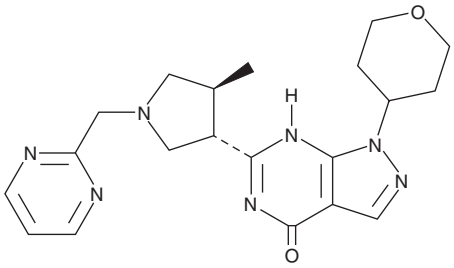
PRODUCT INFORMATION

PF-04447943

Item No. 24299

CAS Registry No.:	1082744-20-4
Formal Name:	1,5-dihydro-6-[(3S,4S)-4-methyl-1-(2-pyrimidinylmethyl)-3-pyrrolidinyl]-1-(tetrahydro-2H-pyran-4-yl)-4H-pyrazolo[3,4-d]pyrimidin-4-one
MF:	$C_{20}H_{25}N_7O_2$
FW:	395.5
Purity:	≥98%
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PF-04447943 is supplied as a solid. A stock solution may be made by dissolving the PF-04447943 in the solvent of choice. PF-04447943 is soluble in the organic solvent DMSO, which should be purged with an inert gas, at a concentration of approximately 50 mg/ml.

Description

PF-04447943 is a brain-permeable phosphodiesterase (PDE) inhibitor that is selective for PDE9A (IC_{50} = 12 nM) over other PDEs (IC_{50}s = >940 nM) in enzymatic assays of second messenger hydrolysis.[1] It is over 1,000-fold more selective for PDE9A over 79 non-PDE targets, with the exception of the melatonin MT_3/ML2 receptor (K_i = 3,800 nM). PF-04447943 also inhibits rat and rhesus monkey PDE9A (K_is = 18.1 and 4.5 nM, respectively).[2] It increases neurite outgrowth and the density of synapsin puncta in primary rat hippocampal neurons when used at a concentration of 0.03 µM. PF-04447943 increases the cGMP level in the striatum and frontal cortex of mice and in the cerebrospinal fluid (CSF) of rats when administered at 10 and 1 mg/kg, respectively.[1] It improves deficits in episodic memory induced by scopolamine (Item No. 14108) in rats and increases the time spent exploring the novel object in the novel object recognition (NOR) test when administered at a dose of 1 mg/kg. PF-04447943 (3.2 mg/kg) also improves spatial memory in the Morris water maze (MWM) and decreases the distance traveled to the hidden platform.

References

1. Kleiman, R.J., Chapin, D.S., Christoffersen, C., *et al.* Phosphodiesterase 9A regulates central cGMP and modulates responses to cholinergic and monoaminergic perturbation *in vivo*. *J. Pharmacol. Exp. Ther.* **341(2)**, 396-409 (2012).
2. Hutson, P.H., Finger, E.N., Magliaro, B.C., *et al.* The selective phosphodiesterase 9 (PDE9) inhibitor PF-04447943 (6-[(3S,4S)-4-methyl-1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl]-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one) enhances synaptic plasticity and cognitive function in rodents. *Neuropharmacology* **61(4)**, 665-676 (2011).

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