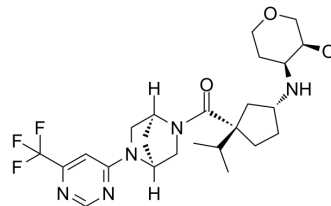


PF-04634817

Cat. No.:	HY-117621		
CAS No.:	1228111-63-4		
Molecular Formula:	C ₂₅ H ₃₆ F ₃ N ₅ O 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)			
		Solvent Concentration	Mass	
			1 mg	5 mg
	Preparing Stock Solutions		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	<ol style="list-style-type: none"> 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 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 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] .	
IC₅₀ & 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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