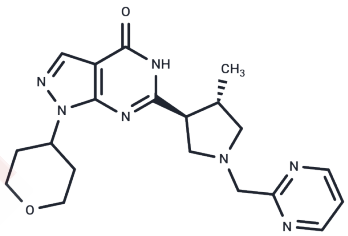
Data Sheet (Cat.No.T16478)

TargetMol

PF-04447943

Chemical Properties



CAS No. : 1082744-20-4

Formula: C20H25N7O2

Molecular Weight: 395.46

Storage: Pure form: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PF-04447943 (Edelinontrine) is a potent and selective phosphodiesterase 9A inhibitor with an IC50 of 12 nM, which is 78-fold more selective than that used for other PDE family members (IC50>1000 nM).PF-04447943 exhibits anti-inflammatory activity, attenuates inflammatory responses by inhibiting oxidative stress, inflammation, and modulating T-cell polarization, and may be useful for research on sickle cell anemia.
Targets(IC50)	PDE
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 increased 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: 55 mg/mL (139.08 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 2.5 mg/mL (6.32 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5287 mL	12.6435 mL	25.287 mL
5 mM	0.5057 mL	2.5287 mL	5.0574 mL
10 mM	0.2529 mL	1.2644 mL	2.5287 mL
50 mM	0.0506 mL	0.2529 mL	0.5057 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.

Hutson PH, 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 cognitive function in rodents. Neuropharmacology. 2011 Sep;61(4):665-76.