PF-06445974

Cat. No.: HY-119190

CAS No.: 2055776-17-3

Molecular Formula: $C_{20}H_{15}FN_4O$

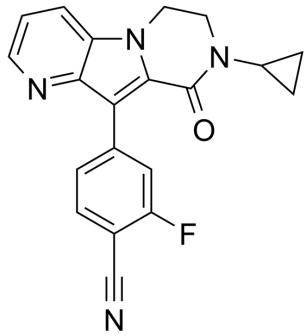
Molecular Weight: 346.36

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 : 33.33 mg/mL (96.23 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8872 mL	14.4358 mL	28.8717 mL
	5 mM	0.5774 mL	2.8872 mL	5.7743 mL
	10 mM	0.2887 mL	1.4436 mL	2.8872 mL

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

BIOLOGICAL ACTIVITY

Description

PF-06445974, a promising positron emission tomography (PET) lead, has exquisite potency at PDE4B with an IC_{50} <1 nM. The IC_{50} values are 36, 4.7 and 17 nM for PDE4D, PDE4A and PDE4C, respectively. PF-06445974 has good selectivity over PDE4D, excellent brain permeability, and a high level of specific binding in the "cold tracer" study[1].

IC_{50} & Target

PDE4B	PDE4D	PDE4A	PDE4C
<1 nM (IC_{50})	36 nM (IC_{50})	4.7 nM (IC_{50})	17 nM (IC_{50})

In Vitro

PF-06445974 demonstrates minimal off-target activities in broad-spectrum selectivity panels, with only weak μM activities at PDE10 (IC_{50}=2290 nM), PDE5A (IC_{50}=4640 nM) and GABAA (K_i=3850 nM)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PF-06445974 exhibits high central nervous system (CNS) PET MPO score (4.0). PF-06445974 is a promising radiotracer lead for specific binding assessment. Neuropharmacokinetic study in rats (0.1 mg/kg, IV) confirms high brain permeability with a total brain to plasma ratio of 0.76, corresponding to a free brain to plasma ratio of 0.70[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Twenty-five drug-naive male 129/B6 PDE4D KO mice (25-35 g)[1]
Dosage:	10 μg/kg
Administration:	Dosed intravenously at 10 μg/kg in a 5 mL/kg dosing volume
Result:	Showed excellent brain uptake and reached peak concentrations at around 20 minutes.

REFERENCES

[1]. Lei Zhang, et al. The Discovery of a Novel Phosphodiesterase (PDE) 4B-Preferring Radioligand for Positron Emission Tomography (PET) Imaging. J Med Chem. 2017 Oct 26;60(20):8538-8551.

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