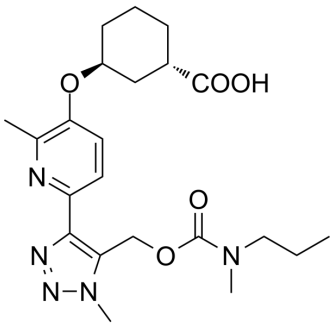
BMS-986278

Cat. No.:	HY-139853
CAS No.:	2170126-74-4
Molecular Formula:	$C_{22}H_{31}N_5O_5$
Molecular Weight:	445.51
Target:	LPL Receptor
Pathway:	GPCR/G Protein
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 (224.46 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2446 mL	11.2231 mL	22.4462 mL
	5 mM	0.4489 mL	2.2446 mL	4.4892 mL
	10 mM	0.2245 mL	1.1223 mL	2.2446 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 (5.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.61 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-986278 is a potent and orally active lysophosphatidic acid receptor 1 (LPA1) antagonist, with K_bs of 6.9 nM and 4.0 nM for human and mouse LPA1, respectively. BMS-986278 can be used for the research of pulmonary fibrotic diseases[1].

IC_{50} & Target

Kb: 6.9 nM (human LPA1), 4.0 nM (mouse LPA1)[1]

In Vitro

BMS-986278 is a high-affinity LPA1 antagonist, with K_bs of 6.9 nM and 4.0 nM for human and mouse LPA1 in CHO cells overexpressing LPA1[1].

BMS-986278 antagonizes Lysophosphatidic acid (LPA)-stimulated calcium flux in normal human lung fibroblasts, with a K_b of 5.8 nM[1].

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

In Vivo

BMS-986278 (0.1-10 mg/kg; a single p.o.) completely inhibits LPA-stimulated systemic histamine release in a concentration-dependent manner in CD1 mice[1].

BMS-986278 (3-30 mg/kg; p.o. twice daily for 14 d) decreases Bleomycin-induced collagen deposition/lung fibrosis in rats[1].

Pharmacokinetics of BMS-986278 in preclinical species[1]

	plasma clearance ((mL/min)/kg)	V_{ss} (L/kg)	oral bioavailability (%)	$T_{1/2}$ (h)	plasma protein binding (% free)
mouse	37	5.5	70	2.5	31.4
rat	15	3.5	100	4.5	12.6
monkey	2.0	1.6	79	11	0.8

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

Animal Model:	Male Sprague-Dawley rats (10 weeks) were administered Bleomycin[1]
Dosage:	3, 10, and 30 mg/kg
Administration:	P.o. twice daily for 14 days
Result:	Resulted in significant decreases in the lung section percent fibrotic area for the 3 mg/kg (48%) and 10 mg/kg (56%) dose groups.

REFERENCES

[1]. Cheng PTW, et, al. Discovery of an Oxycyclohexyl Acid Lysophosphatidic Acid Receptor 1 (LPA1) Antagonist BMS-986278 for the Treatment of Pulmonary Fibrotic Diseases. J Med Chem. 2021 Nov 11;64(21):15549-15581.

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