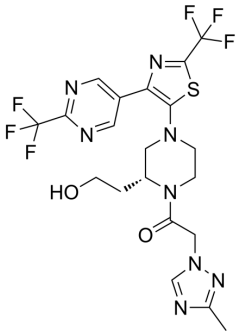
ACT-777991

Cat. No.:	HY-149055
CAS No.:	1967811-46-6
Molecular Formula:	$C_{20}H_{20}F_6N_8O_2S$
Molecular Weight:	550.48
Target:	CXCR
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 : 100 mg/mL (181.66 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8166 mL	9.0830 mL	18.1660 mL
	5 mM	0.3633 mL	1.8166 mL	3.6332 mL
	10 mM	0.1817 mL	0.9083 mL	1.8166 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 (4.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ACT-777991 is an orally active and selective CXCR3 antagonist. ACT-777991 has microsomes and hepatocytes stability across animal models. ACT-777991 inhibits the migration of activated T cells toward CXCL11[1].

IC_{50} & Target

CXCR3

In Vitro

ACT-777991 inhibits hEGR with an IC_{50} value of 26 μM in CHO cells[1].
ACT-777991 (1 μM; 45 min) is stable in microsomes and hepatocytes across humans, rats, and dogs[1].

	ACT-777991 (0.01-1 μM;) inhibits the migration of both human and mouse-activated T cells toward CXCL11 with IC_{50}s range of 3.2-64 nM and 4.9-21 nM, respectively[1]. ACT-777991 (1 nM, 5 nM, 20 nM, and 50 nM) inhibits CXCR3-mediated chemotaxis of human and mouse T cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ACT-777991 (0.5 mg/kg, 1 mg/kg; i.v.; single dose) has low in vivo plasma clearance in male Wistar rats (14/156) or Beagle dogs (5/15)[1]. ACT-777991 (0.006-2 mg/g food; po; started 3 days before and 72 h post LPS challenge) dose-dependently inhibits chemotaxis of $CXCR^{3+}$ T cells in vivo in mouse model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	LPS challenge model in mice[1]
Dosage:	0.006, 0.02, 0.06, 0.2, 0.6, and 2 mg per g of food
Administration:	PO; started 3 days before LPS challenge and continued up to the end of the study (72 h post LPS challenge)
Result:	Reduced the number of BAL CD^{8+} T cells in a dose-dependent manner.

REFERENCES

[1]. Meyer EA, et al. Discovery of Clinical Candidate ACT-777991, a Potent CXCR3 Antagonist for Antigen-Driven and Inflammatory Pathologies. J Med Chem. 2023 Mar 23;66(6):4179-4196.

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