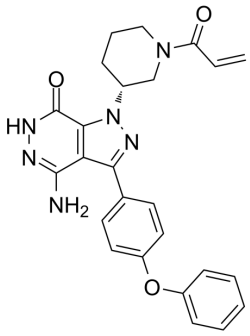
BTK inhibitor 17

Cat. No.:	HY-131705
CAS No.:	1858206-76-4
Molecular Formula:	$C_{25}H_{24}N_6O_3$
Molecular Weight:	456.5
Target:	Btk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (219.06 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1906 mL	10.9529 mL	21.9058 mL
	5 mM	0.4381 mL	2.1906 mL	4.3812 mL
	10 mM	0.2191 mL	1.0953 mL	2.1906 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 (5.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BTK inhibitor 17 is a potent and orally active irreversible BTK inhibitor with an IC_{50} of 2.1 nM. BTK inhibitor 17 can be used for rheumatoid arthritis research[1].

IC_{50} & Target

IC50: 2.1 nM (BTK)[1]

In Vitro

BTK inhibitor 17 (compound 8) could covalently bind to Cys481 and formed an HB network with hinge key residues Met477, Glu475, and gatekeeper Thr474[1].

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

In Vivo

BTK inhibitor 17 (compound 8; 3-10 mg/kg; oral gavage; daily; for 28 days) treatment inhibits the significant progression of the disease and exhibits a clear dose-dependent reduction per paw clinical scores, and no significant body weight loss is observed for all different dosages[1].

BTK inhibitor 17 (compound 8) shows >95% plasma protein binding across three species of human, rat, and mouse. After an intravenous injection, the half-life (rat, 0.32 h; mice, 0.42 h), clearance (rat, 54.6 mL/min/kg; mice, 31.3 mL/min/kg), volume of distribution (rat, 1.55 L/kg; mice, 0.82 L/kg), and AUC exposure (rat, 604 ng.h/mL; mice, 576 ng.h/mL) are observed in two species. After oral administration, BTK inhibitor 17 exhibits higher C_{max} (rat, 466 ng/mL; mice, 252 ng/mL) and plasma exposure (rat, 642 ng.h/mL; mice, 128 ng.h/mL) with a favorable oral bioavailability (rat, 23.7%; mice, 11.2%)[1].

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

Animal Model:	Male Balb/C mice injected with collagen[1]
Dosage:	3 mg/kg or 10 mg/kg
Administration:	Oral gavage; daily; for 28 days
Result:	Inhibited the significant progression of the disease and exhibited a clear dose-dependent reduction per paw clinical scores.

REFERENCES

[1]. Xuejun Zhang, et al. Discovery and Evaluation of Pyrazolo[3,4- d]pyridazinone as a Potent and Orally Active Irreversible BTK Inhibitor. ACS Med Chem Lett. 2019 Dec 11;11(10):1863-1868.

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