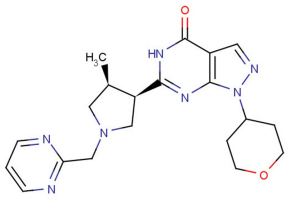
Data Sheet (Cat.No.T16478)

PF-04447943

Chemical Properties



CAS No.:	1082744-20-4
Formula:	C20H25N7O2
Molecular Weight:	395.46
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	PF-04447943 is an effective inhibitor of human recombinant PDE9A (IC50=12 nM). It has >78-fold selectivity, compared to other PDE family members (IC50>1000 nM).
Targets(IC_{50})	PDE9A: 12 nM
In vitro	PF-04447943 inhibits ANP (0.3 μM) stimulated cGMP (IC50: 375±36.9 nM (n=16)), in HEK whole cells expressing rhesus PDE9A2. PF-04447943 is found to be highly selective over other PDE enzymes (PDE1, Ki=8600±2121 nM, n = 5; PDE2A3, Ki>99,000 nM; PDE3A, Ki>50,000 nM; PDE4A, Ki>29,000 nM; PDE5A, Ki=14,980±5025 nM, n=5; PDE6C, Ki=5324±2612 nM, n=4; PDE7A2, Ki>75,000 nM; PDE8A, Ki>50,000 nM; PDE10, Ki>51,250±20,056 nM, n=4; PDE11, Ki>80,000 nM) and no other significant activity at ~60 other receptors/enzymes. Using recombinant human, rhesus, and rat PDE9A2 in a cell free assay PF-04447943 is shown to have a Ki of 2.8±0.26, 4.5±0.13, and 18.1±1.9 nM (n=4, 11 and 9 respectively) [2].
In vivo	PF-04447943 concentrations dose-dependently increase in blood, brain, and cerebrospinal fluid (CSF), thirty minutes following oral administration in rats (1-30 mg/kg). In mice, PF-04447943 (3, 10, 30 mg/kg p.o.) dose-dependently enhances plasma and brain concentrations of PF-04447943 while the brain to plasma ratio ranged from 0.26 to 0.7 although this is not entirely dosed dependent. Based on i.v. and p.o. dosing, pharmacokinetic studies with PF-04447943 in the rat indicate a Tmax of 0.3 h, T1/2 of 4.9 h, Cl of 21.7 mL/min/kg, and oral bioavailability of 47%. The brain: plasma exposure ratios 30 min after dosing range from 0.13 at the 1 mg/kg dose to 0.33 at the 30 mg/kg dose. CSF levels are approximately 50% of brain levels. CSF cGMP levels increase in a dose-dependent manner from a basal level of 3 pmol/mL to 13.3 pmol/mL (3.5-fold) at the 30 mg/kg dose. CSF cGMP levels also increase in a dose-dependent manner from a basal level of 3 pmol/mL in vehicle-treated animals to 13.3 pmol/mL (3.5-fold) at the 30 mg/kg dose. CSF cGMP levels are elevated at all doses tested with a maximal effect of 3.5 fold increase above controls at 30 mg/kg [2].

Solubility Information

Solubility	DMSO: 54.6 mg/mL (138.07 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.529 mL	12.644 mL	25.287 mL
5 mM	0.506 mL	2.529 mL	5.057 mL
10 mM	0.253 mL	1.264 mL	2.529 mL
50 mM	0.051 mL	0.253 mL	0.506 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Kleiman RJ, et al. Phosphodiesterase 9A regulates central cGMP and modulates responses to cholinergic and monoaminergic perturbation in vivo. J Pharmacol Exp Ther. 2012 May;341(2):396-409.
2. Hutson, P. H, et al. The selective phosphodiesterase 9 (PDE9) inhibitor PF-04447943 (6-[(3S,4S)-4-methyl-1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl]-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one) enhances synaptic plasticity and

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