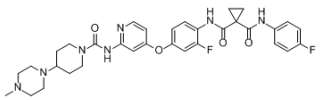
Golvatinib

Cat. No.:	HY-13068
CAS No.:	928037-13-2
Molecular Formula:	$C_{33}H_{37}F_2N_7O_4$
Molecular Weight:	633.69
Target:	c-Met/HGFR; VEGFR
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 (**78.90 mM;** Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5781 mL	7.8903 mL	15.7806 mL
	5 mM	0.3156 mL	1.5781 mL	3.1561 mL
	10 mM	0.1578 mL	0.7890 mL	1.5781 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: ≥ 3 mg/mL (4.73 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 3 mg/mL (4.73 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 3 mg/mL (4.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Golvatinib (E-7050) is a potent dual inhibitor of both **c-Met** and **VEGFR2** kinases with **IC_{50}**s of 14 and 16 nM, respectively.

IC_{50} & Target		
	VEGFR2 16 nM (IC_{50})	c-Met 14 nM (IC_{50})

In Vitro	Golvatinib (E-7050) potently inhibits phosphorylation of both c-Met and VEGFR-2. Golvatinib also potently represses the growth of both c-met amplified tumor cells and endothelial cells stimulated with either HGF or VEGF. Golvatinib strongly inhibits the growth of MKN45, EBC-1, Hs746T, and SNU-5 tumor cells with IC_{50} values of 37, 6.2, 23, and 24 nM, respectively. The growth of A549, SNU-1 and 0MKN74 tumor cells is inhibited by Golvatinib with much higher IC_{50} values[1]. Golvatinib circumvents resistance to all of the reversible, irreversible, and mutant-selective EGFR-TKIs induced by exogenous and/or endogenous HGF in EGFR mutant lung cancer cell lines, by blocking the Met/Gab1/PI3K/Akt pathway in vitro. Golvatinib also prevents the emergence of gefitinib-resistant HCC827 cells induced by continuous exposure to HGF[2].
In Vivo	Golvatinib (E-7050) shows inhibition of the phosphorylation of c-Met and VEGFR-2 in tumors, and strong inhibition of tumor growth and tumor angiogenesis in xenograft models. Treatment of some tumor lines containing c-met amplifications with high doses of Golvatinib (50-200 mg/kg) induced tumor regression and disappearance. In a peritoneal dissemination model, Golvatinib shows an antitumor effect against peritoneal tumors as well as a significant prolongation of lifespan in treated mice[1]. Golvatinib (E7050) plus Gefitinib results in marked regression of tumor growth associated with inhibition of Akt phosphorylation in cancer cells[2].

PROTOCOL

Cell Assay [1]	Cells (1000-3000 cells/100 μL/well) are seeded on 96-well culture plates with various concentrations of Golvatinib and cultured for 3 days. Then, 10 μL of WST-8 reagent is added to each well, and absorbance is measured at 450 nm compared with a reference measurement at 660 nm using a MTP-500 microplate reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Nude mice bearing MKN45, Hs746T, SNU-5, or EBC-1 tumors are administered Golvatinib (25, 50, 100, 200 mg/kg) or vehicle only as a control, once a day. Tumor volume is measured using calipers on the indicated days (0-15 days)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Science**. 2017 Dec 1;358(6367). pii: eaan4368.
- **Sci Transl Med**. 2018 Jul 18;10(450). pii: eaaq1093.
- **PLoS Biol**. 2019 Apr 30;17(4):e3000229.
- **Technical University of Munich**. 24.01.2018.

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REFERENCES

[1]. Nakagawa T et al. E7050: a dual c-Met and VEGFR-2 tyrosine kinase inhibitor promotes tumor regression and prolongs survival in mouse xenograft models. Cancer Sci, 2010, 101(1), 210-215.

[2]. Wang W et al. Met kinase inhibitor E7050 reverses three different mechanisms of hepatocyte growth factor-induced tyrosine kinase inhibitor resistance in EGFR mutant lung cancer. Clin Cancer Res, 2012, 18(6), 1663-1671.

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

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