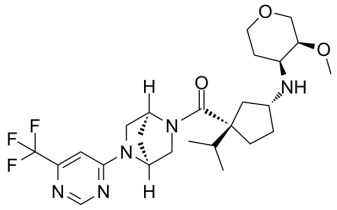
PF-04634817

Cat. No.:	HY-117621
CAS No.:	1228111-63-4
Molecular Formula:	$C_{25}H_{36}F_3N_5O_3$
Molecular Weight:	511.58
Target:	CCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
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 (97.74 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9547 mL	9.7736 mL	19.5473 mL
	5 mM	0.3909 mL	1.9547 mL	3.9095 mL
	10 mM	0.1955 mL	0.9774 mL	1.9547 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 (4.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.89 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-0463481 is a potent and orally active dual CCR2/CCR5 antagonist with comparable human and rodent CCR2 potency (rat IC_{50}=20.8 nM), and displays 10-20 fold less rodent CCR5 potency (rat IC_{50}=470 nM). PF-0463481 is safe and well-tolerated and has the potential for the study of diabetic nephropathy[3].

IC_{50} & Target		
	Rat CCR2 20.8 nM (IC_{50})	CCR5 470 nM (IC_{50})

In Vivo

PF-04634817 (oral administration; 30 mg/kg; once daily; 31 days intervention (weeks 2-15 after Streptozotocin)) intervention at the onset of diabetes (week 2) has no impact on the fasting blood glucose levels in diabetic $Nos3^{-/-}$ 221 mice. The development of diabetes results in a marked increase in the levels of glycated haemoglobin (HbA1c) in $Nos3^{-/-}$ mice. Early intervention with PF-04634817 induces an additional increase in glycated hemoglobin (HbA1c) levels[1].

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

Animal Model:	$Nos3^{-/-}$ mice on the C57BL/6 background[1]
Dosage:	30 mg/kg
Administration:	Oral administration; once daily; 31 days intervention (weeks 2-15 after Streptozotocin)
Result:	Had no impact on the fasting blood glucose levels, but induced an additional increase in HbA1c levels.

REFERENCES

[1]. Gale JD, et al. A CCR2/5 Inhibitor, PF-04634817, Is Inferior to Monthly Ranibizumab in the Treatment of Diabetic Macular Edema. Invest Ophthalmol Vis Sci. 2018 May 1;59(6):2659-2669.

[2]. Gale JD, et al. Effect of PF-04634817, an Oral CCR2/5 Chemokine Receptor Antagonist, on Albuminuria in Adults with Overt Diabetic Nephropathy. Kidney Int Rep. 2018 Aug 3;3(6):1316-1327.

[3]. Tesch GH, et al. Combined inhibition of CCR2 and ACE provides added protection against progression of diabetic nephropathy in Nos3-deficient mice.Am J Physiol Renal Physiol. 2019 Dec 1;317(6):F1439-F1449.

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