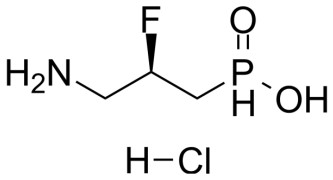
# Lesogaberan hydrochloride

| | |
|---|---|
| **Cat. No.:** | HY-10061B |
| **CAS No.:** | 2925644-17-1 |
| **Molecular Formula:** | $C_3H_{10}ClFNO_2P$ |
| **Molecular Weight:** | 177.54 |
| **Target:** | GABA Receptor |
| **Pathway:** | Membrane Transporter/Ion Channel; Neuronal Signaling |
| **Storage:** | 4°C, stored under nitrogen<br>* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen) |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 240 mg/mL (1351.81 mM; Need ultrasonic)
$H_2O$ : 100 mg/mL (563.25 mM; Need ultrasonic)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 5.6325 mL | 28.1627 mL | 56.3253 mL |
| 5 mM | 1.1265 mL | 5.6325 mL | 11.2651 mL |
| 10 mM | 0.5633 mL | 2.8163 mL | 5.6325 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (563.25 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6 mg/mL (33.80 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Lesogaberan (AZD-3355) hydrochloride is a potent and selective $GABA_B$ receptor agonist with an $EC_{50}$ of 8.6 nM for human recombinant $GABA_B$ receptor. The affinity ($K_i$s) of Lesogaberan hydrochloride for rat $GABA_B$ and $GABA_A$ receptors, as measured by displacement of [$^3$H]GABA binding in brain membranes: 5.1 nM and 1.4 μM, respectively. Lesogaberan hydrochloride inhibits transient lower esophageal sphincter relaxation through a peripheral mode of action[1].

**$IC_{50}$ & Target**

Ki: 5.1±1.2 nM (rat $GABA_B$), 1.4±0.3 μM (rat $GABA_A$)[1]

| | |
|---|---|
| | EC50: 8.6±0.77 nM (human $GABA_B$ receptor)[1] |
| **In Vitro** | Lesogaberan hydrochloride (3-30 nM) enhances human islet cell proliferation in vitro[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only.<br>Cell Proliferation Assay[2] |

| | |
|---|---|
| Cell Line: | Human islet cells |
| Concentration: | 3, 10, and 30 nM |
| Incubation Time: | 4 days |
| Result: | Had a small but nonsignificant promitotic effect at 3 nM, while treatment at higher dosages (10 and 30 nM) led to a 2-3-fold increase in proliferation relative to that of islets cultured in medium alone. |

**In Vivo**

Lesogaberan hydrochloride potently stimulates recombinant human $GABA_B$ receptors and inhibits transient lower esophageal sphincter relaxation (TLESR) in dogs, with a biphasic dose-response curve[1].
Oral Lesogaberan (0.08 mg/mL; 48 hours) hydrochloride protects human islet β-cells from apoptosis in islet grafts in mice[2].
Lesogaberan (7 μmol/kg) hydrochloride shows high oral availability (88% in the dog and 100% in the rat) and relatively low systemic clearance in female Sprague Dawley rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | Diabetic NOD/scid mice were implanted with human islets[2] |
| Dosage: | 0.08 mg/mL |
| Administration: | 48 hours |
| Result: | Significantly reduced the percentages of apoptotic islet cells and increased the frequency of $insulin^+$ β-cells in human islet grafts. |

| | |
|---|---|
| Animal Model: | Female Sprague Dawley rats[1] |
| Dosage: | 7 μmol/kg (Pharmacokinetic Analysis) |
| Administration: | Oral |
| Result: | High oral availability (88% in the dog and 100% in the rat) and relatively low systemic clearance. Plasma protein binding was 1% in rat and human plasma. |

## REFERENCES


[1]. Lehmann A, et al. (R)-(3-amino-2-fluoropropyl) phosphinic acid (AZD3355), a novel GABAB receptor agonist, inhibits transient lower esophageal sphincter relaxation through a peripheral mode of action. J Pharmacol Exp Ther. 2009 Nov;331(2):504-12.

[2]. Tian J, et al. Repurposing Lesogaberan to Promote Human Islet Cell Survival and β-Cell Replication. J Diabetes Res. 2017;2017:6403539.





Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA