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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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