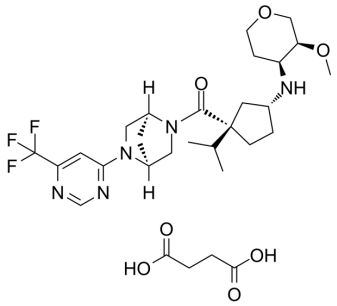
PF-04634817 succinate

Cat. No.:	HY-117621A
CAS No.:	2140301-98-8
Molecular Formula:	$C_{29}H_{42}F_3N_5O_7$
Molecular Weight:	629.67
Target:	CCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



BIOLOGICAL ACTIVITY

Description	PF-0463481 succinate 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 succinate 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 succinate (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]. 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.

[2]. 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.

[3]. 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.

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

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