

PF-04447943

Catalog No: tcsc0942



Available Sizes

Size: 5mg

Size: 10mg

Size: 25mg

Size: 50mg



Specifications

CAS No:

1082744-20-4

Formula:

$C_{20}H_{25}N_7O_2$

Pathway:

Metabolic Enzyme/Protease

Target:

Phosphodiesterase (PDE)

Purity / Grade:

>98%

Solubility:

DMSO : \geq 54.6 mg/mL (138.07 mM)

Observed Molecular Weight:

395.46

Product Description

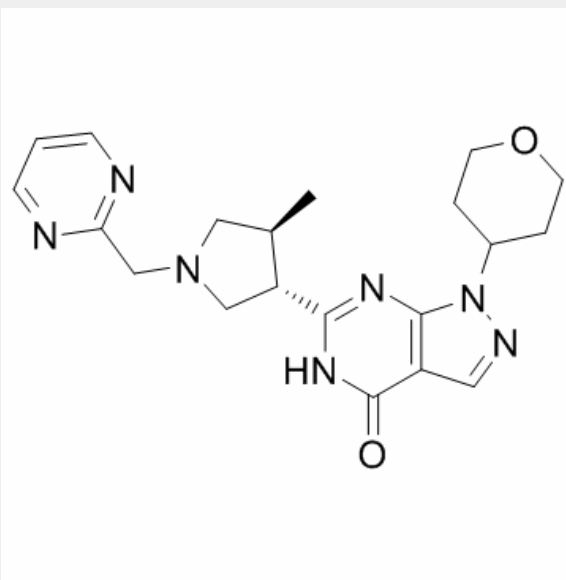
PF-04447943 is a potent inhibitor of human recombinant **PDE9A** (IC_{50} =12 nM) with >78-fold selectivity, respectively, over other

PDE family members (**IC₅₀**>1000 nM).

IC50 & Target: IC50: 12 nM (PDE9A)^[1]

In Vitro: Using recombinant human, rhesus, and rat PDE9A2 in a cell free assay PF-04447943 is shown to have a K_i of 2.8 ± 0.26 , 4.5 ± 0.13 , and 18.1 ± 1.9 nM (n=4, 11 and 9 respectively). PF-04447943 is found to be highly selective over other PDE enzymes (PDE1, $K_i = 8600 \pm 2121$ nM, n = 5; PDE2A3, $K_i > 99,000$ nM; PDE3A, $K_i > 50,000$ nM; PDE4A, $K_i > 29,000$ nM; PDE5A, $K_i = 14,980 \pm 5025$ nM, n=5; PDE6C, $K_i = 5324 \pm 2612$ nM, n=4; PDE7A2, $K_i > 75,000$ nM; PDE8A, $K_i > 50,000$ nM; PDE10, $K_i > 51,250 \pm 20,056$ nM, n=4; PDE11, $K_i > 80,000$ nM) and no other significant activity at ~60 other receptors/enzymes. In HEK whole cells expressing rhesus PDE9A2, PF-04447943 inhibits ANP (0.3 μ M) stimulated cGMP with an IC_{50} of 375 ± 36.9 nM (n=16)^[2].

In Vivo: Based on i.v. and p.o. dosing, pharmacokinetic studies with PF-04447943 in the rat indicates a T_{max} of 0.3 h, $T_{1/2}$ of 4.9 h, Cl of 21.7 mL/min/kg and an oral bioavailability of 47%. Thirty minutes following oral administration in rats (1-30 mg/kg), PF-04447943 concentrations dose-dependently increase in blood, brain and cerebrospinal fluid (CSF). 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. In mice, PF-04447943 (3, 10, 30 mg/kg p.o.) dose-dependently increases 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 dose dependent. 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].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!