Epertinib hydrochloride

Cat. No.: HY-107367A

CAS No.: 2071195-74-7

Molecular Formula: $C_{30}H_{28}Cl_2FN_5O_3$

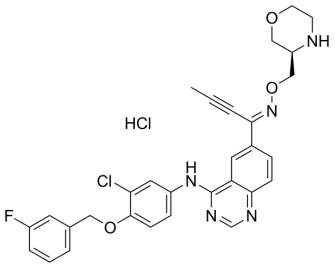
Molecular Weight: 596.48

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (209.56 mM; Need ultrasonic)

H_2O : 33.33 mg/mL (55.88 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6765 mL	8.3825 mL	16.7650 mL
5 mM	0.3353 mL	1.6765 mL	3.3530 mL
10 mM	0.1677 mL	0.8383 mL	1.6765 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 (3.49 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Epertinib (S-22611) hydrochloride is a potent, orally active, reversible, and selective tyrosine kinase inhibitor of EGFR, HER4 and HER2, with IC_{50}s of 1.48 nM, 2.49 nM and 7.15 nM, respectively. Epertinib hydrochloride shows potent antitumor activity [1][2]. Epertinib (hydrochloride) is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

EGFR	HER4	HER2
1.48 ± 0.0 nM (IC_{50})	2.49 ± 0.1 nM (IC_{50})	7.15 nM (IC_{50})

In Vitro

Epertinib hydrochloride inhibits the phosphorylation of EGFR and HER2 in NCI-N87 cells, with IC_{50} values of 4.5 and 1.6 nM, respectively[2].

Epertinib hydrochloride shows inhibitory activity against MDA-MB-361 cell, with an IC_{50} of 26.5 nM[1].
Epertinib hydrochloride (0-10 μM, 72 h) can selectively inhibit the proliferation of a range of cancer cell lines expressing EGFR and/or HER2[2].

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

Cell Proliferation Assay[2]

Cell Line:	NCI-N87 (stomach), BT-474 (breast), SK-BR-3 (breast), MDA-MB-453 (breast), MDA-MB-175VII (breast), HT115 (colon), Calu-3 (lung), fR2 (breast), and MRC-5 (lung)
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Inhibited the growth of NCI-N87, BT-474, SK-BR-3, MDA-MB-453, MDA-MB-175VII, HT115, Calu-3, fR2, and MRC-5, with IC_{50} values of 8.3 ± 2.6, 9.9 ± 0.8, 14.0 ± 3.6, 48.6 ± 3.1, 21.6 ± 4.3, 53.3 ± 8.6, 241.5 ± 29.2, 5366.7 ± 65.2, and 4964.6 ± 340.3.

In Vivo

Epertinib hydrochloride (0-100 mg/kg, Orally, once daily for 28 days) shows antitumor activity[1].
Epertinib hydrochloride (50 mg/kg, Orally, once daily for 30 days) significantly reduces the brain tumor volume[1].
Epertinib hydrochloride (0-50 mg/kg, Orally, once daily for 10-28 days) significantly inhibits the tumor growth in a dose-dependent manner[2].

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

Animal Model:	Nude mice (BALB/cAJcl-nu/nu, implanted intracranially with MDA-MB-361 or BR2 cells)[1]
Dosage:	12.5, 25, 50, 100 mg/kg
Administration:	Orally, once daily for 28 days
Result:	Showed antitumor activity in the mammary fat pad implantation model using both cell lines and the ED_{50} values were comparable (24.1 mg/kg and 26.5 mg/kg for MDA-MB-361 and BR2 (MDA-MB-361-luc-BR2), respectively).

Animal Model:	Nude mice (BALB/cAJcl-nu/nu, implanted intracranially with MDA-MB-361 or BR2 cells)[1]
Dosage:	50 mg/kg
Administration:	Orally, once daily for 30 days
Result:	Significantly reduced the brain tumor volume, indicating that epertinib could have potent antitumor activity in brain metastasis even in the presence of an intact BTB (blood-tumor barrier).

Animal Model:	Nude mice (BALB/cAJcl-nu/nu, prepared by subcutaneous implantation of human gastric cancer cells, NCI-N87 into the back of nude mice)[2]
Dosage:	0, 6.25, 12.5, 25, and 50 mg/kg
Administration:	Oral gavage, daily for 10-28 days
Result:	Significantly inhibited the tumor growth in a dose-dependent manner.

REFERENCES

[1]. Tanaka H, et al. Preclinical antitumor activity of S-222611, an oral reversible tyrosine kinase inhibitor of epidermal growth factor receptor and human epidermal growth factor receptor 2. Cancer Sci. 2014 Aug;105(8):1040-8.

[2]. Tanaka Y, et al. Distribution analysis of epertinib in brain metastasis of HER2-positive breast cancer by imaging mass spectrometry and prospect for antitumor activity. Sci Rep. 2018 Jan 10;8(1):343.

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