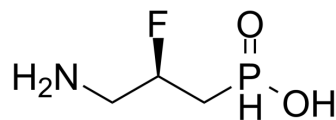


Lesogaberan

Cat. No.:	HY-10061
CAS No.:	344413-67-8
Molecular Formula:	C ₃ H ₉ FNO ₂ P
Molecular Weight:	141.08
Target:	GABA Receptor
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Lesogaberan (AZD-3355) is a potent and selective GABA _B receptor agonist with an EC ₅₀ of 8.6 nM for human recombinant GABA _B receptors. The affinity (K _i s) of Lesogaberan 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 inhibits transient lower esophageal sphincter relaxation through a peripheral mode of action ^[1] .								
IC₅₀ & 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	<p>Lesogaberan (3-30 nM) enhances human islet cell proliferation in vitro^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Cell Proliferation Assay^[2]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>Human islet cells</td> </tr> <tr> <td>Concentration:</td> <td>3, 10, and 30 nM</td> </tr> <tr> <td>Incubation Time:</td> <td>4 days</td> </tr> <tr> <td>Result:</td> <td>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.</td> </tr> </table>	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.
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In Vivo	<p>Lesogaberan (AZD3355) 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) protects human islet β-cells from apoptosis in islet grafts in mice^[2]. Lesogaberan (7 μmol/kg) shows high oral availability (88% in the dog and 100% in the rat) and relatively low systemic clearance in female SpragueDawley rats^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Diabetic NOD/scid mice were implanted with human islets^[2]</td> </tr> <tr> <td>Dosage:</td> <td>0.08 mg/mL</td> </tr> </table>	Animal Model:	Diabetic NOD/scid mice were implanted with human islets ^[2]	Dosage:	0.08 mg/mL				
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Administration:	Oral feeding; 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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