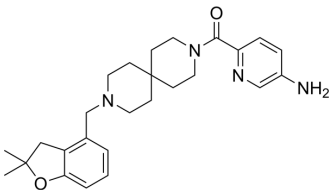
AZ084

Cat. No.:	HY-119217
CAS No.:	929300-19-6
Molecular Formula:	$C_{26}H_{34}N_4O_2$
Molecular Weight:	434.57
Target:	CCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (575.28 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3011 mL	11.5056 mL	23.0113 mL
	5 mM	0.4602 mL	2.3011 mL	4.6023 mL
	10 mM	0.2301 mL	1.1506 mL	2.3011 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: ≥ 2.08 mg/mL (4.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZ084 is a potent, selective, allosteric and oral active CCR8 allosteric antagonist, with a K_i of 0.9 nM. Has potential to treat asthma[1]. AZ084 restrains the formation of the immunologically tolerant pre-metastatic niche (PMN) and tumor cells metastasis in lung by downregulating Treg differentiation. AZ084 can be used in studies of asthma and cancer[1][2].

IC_{50} & Target

CCR8
0.9 nM (Ki)

In Vitro

AZ084 (5 μg/mL; single daily for 4 days) suppresses proportion of Tregs and reduces T cells that expresses CCR8 (co-cultured in vitro with LLC-exo MPF CM)[1].

?AZ084 (0-10 μM) inhibits AML, DC and T cells with IC_{50}s of 1.3, 4.6 and 5.7 nM, respectively[2].

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

Cell Viability Assay[1]

Cell Line:	Splenic T cells
Concentration:	5 μg/mL (single daily)
Incubation Time:	4 days
Result:	Reversed the increased proportion of Tregs among the CD4+ T cells co-cultured in vitro with LLC-exo MPF CM. Reduced T cells that expressed CCR8 (cultured in vitro with by LLC-exo MPF CM).

Cell Viability Assay[2]

Cell Line:	AML, DC and T cells
Concentration:	0-10 μM
Incubation Time:	
Result:	Showed high potency with pronounced dose-response dependent inhibition of chemotaxis with an IC_{50} of 1.3 nM in AML cells.

In Vivo

AZ084 (5 mg/kg; i.p.; every third day for 9 or 21 days) restrains the formation of the immunologically tolerant PMN and tumor cells metastasis in lung by downregulating Treg differentiation[1].

?AZ084 (434.57-869.14 mg/kg; i.v.; single) shows a bioavailability >70% in rats[2].

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

Animal Model:	C57BL/6 J mice (subcutaneous LLC tumor model)[1].
Dosage:	5 mg/kg
Administration:	Intraperitoneal injection, every third day for 9 or 21 days.
Result:	Inhibited Treg differentiation and tumor cell colonization of the lungs and reduced the number of CD4+Foxp3+ Tregs in the lungs of LLC-exo pre-injected mice (every third day for 9 days). Inhibited the LLC-exo-induced LLC cell seeding in lung and also significantly reduced Treg accumulation in LLC-exo stimulated mouse lungs(every third day for 21 days).

Animal Model:	Female Balb/C mice, male Wistar rats and female Beagle dogs[2].
Dosage:	434.57-869.14 mg/kg (in 0.9% NaCl)
Administration:	Intravenous injection, single.
Result:	Pharmacokinetic Parameters of AZ084 in Female Balb/C mice, male Wistar rats and female Beagle dogs[2].

	IV (434.57-869.14 mg/kg)

Dog plasma protein binding (% free)	45.7
Mu plasma protein binding (% free)	55.6
Hu plasma protein binding (% free)	31.0
Rat plasma protein binding (% free)	47.0
Rat HW plasma PK CL (mL/min/kg)	15.0
Rat HW plasma PK V_{ss} (L/kg)	6.0
Rat HW plasma PK $T_{1/2}$ (h)	5.4
Rat HW plasma PK C_{max} (μM)	0.5
Rat HW plasma PK bioavailability (%)	68.0

CUSTOMER VALIDATION

- Nat Commun. 2021 Dec 8;12(1):7122.
- Nat Commun. 2020 May 1;11(1):2177.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Wang M, et al. Tumor-derived exosomes drive pre-metastatic niche formation in lung via modulating CCL1+ fibroblast and CCR8+ Treg cell interactions. Cancer Immunol Immunother. 2022 Apr 15.

[2]. Connolly S, et al. Orally bioavailable allosteric CCR8 antagonists inhibit dendritic cell, T cell and eosinophil migration. Biochem Pharmacol. 2012 Mar 15;83(6):778-87.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA