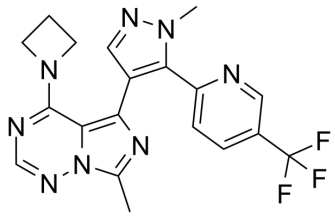
PF-05180999

Cat. No.:	HY-111371
CAS No.:	1394033-54-5
Molecular Formula:	$C_{19}H_{17}F_3N_8$
Molecular Weight:	414
Target:	Phosphodiesterase (PDE)
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (120.77 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4155 mL	12.0773 mL	24.1546 mL
	5 mM	0.4831 mL	2.4155 mL	4.8309 mL
	10 mM	0.2415 mL	1.2077 mL	2.4155 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.04 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-05180999 (PF-999) is a phosphodiesterase 2A (PDE2A) inhibitor, with an IC_{50} of 1.6 nM.

IC_{50} & Target

PDE2A	PDE10A1	PDE11A4	PDE7B
1.6 nM (IC_{50})	2.03 μM (IC_{50})	26.969 μM (IC_{50})	50.09 μM (IC_{50})

In Vitro

PF-05180999 is a phosphodiesterase 2A (PDE2A) inhibitor, with an IC_{50} of 1.6 nM. PF-05180999 binds to the rat, dog and monkey PDE2A, with K_is of 4.2, 8.4, and 5.5 nM and IC_{50}s of 2.6, 5.2, and 3.4 nM, respectively. PF-05180999 shows weak

	activity against PDE, with IC_{50}s of 2.03 μM (PDE10A1), 26.969 μM (PDE7B), 50.09 μM (PDE11A4), and >56.25 μM (PDE1B1, PDE3A1, PDE4D3, PDE5A1, PDE6 (bovine), PDE8B, PDE9A1), respectively. PF-05180999 is also a weak inducer of CYP3A4, and with no direct inhibition of human recombinant cytochrome P450 (CYP) enzymes (1A2, 2B6, 2C8, 2C9, 2C19, 2D6, and 3A) and no induction of CYP1A2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PF-05180999 (Compound 30; 0.032-0.32 mg/kg mg/kg, s.c.) dramatically reduces the working memory errors produced by ketamine in a working memory radial arm maze (RAM) model in rats. PF-05180999 causes acute and exposure-dependent elevation in the accumulation of cGMP bulk levels in the cortex, striatum, and hippocampus, but with no changes in cAMP and the associated downstream phospho-cAMP response element-binding protein (p-CREB) in mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] Male Sprague-Dawley rats (weighing 250-320 g) under urethane anesthesia at 1.5 g/kg intraperitoneal (ip) are placed in a stereotaxic frame, where craniotomies are performed above the region of the medial prefrontal cortex (mPFC) and ipsilateral (CA)1/subiculum. Body temperature of the rat is maintained at 37°C with an electrical heating pad. The femoral vein is cannulated for administration of test drugs (PF-05180999, etc.). After the conclusion of the experiments animals are euthanized with an iv bolus of urethane[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Helal CJ, et al. Identification of a Potent, Highly Selective, and Brain Penetrant Phosphodiesterase 2A Inhibitor Clinical Candidate. J Med Chem. 2018 Feb 8;61(3):1001-1018.

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