Roblitinib

Cat. No.: HY-101568

CAS No.: 1708971-55-4

Molecular Formula: $C_{25}H_{30}N_8O_4$

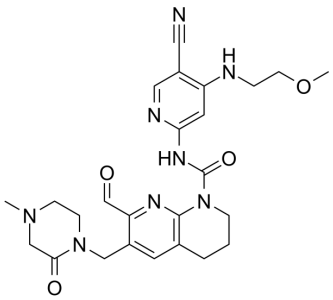
Molecular Weight: 506.56

Target: FGFR

Pathway: Protein Tyrosine Kinase/RTK

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 : 5 mg/mL (9.87 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9741 mL	9.8705 mL	19.7410 mL
	5 mM	0.3948 mL	1.9741 mL	3.9482 mL
	10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Roblitinib (FGF-401) is an orally active and highly selective FGFR4 inhibitor with an IC_{50} of 1.9 nM[1]. Roblitinib has antitumor activity[2].

IC_{50} & Target

FGFR4 1.9 nM (IC_{50})	FGFR1 >10 μM (IC_{50})	FGFR2 >10 μM (IC_{50})	FGFR3 >10 μM (IC_{50})
rat FGFR4 >10 μM (IC_{50})			

In Vitro

Roblitinib (FGF-401; Compound Example 83) is a highly selective and potent FGFR4 inhibitor (IC_{50}= 1.9 nM)[1].
Roblitinib shows no activity FGFR1, FGFR2, FGFR3, rat FGFR4, C552A FGFR4 (all IC_{50}>10 uM)[1].
Roblitinib inhibits HUH7 (IC_{50}=12 nM), Hep3B (IC_{50}=9 nM), JHH7 (IC_{50}=9 nM), HEPG2 (IC_{50}>10 uM), JHH (IC_{50}>10 uM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Roblitinib (gavage; 10-100 mg/kg; b.i.d.; for 10 days) with the 30 mg/kg has the maximal level of inhibition of FGFR4-

dependent tumor growth in the Hep3B xenograft model[1].
Roblitinib causes blood concentrations dropped below the IC90 threshold level within 8 h of dosing, and controlles tumor growth to the level of stasis at the lowest dose of 10 mg/kg for 6 days[1].
Roblitinib (iv at 1 mg/kg; po at 3 mg/kg) has a $T_{1/2}$ of 1.4 hours, a CL of 28 mL/min•kg, and a V_{ss} of 2.3 L/kg for Male mice (C57BL/6) [1].
Roblitinib (iv at 0.5 mg/kg; po at 3 mg/kg) has a $T_{1/2}$ of 4.4 hours, a CL of 19 mL/min•kg, and a V_{ss} of 3.9 L/kg for male SD rats [1].

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

Animal Model:	Male Wistar Hannover rats (Hep3B xenograft model)[1]
Dosage:	10, 30, 100 mg/kg
Administration:	Gavage; for 10 days
Result:	Caused blood concentrations dropped below the IC90 threshold between 8 and 12 h following dosing. Had the maximal level of inhibition of FGFR4-dependent tumor growth in the Hep3B xenograft model.

Animal Model:	Male mice (C57BL/6)[1]
Dosage:	1 mg/kg or 3 mg/kg (Pharmacokinetic Analysis)
Administration:	IV at 1 mg/kg; PO at 3 mg/kg
Result:	Had a $T_{1/2}$ of 1.4 hours, a CL of 28 mL/min•kg, and a V_{ss} of 2.3 L/kg.

CUSTOMER VALIDATION

- Nat Commun. 2022 May 13;13(1):2672.
- Mol Syst Biol. 2023 Dec 18.
- J Cancer. 2022 Feb 14;13(4):1370-1384.
- Biochemistry for Health, NOVA University of Lisbon. 2019 Jul.

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REFERENCES

[1]. Nicole Buschmann, et al. Ring-fused bicyclic pyridyl derivatives as fgfr4 inhibitors. WO2015059668A1.

[2]. Robin A Fairhurst, et al. Discovery of Roblitinib (FGF401) as a Reversible-Covalent Inhibitor of the Kinase Activity of Fibroblast Growth Factor Receptor 4. J Med Chem. 2020 Nov 12;63(21):12542-12573.

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