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Zuschläge

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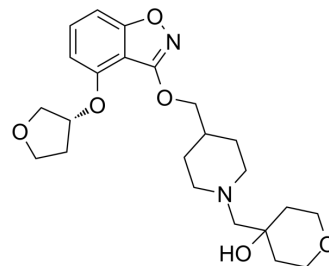
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PF-04995274

Cat. No.:	HY-18137
CAS No.:	1331782-27-4
Molecular Formula:	C ₂₃ H ₃₂ N ₂ O ₆
Molecular Weight:	432.51
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (231.21 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	2.3121 mL	11.5604 mL	23.1209 mL
		5 mM	0.4624 mL	2.3121 mL	4.6242 mL
		10 mM	0.2312 mL	1.1560 mL	2.3121 mL
Please refer to the solubility information to select the appropriate solvent.					
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution				
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	PF-04995274 is a potent, high-affinity, orally active and partial serotonin 4 receptor (5-HT ₄ R) agonist. PF-04995274 has an EC ₅₀ range of 0.26-0.47 nM for human 5-HT _{4A/4B/4D/4E} (K _i range of 0.15-0.46 nM), and has an EC ₅₀ range of 0.59-0.65 nM for rat 5-HT _{4S/4L/4E} (K _i of 0.30 nM for rat 5-HT _{4S}). PF-04995274 is brain penetrant and can be used for cognitive disorders associated with Alzheimer's disease ^{[1][2][3]} .
IC ₅₀ & Target	5-HT ₄ Receptor

In Vitro	PF-04995274 has EC₅₀ values of 0.47 nM, 0.36 nM, 0.37 nM, 0.26 nM, 0.59 nM, 0.65 nM and 0.62 nM for human 5-HT_{4A/4B/4D/4E} and rat 5-HT_{4S/4L/4E}, respectively. PF-04995274 has K_i values of 0.36 nM, 0.46 nM, 0.15 nM, 0.32 nM and 0.3nM for human 5-HT_{4A/4B/4D/4E} and rat 5-HT_{4S}, respectively^[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.									
In Vivo	PF-04995274 (3-10 mg/kg; intravenous injection; for 17 days; male 129S6/SvEv mice) treatment results in prophylactic efficacy by attenuating learned fear and decreasing stress-induced depressive-like behavior^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. <table><tr><td>Animal Model:</td><td>Male 129S6/SvEv mice (7-8 weeks) treated with contextual fear conditioning (CFC) and forced swim test (FST)^[1]</td></tr><tr><td>Dosage:</td><td>3 mg/kg, 10 mg/kg</td></tr><tr><td>Administration:</td><td>Intravenous injection; for 17 days</td></tr><tr><td>Result:</td><td>Attenuated learned fear and decreased stress-induced depressive-like behavior.</td></tr></table>		Animal Model:	Male 129S6/SvEv mice (7-8 weeks) treated with contextual fear conditioning (CFC) and forced swim test (FST) ^[1]	Dosage:	3 mg/kg, 10 mg/kg	Administration:	Intravenous injection; for 17 days	Result:	Attenuated learned fear and decreased stress-induced depressive-like behavior.
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Dosage:	3 mg/kg, 10 mg/kg									
Administration:	Intravenous injection; for 17 days									
Result:	Attenuated learned fear and decreased stress-induced depressive-like behavior.									

REFERENCES

- [1]. Chen BK, et al. Prophylactic efficacy of 5-HT₄R agonists against stress. Neuropsychopharmacology. 2019 Oct 10.
- [2]. Grimwood S, et al. Translational receptor occupancy for the 5-HT₄ partial agonist PF-04995274 in rats, non-human primates and healthy volunteers. Alzheimer's Dement: J Alzheimer's Assoc. 2011;7:S653.
- [3]. Timothy Nicholas1, et al. Systems pharmacology modeling in neuroscience: Prediction and outcome of PF-04995274, a 5-HT₄ partial agonist, in a clinical scopolamine impairment trial. Advances in Alzheimer's Disease. Vol.2 No.3(2013).

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

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