



BDG SYNTHESIS

Certificate of Analysis

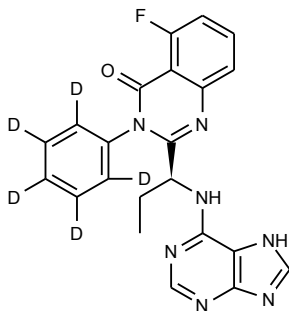
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
3 July 2014

Name: Idelalisib-d₅
CAS Number: 870281-82-6 (unlabelled)

Structure:



Molecular Weight: C₂₂H₁₃D₅FN₇O = 420.45
Lot Number: BDG 15039.4
Appearance: Off-white, amorphous powder
Corrected Purity: 99.5 % (HPLC) - 1.1 % (hexanes) - 1.3 % (water) = 97.1 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 3 July 2019
Storage and Handling: Temperature: refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity: not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
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.

Isotopic Labelling: signals at the sites of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: a small amount of hexanes (1.1 % w/w) is observed.

Impurities: traces of unidentified impurities are seen in the baseline.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic Labelling: signals at the sites of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found m/z 421.1941. $C_{22}H_{14}D_5FN_7O$ $[M+H]^+$ requires m/z 421.1949. The deviation of 1.9 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for d_0 material was seen (detection limit about 0.5 %).

HPLC

A sharp, slightly tailing peak is observed (99.5 %). 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 62.10, H 3.35, D 2.47, N 22.15 %
$C_{22}H_{13}D_5FN_7O \cdot 0.3H_2O$	Requires:	C 62.05, H 3.22, D 2.36, N 23.02 %, H_2O 1.27 %
$C_{22}H_{13}D_5FN_7O$	Requires:	C 62.85, H 3.12, D 2.40, N 23.32 %

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. In the absence of a Karl-Fischer water analysis, we recommend that the "best-fit" water content be used when determining corrected purity.

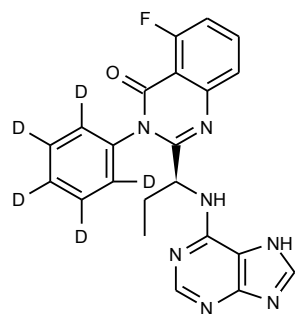
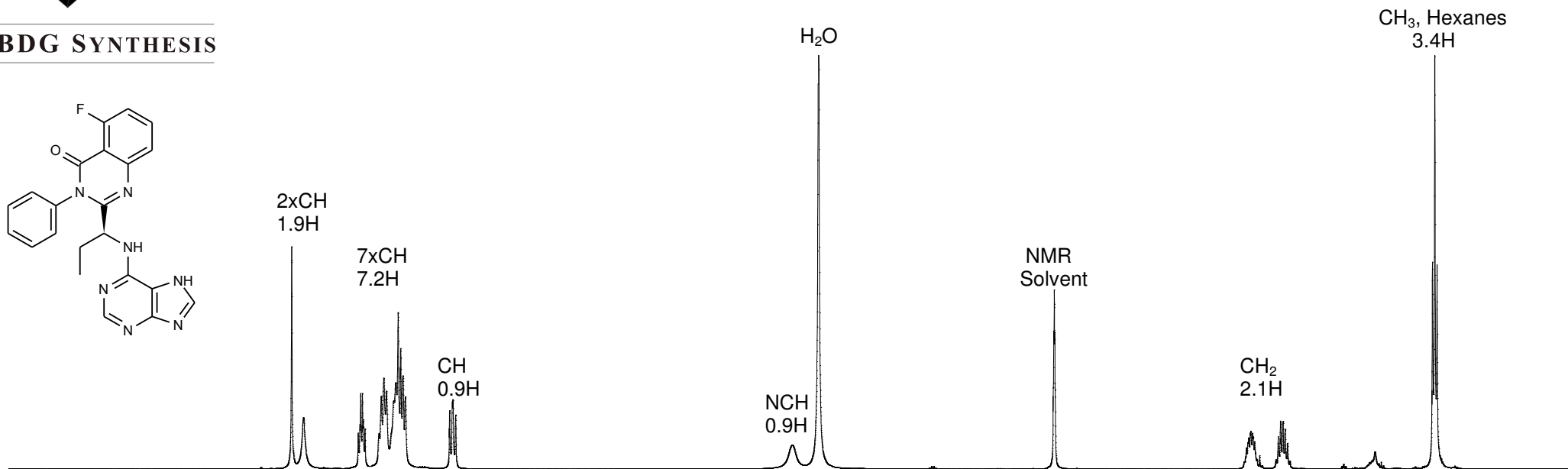
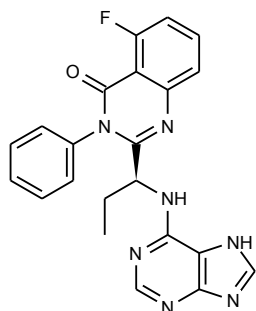
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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.

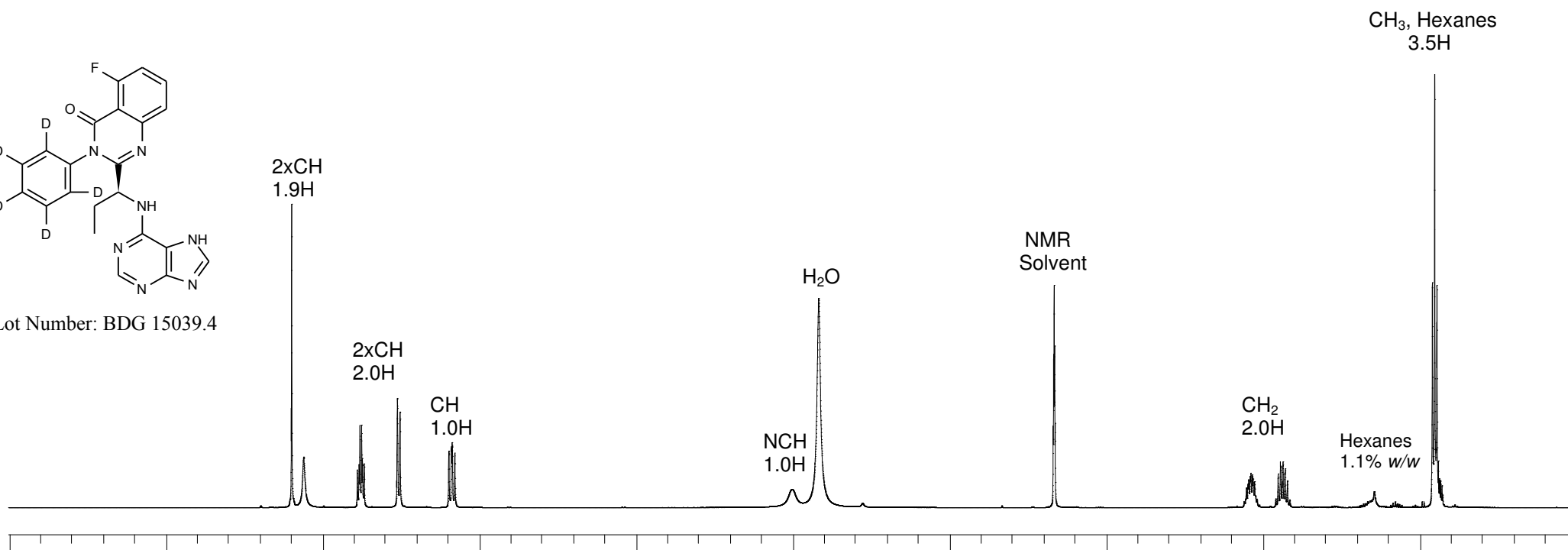


Proton NMR Spectrum of Idelalisib (top) and Idelalisib-d₅ (bottom) in Methanol-d₄

BDG SYNTHESIS



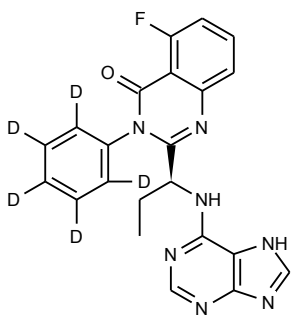
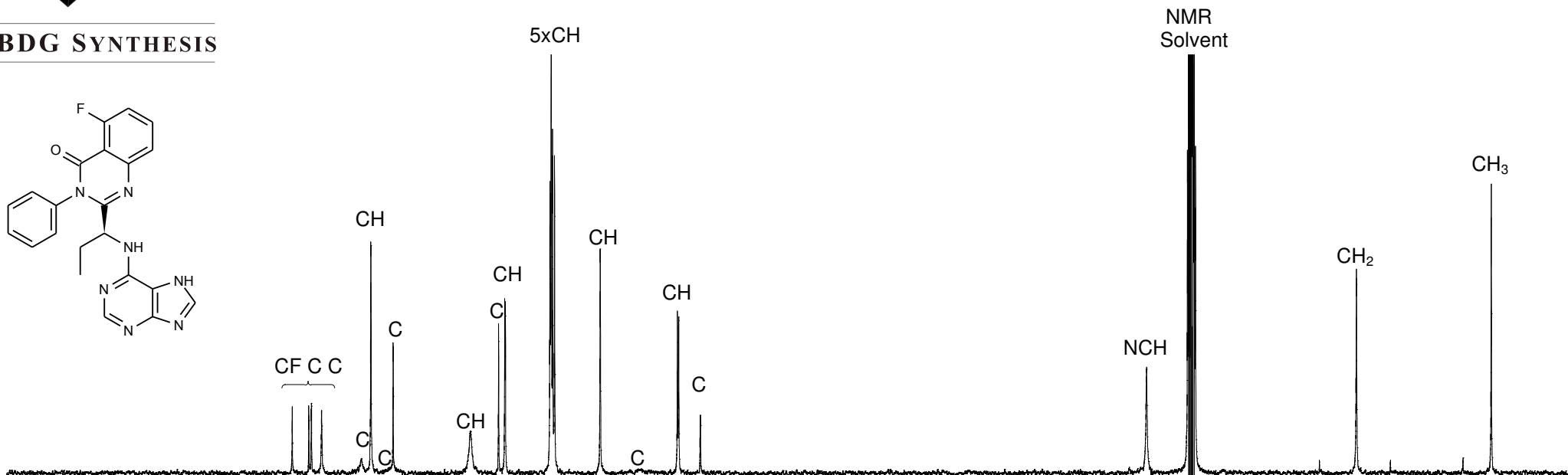
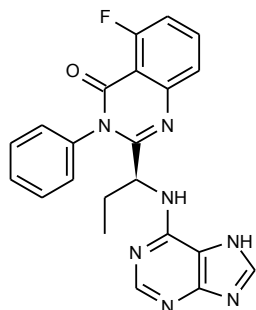
Lot Number: BDG 15039.4



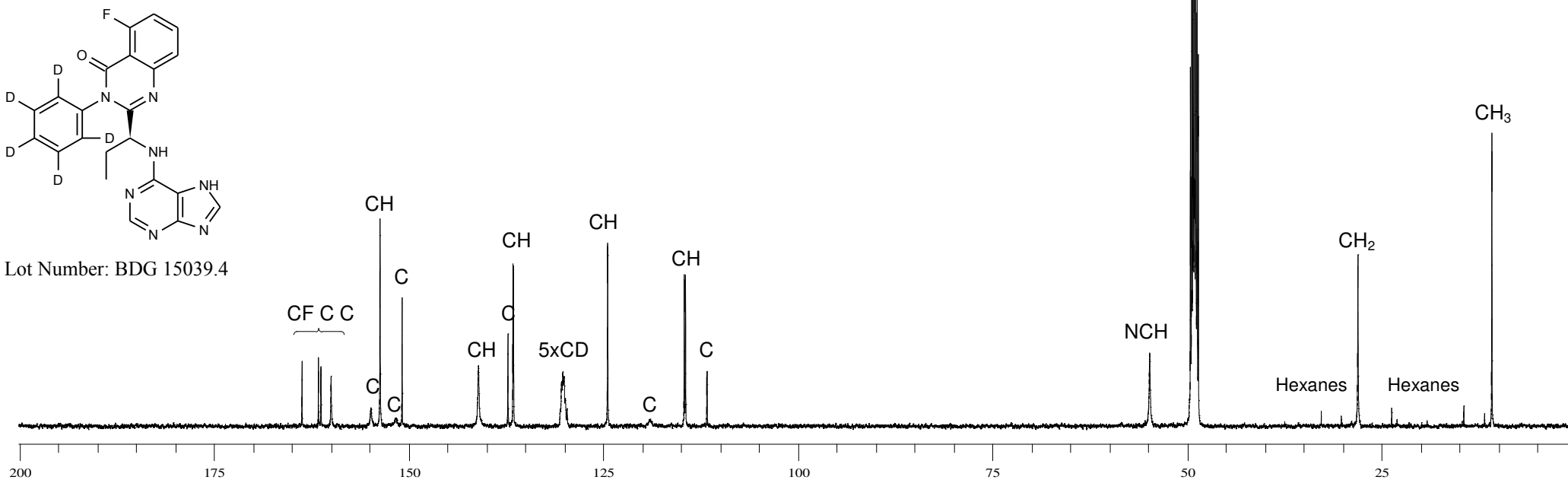


Carbon-13 NMR Spectrum of Idelalisib (top) and Idelalisib-d₅ (bottom) in Methanol-d₄

BDG SYNTHESIS



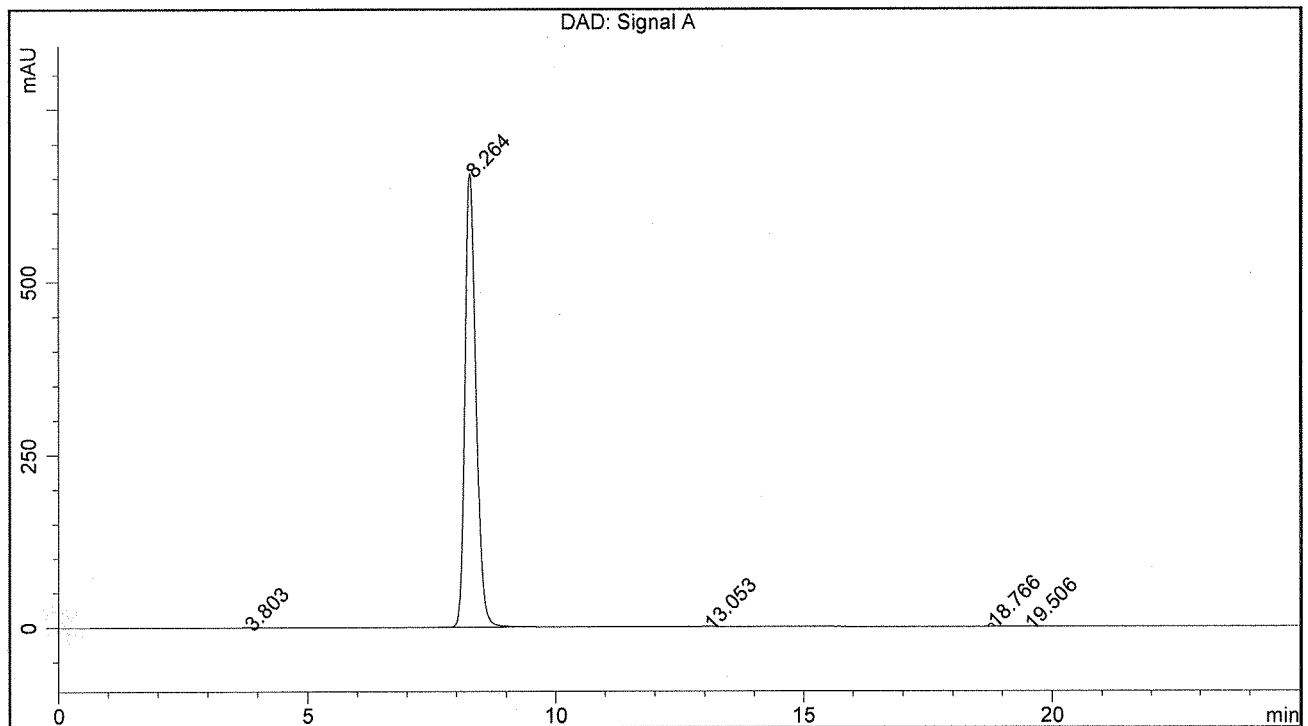
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BDG - Analysis of Idelalisib-d5

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase A : 70:30:0.05 Water : Acetonitrile : Trifluoroacetic Acid
 Mobile Phase B : 30:70:0.05 Water : Acetonitrile : Trifluoroacetic Acid
 Gradient (A:B) : T0=100:0, T12=80:20, T18=0:100, T24=0:100, T26=100:0, T30=100:0
 Flow Rate : 1.0 mL/min.
 Sample Solvent : 70:30 Water : Acetonitrile
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 278 nm

Sample Name	BDG 15039.4	Instrument	AnalyticalLC01
Acquisition	03/07/2014, 10:42:35	Method (rev.)	LC10615a (12)
Sequence	BDG_03Jul2014b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.80 min	0.9407	12.3752	0.2035 min	0.122 %
2	8.26 min	656.5873	10058.4975	0.2327 min	99.516 %
3	13.05 min	0.4423	8.2502	0.2416 min	0.082 %
4	18.77 min	4.0806	26.0940	0.0966 min	0.258 %
5	19.51 min	0.3161	2.2301	0.1043 min	0.022 %