BDG SYNTHESIS

# Certificate of Analysis

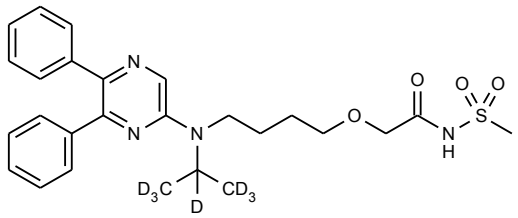
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
29 March 2017

**Name:** **Selexipag-$d_7$**

**CAS Number:** 475086-01-2 (unlabelled)

**Structure:**



**Molecular Weight:** $C_{26}H_{25}D_7N_4O_4S$ = 503.67

**Lot Number:** BDG 16867.3

**Appearance:** Pale yellow, crystalline solid

**Corrected Purity:** 99.2 % (HPLC) - 1.5 % (ethanol) = 97.7 %

**Isotopic Purity:** Under 0.5 % $d_0$

**Re-test Date:** 29 March 2022

**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. Solutions of this material are light sensitive. |

## 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 what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of ethanol (1.5 % *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.
Isotopic Labelling: signals at the sites of deuteration have collapsed to small multiplets compared with what would be expected for unlabelled material, indicating clean deuteration.

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

Found *m/z* 504.2676. $C_{26}H_{26}D_7N_4O_4S$ $[M+H]^+$ requires *m/z* 504.2656. The deviation of 3.9 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 (99.2 %). 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 62.87, H 5.27, D 2.98, N 11.38 % |
| $C_{26}H_{25}D_7N_4O_4S$ | Requires: | C 62.00, H 5.00, D 2.80, N 11.12 % |

The elemental analyses fall within generally accepted limits (+/- 0.4 %) for establishing the molecular formula given, except the result for carbon. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

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.

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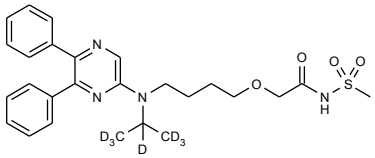
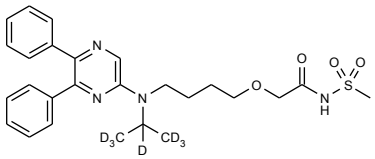
Proton NMR Spectrum of Selexipag-$d_7$ in DMSO-$d_6$



Lot Number: BDG 16867.3

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Selexipag-$d_7$ in DMSO-$d_6$

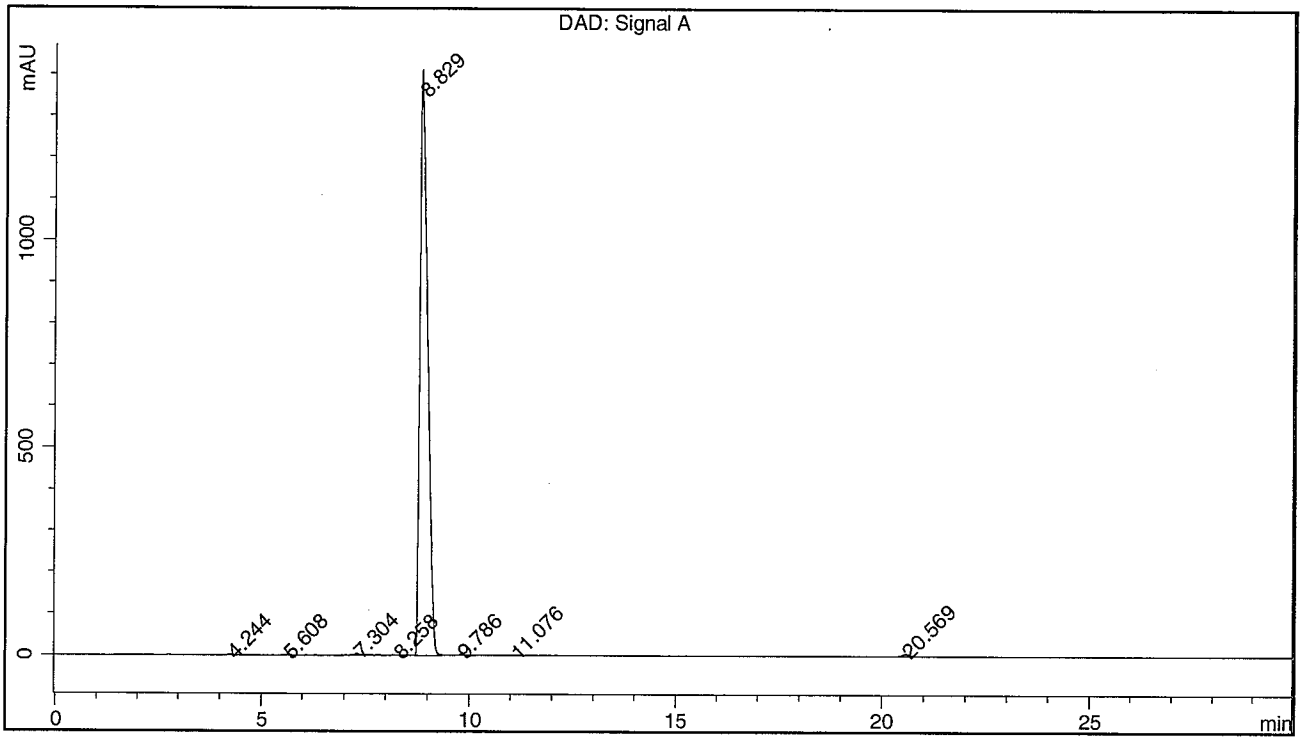


Lot Number: BDG 16867.3

BDG - Analysis of Selexipaq-d7

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 4 x 3 mm
Mobile Phase A : 50:50 20 mM diPotassium Hydrogen Phosphate pH = 7.0 : Acetonitrile
Mobile Phase B : 30:70 20 mM diPotassium Hydrogen Phosphate pH = 7.0 : Acetonitrile
Gradient (A:B) : T0=100:0, T15=0:100, T25=0:100, T26=100:0, T30=100:0
Flow Rate : 1.0 mL/min
Sample Solvent : 1:1 Water : Acetonitrile
Column Temperature : 20 C
Injection Volume : 10 uL
Detection : UV at 300 nm

| Sample Name | BDG 16867.3 | Instrument | AnalyticalLC01 |
|---|---|---|---|
| Acquisition | 29/03/2017, 16:03:28 | Method (rev.) | LC10705a ( 6) |
| Sequence | BDG_29Mar2017b - Reprocessed | Vial Position | 1 |
| Operator | solvation010\cerityadmin | Injection | 1 of 1 |




**Area Percent Report**

| Peak# | RT | Peak Height | Peak Area | Width | Area % |
|---|---|---|---|---|---|
| 1 | 4.24 min | 0.4617 | 6.7168 | 0.2137 min | 0.037 % |
| 2 | 5.61 min | 0.9315 | 8.7865 | 0.1380 min | 0.048 % |
| 3 | 7.30 min | 4.1690 | 30.2251 | 0.1106 min | 0.166 % |
| 4 | 8.26 min | 0.3838 | 6.2149 | 0.2109 min | 0.034 % |
| 5 | 8.83 min | 1409.9239 | 18055.8202 | 0.1954 min | 99.232 % |
| 6 | 9.79 min | 1.0930 | 8.8264 | 0.1222 min | 0.049 % |
| 7 | 11.08 min | 0.4202 | 6.5714 | 0.1945 min | 0.036 % |
| 8 | 20.57 min | 5.5376 | 72.4425 | 0.2006 min | 0.398 % |