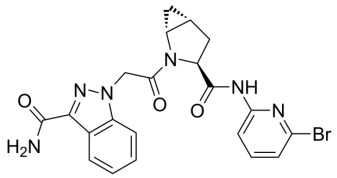
Complement factor D-IN-1

Cat. No.:	HY-102034
CAS No.:	1386455-76-0
Molecular Formula:	$C_{21}H_{19}BrN_6O_3$
Molecular Weight:	483.32
Target:	Complement System
Pathway:	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 (517.26 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0690 mL	10.3451 mL	20.6902 mL
5 mM	0.4138 mL	2.0690 mL	4.1380 mL
10 mM	0.2069 mL	1.0345 mL	2.0690 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 (4.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Complement factor D-IN-1 is a potent and selective small-molecule reversible factor d inhibitor, with IC_{50}s of 0.006 and 0.05 μM in FD Thioesterolytic Fluorescent Assay and a MAC Deposition Assay, respectively.

IC_{50} & Target

IC50: 0.006 μM (FD), 0.05 μM (MAC)[1]

In Vitro

The highly specific S1 serine protease factor D (FD) plays a central role in the amplification of the complement alternative pathway (AP) of the innate immune system. Complement factor D-IN-1 (compound 2) shows similar potency against human

	and monkey FD (IC_{50}s in FD thioesterolytic assays of 0.005 μM and in 50% serum MAC deposition assays of 0.011 μM for both human and monkey)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Complement factor D-IN-1 displays an excellent oral PK profile in Sprague–Dawley rats and, following an oral dose (10 mg/kg) in Brown Norway rats, demonstrates a good distribution and sustained exposure in ocular tissues including the neural retina and the posterior eye cup (PEC), which comprises the sclera, retinal pigmented epithelium, and choroid. Mean exposure levels in plasma, the PEC, and the retina at 6 h after dosing are 0.36, 0.43, and 0.09 μM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] Complement factor D-IN-1 is tested at 30 mg/kg in the human factor D knock-in mouse pharmacodynamic model. Groups of mice (n=4, female human FD knock-in) are treated either with Complement factor D-IN-1 or dosing vehicle by oral gavage at 24, 16, 12, 8, 6, and 4 h, respectively, prior to the termination of the study. All animals are given intraperitoneal LPS to activate complement 7.5 h prior to study termination. Baseline complement levels are obtained from mice that received oral dosing vehicle and intraperitoneal saline (indicated by PBS line on graph). The positive control group receives oral dosing vehicle and intraperitoneal LPS[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lorthiois E, et al. Discovery of Highly Potent and Selective Small-Molecule Reversible Factor D InhibitorsDemonstrating Alternative Complement Pathway Inhibition in Vivo. J Med Chem. 2017 Jul 13;60(13):5717-5735.

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