BDG SYNTHESIS

Certificate of Analysis

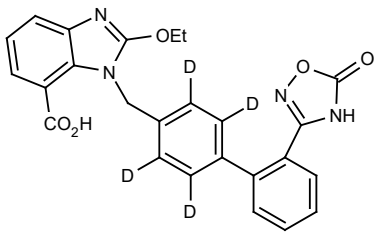
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
6 September 2018

Name: **Azilsartan-d_4**

CAS Number: 147403-03-0 (unlabelled)

Structure:



Molecular Weight: $C_{25}H_{16}D_4N_4O_5$ = 460.47

Lot Number: BDG 17388.2

Appearance: White powder

Corrected Purity: 99.0 % (HPLC) - 0.8 % (ethyl acetate) - 0.6 % (acetic acid) - 3.0 % (water) = 94.6 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 6 September 2023

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:	store in an amber vial and protect from bright light.
Caution:	only experienced laboratory personnel should handle the material.

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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 greatly diminished, compared with what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: small amounts of acetic acid (0.6 % *w/w*) and ethyl acetate (0.8 % *w/w*) are 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.
Isotopic Labelling: signals at the site of deuteration have collapsed to small multiplets compared with what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 461.1780. $C_{25}H_{17}D_4N_4O_5$ $[M+H]^+$ requires *m/z* 461.1763. The deviation of 4.0 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 somewhat broadened, symmetrical peak is observed (99.0 %). 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 62.85, H 3.97, D 1.98, N 11.45 %
$C_{25}H_{16}D_4N_4O_5 \cdot 0.8H_2O$	Requires:	C 63.23, H 3.74, D 1.70, N 11.80 %, H_2O 3.03 %
$C_{25}H_{16}D_4N_4O_5$	Requires:	C 65.21, H 3.50, D 1.75, N 12.17 %

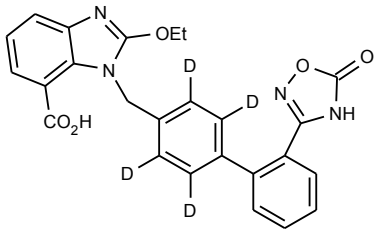
The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend 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.

BDG SYNTHESIS

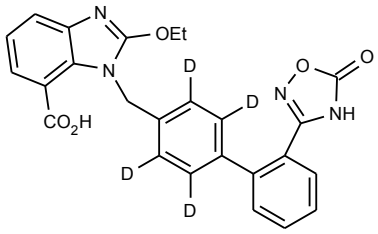
Proton NMR Spectrum of Azilsartan-d_4 in DMSO-d_6



Lot Number: BDG 17388.2

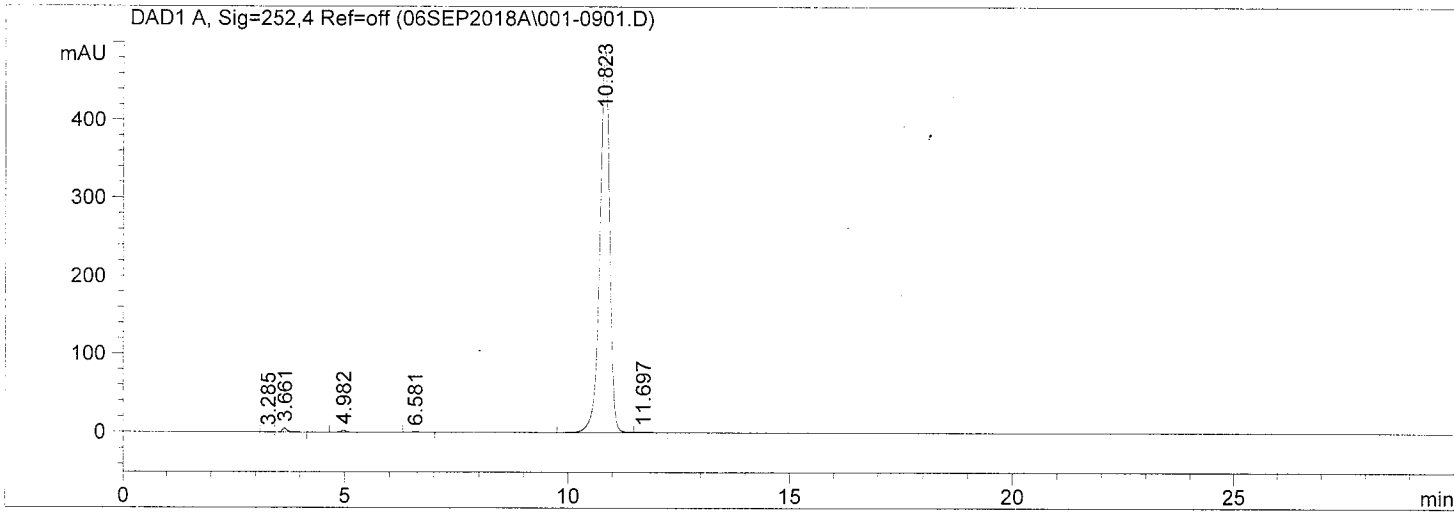
BDG SYNTHESIS

Carbon-13 NMR Spectrum of Azilsartan-d_4 in DMSO-d_6



Lot Number: BDG 17388.2

Injection Date : 9/6/2018 7:06:10 PM Inj : 1
Inj Volume : 10 µl
Acq. Method : C:\CHEM32\1\METHODS\2018\LC20026A.M
Last changed : 9/6/2018 6:00:29 PM by Bruce Hamilton
Analysis Method : C:\CHEM32\1\METHODS\2018\LC20026A.M
Last changed : 9/7/2018 10:26:16 AM by Bruce Hamilton
(modified after loading)
Method Info : BDG - Analysis of Azilsartan-d4
Column : Phenomenex Luna C18(2) 5 um 250 x 4.6 mm : Guard C18RP 4 x 3 mm
Mobile Phase : 43:22:35 20 mM Potassium diHydrogen Phosphate pH=3.0 :
Methanol : Acetonitrile
Flow : 1 ml/min., Column Temperature : 20 C, Injection : 10 ul,
Detection : UV at 252 nm, Sample Solvent : Mobile Phase



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=252,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.285	BB	0.1234	2.32286	2.84174e-1	0.0308
2	3.661	BV R	0.1146	36.85683	4.85154	0.4887
3	4.982	BV R	0.1171	16.90799	2.21475	0.2242
4	6.581	VV R	0.1793	9.70815	8.01287e-1	0.1287
5	10.823	VV R	0.2339	7469.67285	489.73987	99.0382
6	11.697	VV	0.2182	6.74622	3.97181e-1	0.0894
Totals :				7542.21490	498.28880	

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*** End of Report ***