Oritinib

Cat. No.: HY-139920

CAS No.: 2035089-28-0

Molecular Formula: $C_{31}H_{37}N_7O_2$

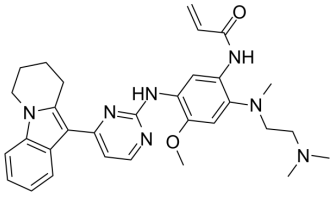
Molecular Weight: 539.67

Target: EGFR

Pathway: JAK/STAT Signaling; 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 : 125 mg/mL (231.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8530 mL	9.2649 mL	18.5298 mL
	5 mM	0.3706 mL	1.8530 mL	3.7060 mL
	10 mM	0.1853 mL	0.9265 mL	1.8530 mL

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

BIOLOGICAL ACTIVITY

Description

Oritinib (SH-1028), an irreversible third-generation EGFR TKI, overcomes T790M-mediated resistance in non-small cell lung cancer. Oritinib (SH-1028), a mutant-selective inhibitor of EGFR kinase activity, inhibits $EGFR^{WT}$, $EGFR^{L858R}$, $EGFR^{L861Q}$, $EGFR^{L858R/T790M}$, $EGFR^{d746-750}$ and $EGFR^{d746-750/T790M}$ kinases, with IC_{50}s of 18, 0.7, 4, 0.1, 1.4 and 0.89 nM, respectively[1].

IC_{50} & Target

EGFR (WT) 18 nM (IC_{50})	$EGFR^{L858R}$ 0.7 nM (IC_{50})	$EGFR^{L861Q}$ 4 nM (IC_{50})	$EGFR^{L858R/T790M}$ 0.1 nM (IC_{50})
$EGFR^{d746-750}$ 1.4 nM (IC_{50})	$EGFR^{d746-750/T790M}$ 0.89 nM (IC_{50})		

In Vitro

Oritinib (SH-1028) binds irreversibly to EGFR kinase by targeting cysteine-797 residue in the ATP binding site via covalent bond formation[1].

Oritinib (0.001-10 μM) potently and selectively targets mutant EGFR cell lines in vitro[1].

Oritinib (0.1 μM) continuously inhibits the phosphorylation of EGFR in PC-9 and NCI-H1975 cells at lower concentrations or even drug-free for at least 6 h[1].

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

Cell Proliferation Assay[1]

Cell Line:	A431 ($EGFR^{WT}$), H3255 ($EGFR^{L858R}$), PC-9 ($EGFR^{d746-750}$) and NCI-H1975 ($EGFR^{L858R/T790M}$) cells
Concentration:	0.001, 0.01, 0.1, 1, and 10 μM
Incubation Time:	72 hours
Result:	Selectively inhibited EGFR-mutated NCI-H1975, H3255 and PC-9 cells, with IC_{50}s of 3.93±1.12, 9.39±0.88 and 7.63±0.18 nmol/L, respectively, which were about 198-, 83- and 102-fold more sensitive than the inhibition of wild-type EGFR in A431 cells (IC_{50} =778.89±134.74 nM).

In Vivo

Oral administration of Oritinib at a daily dose of 5 mg/kg significantly inhibits proliferation of tumor cells with EGFR sensitive mutation (exon 19 del) and resistant mutation (T790 M) for consecutive 14 days, with no TKI-induced weight loss in mouse xenograft models[1].

Oritinib shows good bioavailability, and is distributed extensively from the plasma to the tissues[1].

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

Animal Model:	6-8 weeks old female mice bearing NCI-H1975 and A431 xenograft models [1]
Dosage:	2.5, 5, and 15 mg/kg
Administration:	Orally administrated once daily for consecutive 14 days
Result:	Led to a significant inhibition of tumor cell growth in both PC-9 (exon 19 del) and NCI-H1975 (L858R/T790M) xenograft models.

Animal Model:	NCI-H1975 tumor-bearing mice[1]
Dosage:	2.5, 5, and 15 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration for 1 day or 14 consecutive days.
Result:	The T_{max} is 1.5-2 h, indicating rapidly distributed into tissues, including lung tumor tissues. The AUC_{0-t} values in plasma were 118, 300 and 931 ng×h/mL on Day 1, while 272, 308 and 993 ng×h/ml on Day 14, respectively.

REFERENCES

[1]. Luwei Han, et al. SH-1028, An Irreversible Third-Generation EGFR TKI, Overcomes T790M-Mediated Resistance in Non-Small Cell Lung Cancer. Front Pharmacol. 2021 Apr 27;12:665253.

Caution: Product has not been fully validated for medical applications. For research use only.

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