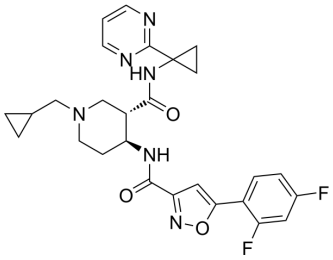
ACT-1004-1239

Cat. No.:	HY-142617
CAS No.:	2178049-58-4
Molecular Formula:	$C_{27}H_{28}F_2N_6O_3$
Molecular Weight:	522.55
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (38.27 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9137 mL	9.5685 mL	19.1369 mL
	5 mM	0.3827 mL	1.9137 mL	3.8274 mL
	10 mM	0.1914 mL	0.9568 mL	1.9137 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 1.67 mg/mL (3.20 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

ACT-1004-1239 is a potent, selective, orally active CXCR7 antagonist with an IC_{50} value of 3.2 nM[1][2].

IC_{50} & Target

CXCR7

In Vitro

ACT-1004-1239 inhibits human, dog, rat, mouse, guinea pig, macaque CXCR7 with IC_{50}s of 3.2, 2.3, 3.1, 2.3, 0.6, 1.5 nM respectively[1].

ACT-1004-1239 (1-10 μM, 30 days) promotes oligodendrocyte precursor cell (OPC) differentiation by increasing CXCL12 levels [2].

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

In Vivo

ACT-1004-1239 (100 mg/kg, p.o.) increase of plasma CXCL12 concentration in naive male DBA/1 mice[1].

ACT-1004-1239 (100 mg/kg, p.o., twice daily) reduces disease severity in myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) model[2].

ACT-1004-1239 (100 mg/kg, p.o., twice daily) increases myelination in the Cuprizone (HY-W115718)-induced demyelination model mice[2].

ACT-1004-1239 (10 mg/kg, p.o., rats) shows a C_{max} of 600 ng/h/mL, T_{max} of 0.5 h, F (%) of 35%[1].

ACT-1004-1239 (1 mg/kg, i.v., rats) shows a Vss of 3.6 L/kg, Cl of 70 mL/min/kg, $T_{1/2}$ of 1.3 h[1].

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

Animal Model:	Myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) model[2]
Dosage:	10-100 mg/kg
Administration:	p.o., twice daily
Result:	Reduced clinical disease scores, and increases survival rate. Increases plasma CXCL12 concentration. Reduces the infiltration of neutrophils, monocytes, monocytes-derived cells (MdCs), plasmacytoid dendritic cells (pDCs), DCs, natural killer (NK) cells, NK T cells, B cells, and T cells. Reduces the number of CXCR4-expressing leukocytes.

REFERENCES

[1]. Pouzol L, et al. ACT-1004-1239, a first-in-class CXCR7 antagonist with both immunomodulatory and promyelinating effects for the treatment of inflammatory demyelinating diseases. FASEB J. 2021 Mar;35(3):e21431.

[2]. Richard-Bildstein S, et al. Discovery of the Potent, Selective, Orally Available CXCR7 Antagonist ACT-1004-1239. J Med Chem. 2020 Dec 24;63(24):15864-15882.

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