Glesatinib hydrochloride

Cat. No.: HY-19642A

CAS No.: 1123838-51-6

Molecular Formula: $C_{31}H_{28}ClF_2N_5O_3S_2$

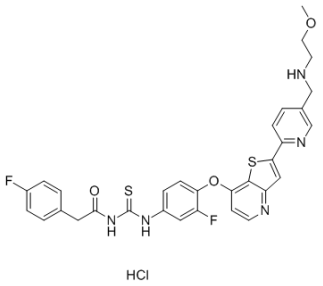
Molecular Weight: 656.17

Target: TAM Receptor; c-Met/HGFR

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 : 50 mg/mL (76.20 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5240 mL	7.6200 mL	15.2400 mL
5 mM	0.3048 mL	1.5240 mL	3.0480 mL
10 mM	0.1524 mL	0.7620 mL	1.5240 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 (3.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.81 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Glesatinib hydrochloride (MGCD265 hydrochloride) is an orally active, potent MET/SMO dual inhibitor. Glesatinib hydrochloride, a tyrosine kinase inhibitor, antagonizes P-glycoprotein (P-gp) mediated multidrug resistance (MDR) in non-small cell lung cancer (NSCLC)[1][2].

IC_{50} & Target

MET

In Vitro

Glesatinib hydrochloride (MGCD265 hydrochloride; 0.01-5 μM; for 72 hours) results in a dose-dependent inhibition of cancer cell growth and shows the low IC_{50} value of 0.08 μM on NSCLC H1299 cells[1].
Glesatinib hydrochloride (0.01, 0.1, 0.5, 1 μM) significantly increases by several-fold the percentage of apoptotic cells in NSCLC H1299 cells[1].
Glesatinib hydrochloride has the cytotoxicity to P-gp overexpressing cancer cells KB-C2, SW620/Ad300, HEK293/ABCB1, and their parent cells KB-3-1, SW620, HEK293 cells with the IC_{50}s fell between 5 and 10 μM[1].
Glesatinib hydrochloride (1, 3 μM; 120 mins) increases the intracellular [^{3}H]-Paclitaxel accumulation and inhibits [^{3}H]-Paclitaxel efflux in cancer cell lines overexpressing P-gp[2].
Glesatinib hydrochloride (0-40 μM) stimulates the ATPase activity of P-gp transporters in a dose-dependent manner[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	NSCLC H1299 cells
Concentration:	0.01, 0.1, 1, 2, 5 μM
Incubation Time:	For 72 hours
Result:	Resulted in a dose-dependent inhibition of cancer cell growth and showed the lowest IC_{50} value of 0.08 μM.

In Vivo

Glesatinib hydrochloride (MGCD265 hydrochloride; 15 mg/kg/day; orally; 40 weeks) causes a significant decrease in tumor size[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	4–6-week old female balb/c athymic (nu/nu) mice with HCC827 NSCLC tumor xenografts[1]
Dosage:	15 mg/kg
Administration:	Orally; daily; 40 weeks
Result:	Caused a significant decrease in tumor size.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.

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REFERENCES

[1]. Morgillo F, et al. Dual MET and SMO Negative Modulators Overcome Resistance to EGFR Inhibitors in Human Nonsmall Cell Lung Cancer. J Med Chem. 2017 Sep 14;60(17):7447-7458.

[2]. Cui Q, et al. Glesatinib, a c-MET/SMO Dual Inhibitor, Antagonizes P-glycoprotein Mediated MultidrugResistance in Cancer Cells. Front Oncol. 2019 Apr 25;9:313.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA