Web: www.taiclone.com
Tel: +886-2-2735-9682
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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 : ≥ 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

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PDE family members (**IC_{50}**>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±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±5025 nM, n=5; PDE6C, K_i=5324±2612 nM, n=4; PDE7A2, K_i>75,000 nM; PDE8A, K_i>50,000 nM; PDE10, K_i>51,250±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 μM) 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]
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