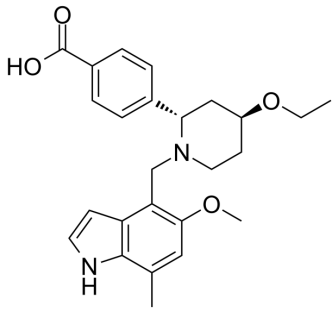
Iptacopan



Cat. No.:	HY-127105
CAS No.:	1644670-37-0
Molecular Formula:	$C_{25}H_{30}N_2O_4$
Molecular Weight:	422.52
Target:	Complement System
Pathway:	Immunology/Inflammation
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months

SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (118.34 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3668 mL	11.8338 mL	23.6675 mL
	5 mM	0.4734 mL	2.3668 mL	4.7335 mL
	10 mM	0.2367 mL	1.1834 mL	2.3668 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: ≥ 5 mg/mL (11.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (11.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Iptacopan (LNP023) is a first-in-class, orally bioavailable, highly potent and highly selective factor B inhibitor with an IC_{50} value of 10 nM. Iptacopan shows direct, reversible, and high-affinity binding to human factor B with a K_D of 7.9 nM. Iptacopan targets the underlying cause of complement 3 glomerulopathy (C3G)[1][2].

IC_{50} & Target

KD: 7.9 nM (factor B)[2]
IC50: 10 nM (factor B)[2]

In Vitro	Iptacopan (LNP023) demonstrates potent inhibition of alternative complement pathway (AP)-induced membrane attack complex (MAC) formation in 50% human serum (IC_{50} value of 130 nM)[2]. ?Iptacopan (LNP023) exhibits excellent selectivity over other proteases affording IC_{50} values of >30 μM across a panel of 41 human proteases, including the AP protein factor D (>100 μM)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Iptacopan (LNP023; 20-180 mg/kg; oral administration) prevents KRN (150 μL)-induced arthritis in mice and is effective upon prophylactic and therapeutic dosing in an experimental model of membranous nephropathy in rats[2]. ?LNP023 exhibits moderate half-lives ($T_{1/2}$; Wistar Han rats 3.4 h, beagle dogs 5.5 h) and C_{max} (Wistar Han rats 410 nM, beagle dogs 2200 nM) following oral administration (rat 30 and, dog 10 mg/kg)[3]. ?Iptacopan exhibits terminal elimination half-lives ($T_{1/2}$; Wistar Han rats 7 h, beagle dogs 5.6 h) due to high plasma clearance (8, and 2 mL/min/kg respectively combined with large volumes of distribution (2.3, and 0.6 L/kg respectively) following intravenous administration (rat 1.0 and, dog 0.1 mg/kg)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice with KRN-induced arthritis[2]
Dosage:	20, 60, and 180 mg/kg
Administration:	Orally gavaged; twice a day (b.i.d.) for 14 days
Result:	Blocked KRN-induced arthritis.

CUSTOMER VALIDATION

- Cell Stem Cell. 2023 Oct 5;30(10):1315-1330.e10.
- Blood Adv. 2024 Jun 12:bloodadvances.2024012874.
- Biomed Pharmacother. September 2022, 113433.
- J Biol Chem. 2024 Jun 12:107467.
- Biomed Chromatogr. 2021 Mar;35(3):e5006.

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REFERENCES

[1]. Dimitrios C Mastellos, et al. Expanding Complement Therapeutics for the Treatment of Paroxysmal Nocturnal Hemoglobinuria. Semin Hematol. 2018 Jul;55(3):167-175.

[2]. Anna Schubart, et al. Small-molecule Factor B Inhibitor for the Treatment of Complement-Mediated Diseases. Proc Natl Acad Sci U S A. 2019 Apr 16;116(16):7926-7931.

[3]. Nello Mainolfi, et al. Discovery of 4-((2 S,4 S)-4-Ethoxy-1-((5-methoxy-7-methyl-1 H-indol-4-yl)methyl)piperidin-2-yl)benzoic Acid (LNP023), a Factor B Inhibitor Specifically Designed To Be Applicable to Treating a Diverse Array of Complement Mediated Diseases. J Med Chem. 2020 Jun 11;63(11):5697-5722.

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