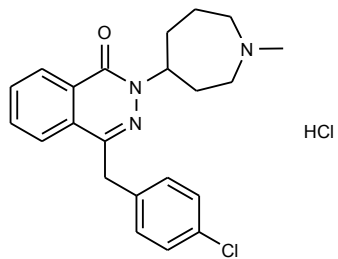
Lot Number: BDG 3925.1



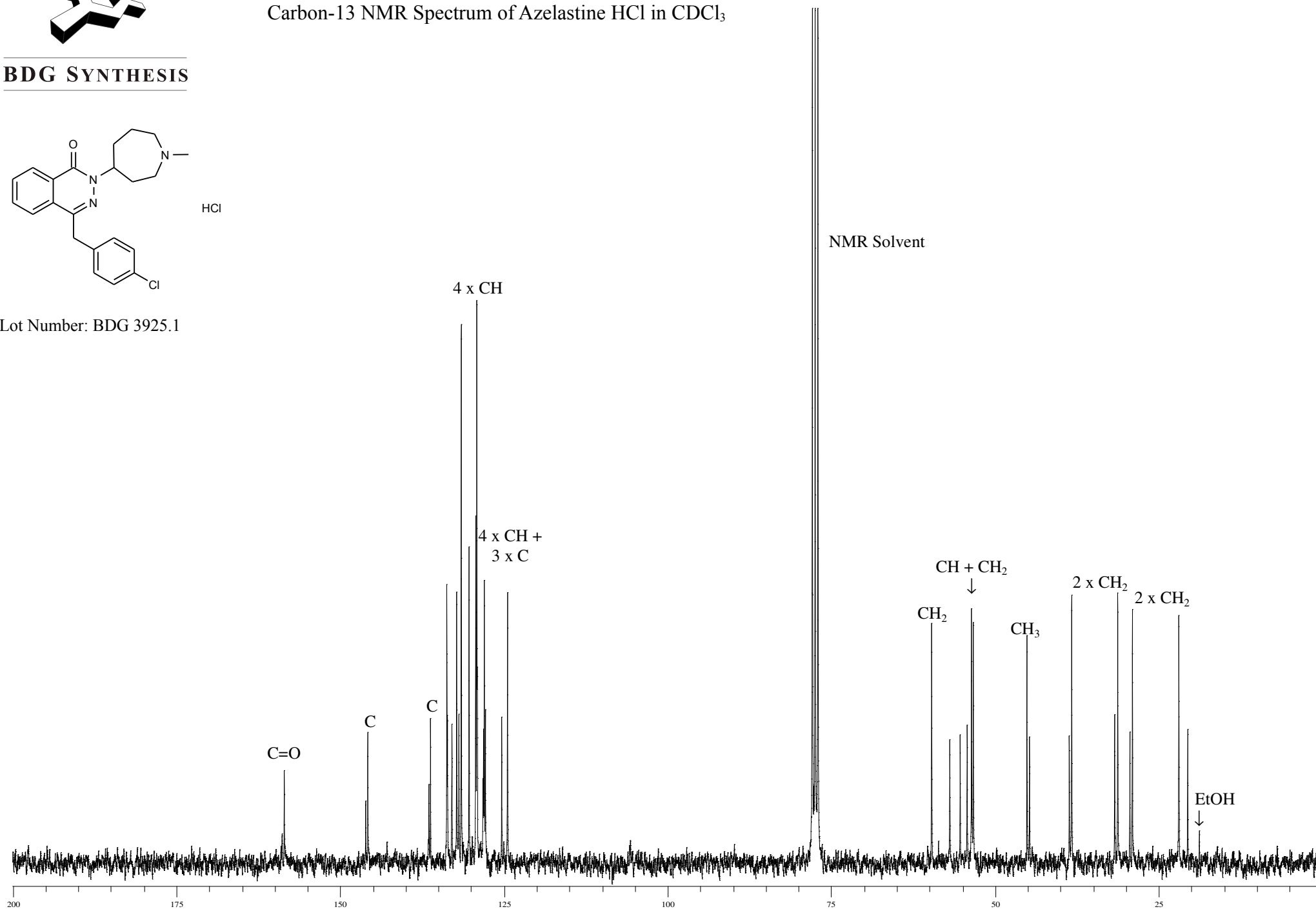


Carbon-13 NMR Spectrum of Azelastine HCl in CDCl₃

BDG SYNTHESIS



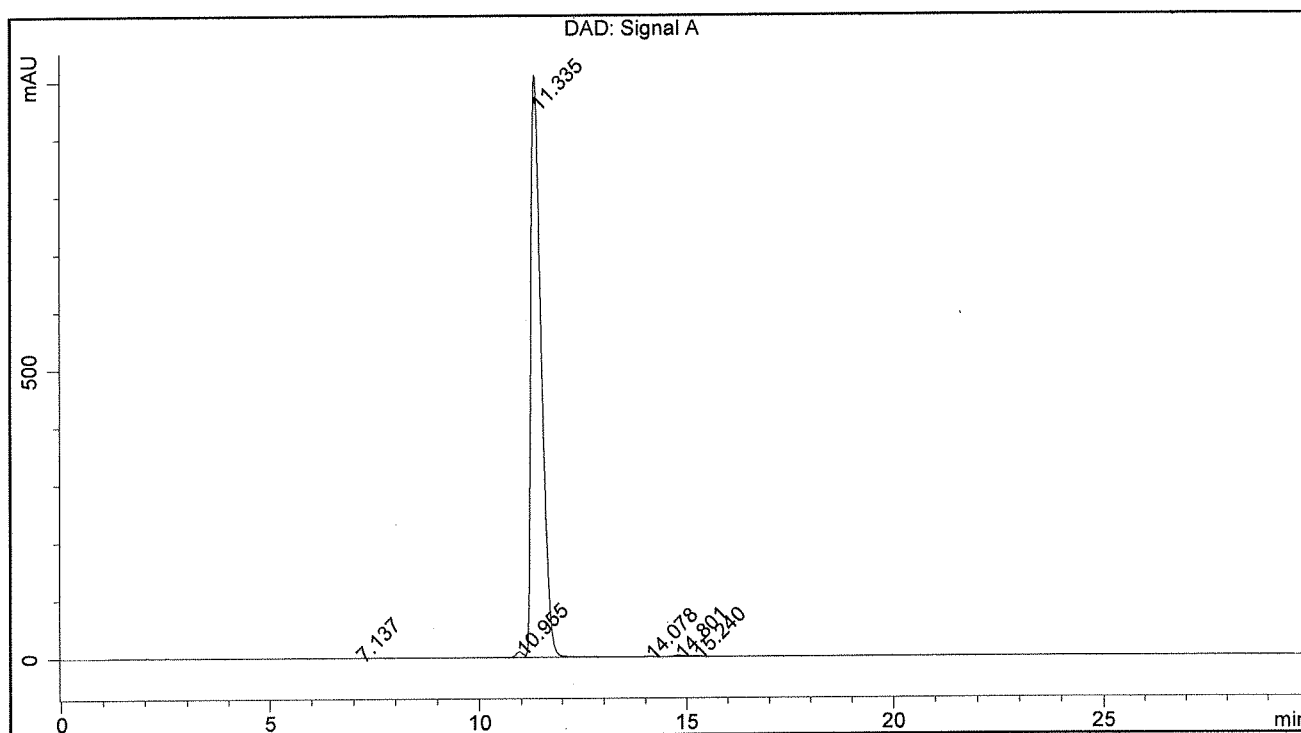
Lot Number: BDG 3925.1



BDG - Analysis of Azelastine HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 60:40 Ion Pair Buffer : Acetonitrile
 IP Buffer : 600ml 2.02g Na Heptanesulphonate + 0.68g Potassium diHydrogen Phosphate pH=3,0 (H3PO4)
 Flow Rate : 1.0 mL/min
 Sample Solvent : 1:1 Water:Acetonitrile
 Column Temperature : 30C
 Injection Volume : 10 uL
 Detection : UV at 210 nm

Sample Name	BDG 3925.1	Instrument	AnalyticalLC01
Acquisition	17/12/2012, 17:25:30	Method (rev.)	LC10549a (4)
Sequence	BDG_17Dec2012a - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.14 min	0.2195	2.4288	0.1591 min	0.014 %
2	10.95 min	9.6415	116.1536	0.1886 min	0.651 %
3	11.33 min	1009.9989	17633.8426	0.2717 min	98.894 %
4	14.08 min	0.4675	8.4791	0.2856 min	0.048 %
5	14.80 min	2.1586	38.3862	0.2735 min	0.215 %
6	15.24 min	1.6317	31.7829	0.2833 min	0.178 %