Dovitinib lactate

Cat. No.: HY-10207

CAS No.: 692737-80-7

Molecular Formula: $C_{24}H_{27}FN_6O_4$

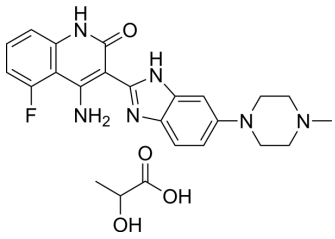
Molecular Weight: 482.51

Target: FGFR; FLT3; c-Kit; VEGFR; PDGFR

Pathway: 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 : 25 mg/mL (51.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0725 mL	10.3625 mL	20.7250 mL
	5 mM	0.4145 mL	2.0725 mL	4.1450 mL
	10 mM	0.2072 mL	1.0362 mL	2.0725 mL

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

BIOLOGICAL ACTIVITY

Description

Dovitinib lactate (TKI258 lactate) is a multi-targeted tyrosine kinase inhibitor with IC_{50}s of 1, 2, 8/9, 10/13/8, 27/210 nM for FLT3, c-Kit, FGFR1/3, VEGFR1/2/3 and PDGFRα/β, respectively[1].

IC_{50} & Target

FLT3 1 nM (IC_{50})	c-Kit 2 nM (IC_{50})	FGFR1 8 nM (IC_{50})	FGFR3 9 nM (IC_{50})
VEGFR1 1 nM (IC_{50})	VEGFR3 8 nM (IC_{50})	VEGFR2 13 nM (IC_{50})	PDGFRα 27 nM (IC_{50})
PDGFRβ 210 nM (IC_{50})			

In Vitro

Dovitinib potently inhibits the FGF-stimulated growth of WT and F384L-FGFR3-expressing B9 cells with IC_{50} values of 25 nM. B9-MINV cells are resistant to the inhibitory activity of Dovitinib at concentrations up to 1 μM. Dovitinib inhibits cell proliferation of KMS11 (FGFR3-Y373C), OPM2 (FGFR3-K650E), and KMS18 (FGFR3-G384D) cells with IC_{50} of values of 90 nM (KMS11 and OPM2) and 550 nM, respectively[1]. Treatment of SK-HEP1 cells with dovitinib results in G2/M cell cycle arrest, inhibition of colony formation in soft agar and blockade of bFGF-induced cell migration. Dovitinib inhibits basal expression

	and FGF-induced phosphorylation of FGFR-1, FRS2-α and ERK1/2[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Dovitinib (10 mg/kg, 30 mg/kg, 60 mg/kg, p.o.) shows significant antitumor effect in the KMS11-bearing mice model, and the growth inhibition is 48%, 78.5%, and 94% in the 10 mg/kg, 30 mg/kg, and 60 mg/kg treatment arms, respectively, compared with the placebo-treated mice[1]. Dovitinib demonstrates significant antitumor and antimetastatic activities in HCC xenograft models. Dovitinib potently inhibits tumor growth of six HCC lines. Inhibition of angiogenesis correlates with inactivation of FGFR/PDGFR-β/VEGFR-2 signaling pathways. Dovitinib also causes dephosphorylation of retinoblastoma, upregulation of p-histone H2A-X and p27, and downregulation of p-cdk-2 and cyclin B1, which results in a reduction in cellular proliferation and the induction of tumor cell apoptosis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	To determine IC_{50} for SK-HEP1 cells, cells are plated at a density of 2×10^4 cells per dish. After 48 h, cells are treated with 0, 0.01, 0.1, 1, 5, 10, 50, 100 μM dovitinib in DMEM containing 1% FBS for 24 h. Cell viability is determined with Cell Proliferation Assay. IC_{50} is calculated by nonlinear regression analysis using GraphPad Prism software[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: Six HCC lines (06-0606, 26-0808A, 26-1004, 25-0705A, 5-1318, 21-0208) are used to establish tumors in male SCID mice. or dose-esponse experiments, mice bearing the 06-0606 xenografts re orally given vehicle (5% dextrose) or two doses of dovitinib (50 and 75 mg/kg) daily for 14 days. For time-dependent inhibition of dovitinib targets, mice bearing 06-0606 tumors are given orally 200 μL of either vehicle (n=6) or 50 mg/kg/day of dovitinib (n=10)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Theranostics. 2018 Jul 30;8(15):4262-4278.
- NPJ Precis Oncol. 2021 Jul 16;5(1):66.
- Front Cell Dev Biol. 2020 May 7;8:287.
- Biochemistry for Health, NOVA University of Lisbon. 2019 Jul.

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REFERENCES

[1]. Trudel S, et al. CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. Blood. 2005, 105(7), 2941-2948.

[2]. Huynh H, et al. Dovitinib demonstrates antitumor and antimetastatic activities in xenograft models of hepatocellular carcinoma. J Hepatol. 2012, 56(3), 595-601.

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