



## BDG SYNTHESIS

### Certificate of Analysis

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

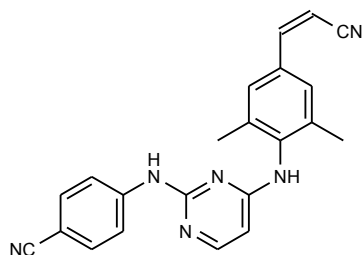
*Neil Beare*

Neil Beare, PhD, Director  
11 July 2017

**Name:** Z-Rilpivirine

**CAS Number:** 500287-94-5

**Structure:**



**Molecular Weight:**  $C_{22}H_{18}N_6 = 366.42$

**Lot Number:** BDG 16738.1

**Appearance:** White, crystalline solid

**Corrected Purity:** 97.3 % (HPLC) - 0.5 % (water) = 96.8 %

**Re-test Date:** 11 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. To avoid isomerization do not heat or store in strongly acidic solutions.

## Identity and Purity

### Proton NMR Spectrum

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

Residual Solvents: no residual solvents are observed.

Impurities: a trace of an unidentified impurity is seen in the baseline. Minor signals for *E*-Rilpivirine are also observed in the spectrum.

### Carbon-13 NMR Spectrum

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

### High-resolution Mass Spectrum (TOF MS ES+)

Found  $m/z$  367.1664.  $C_{22}H_{19}N_6$   $[M+H]^+$  requires  $m/z$  367.1671. The deviation of 1.9 ppm is within normally accepted limits for the establishment of identity by HRMS.

### HPLC

A somewhat broadened, symmetrical peak is observed (97.3 %). A small amount of the *E* isomer is observed (15.05 minutes). 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 71.67, H 4.75, N 22.80 %                |
| $C_{22}H_{18}N_6 \cdot 0.1H_2O$ | Requires: | C 71.76, H 4.98, N 22.82 %, $H_2O$ 0.49 % |
| $C_{22}H_{18}N_6$               | Requires: | C 72.11, H 4.95, N 22.94 %                |

The elemental analyses fall slightly 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.

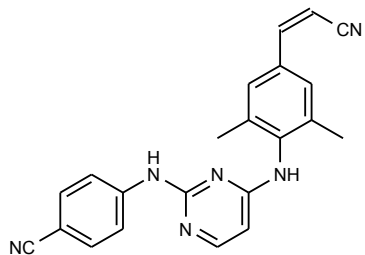
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

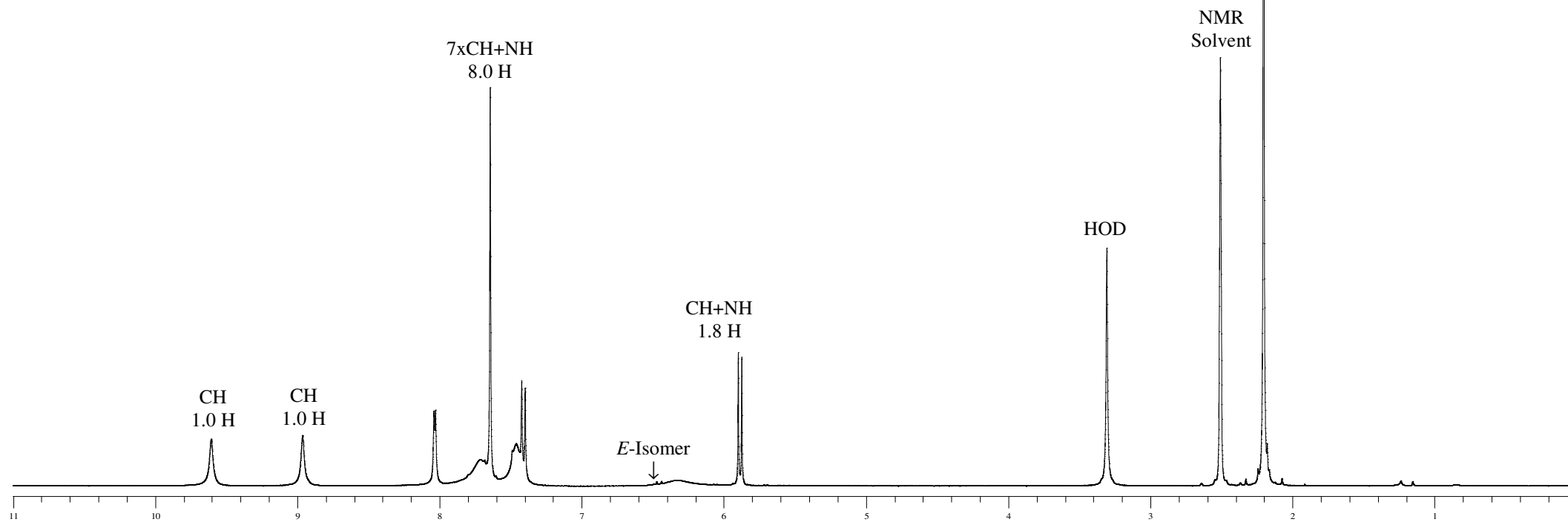


Proton NMR Spectrum of Z-Rilpivirine in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



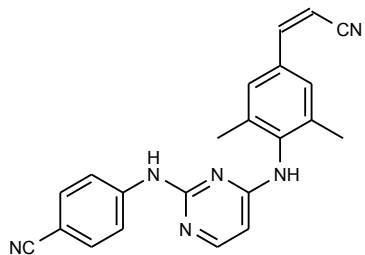
Lot Number: BDG 16738.1



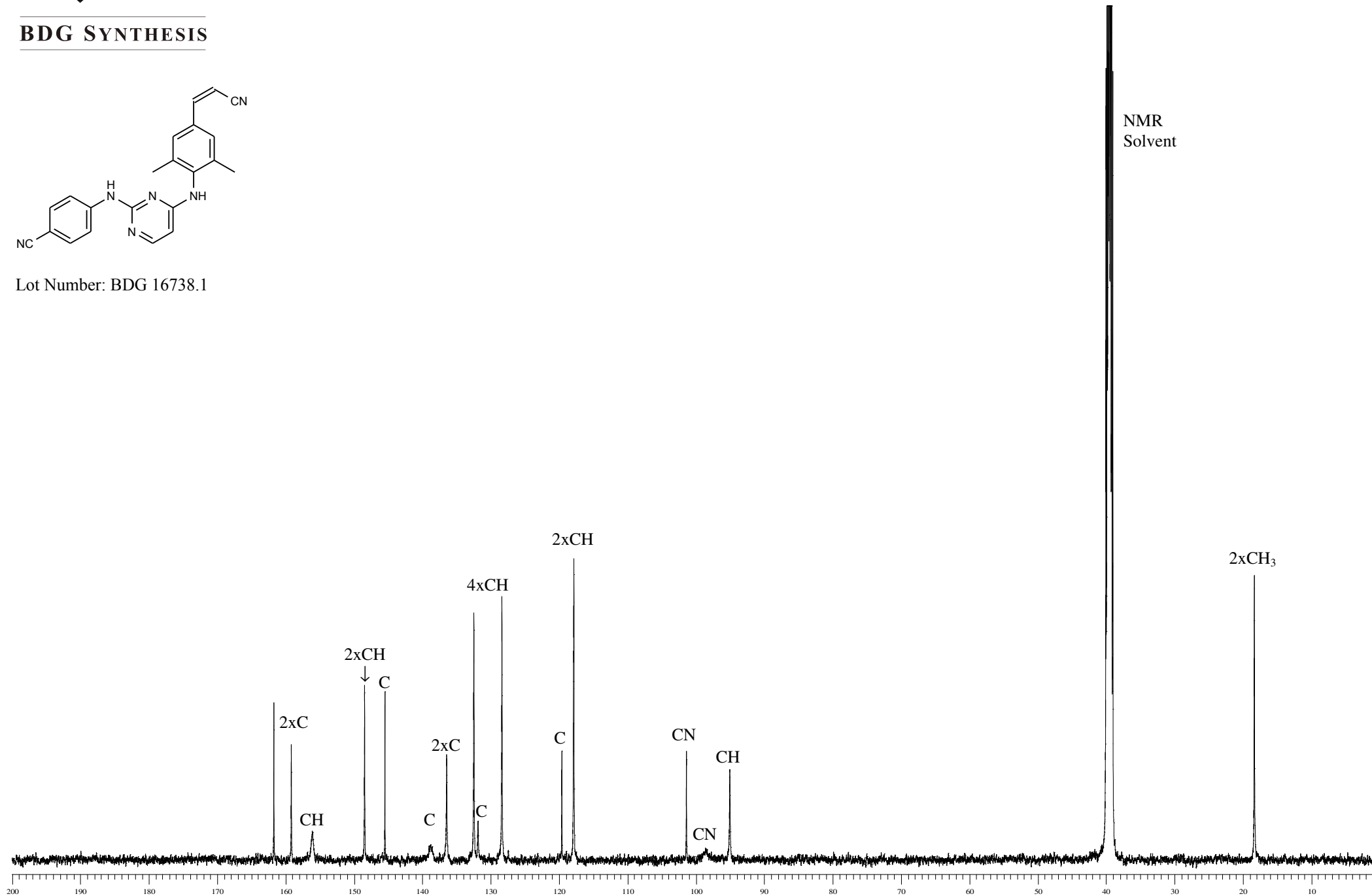


# Carbon-13 NMR Spectrum of Z-Rilpivirine in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



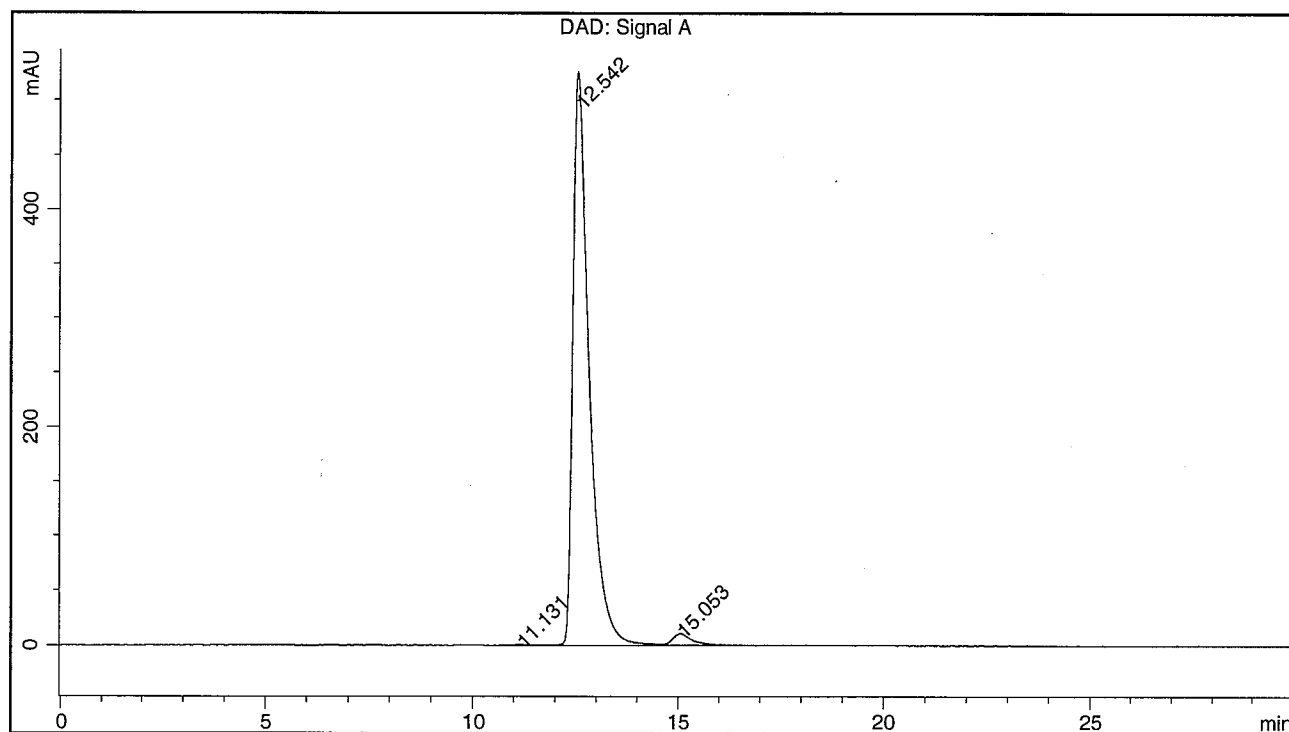
Lot Number: BDG 16738.1



BDG - Analysis of Z-Rilpivirine

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm  
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm  
 Mobile Phase : 50:50:0.05 Water : Methanol : Trifluoroacetic Acid  
 Column Temperature : 30 C . . . . . Flow Rate : 1.0 mL/min . . . . . Injection Volume : 10 uL  
 Sample Solvent : Mobile Phase . . . . . Detection : UV 290 nm

|                    |                              |                      |                |
|--------------------|------------------------------|----------------------|----------------|
| <b>Sample Name</b> | BDG 16738.1                  | <b>Instrument</b>    | AnalyticalLC01 |
| <b>Acquisition</b> | 11/07/2017, 17:32:50         | <b>Method (rev.)</b> | LC10678b ( 19) |
| <b>Sequence</b>    | BDG_11Jul2017b - Reprocessed | <b>Vial Position</b> | 5              |
| <b>Operator</b>    | solvation010\cerityadmin     | <b>Injection</b>     | 1 of 2         |



**Area Percent Report**

| Peak# | RT        | Peak Height | Peak Area  | Width      | Area %   |
|-------|-----------|-------------|------------|------------|----------|
| 1     | 11.13 min | 0.8257      | 20.4476    | 0.3409 min | 0.137 %  |
| 2     | 12.54 min | 527.2831    | 14544.0640 | 0.4018 min | 97.285 % |
| 3     | 15.05 min | 10.6108     | 385.4071   | 0.5238 min | 2.578 %  |