Telatinib

Cat. No.: HY-10527

CAS No.: 332012-40-5

Molecular Formula: $C_{20}H_{16}ClN_5O_3$

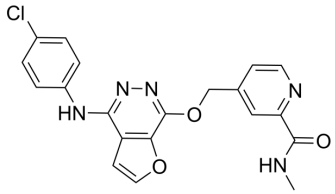
Molecular Weight: 409.83

Target: c-Kit; PDGFR; VEGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 46 mg/mL (112.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4400 mL	12.2002 mL	24.4004 mL
	5 mM	0.4880 mL	2.4400 mL	4.8801 mL
	10 mM	0.2440 mL	1.2200 mL	2.4400 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Telatinib (Bay 57-9352) is an orally active, small molecule inhibitor of VEGFR2, VEGFR3, PDGFα, and c-Kit with IC_{50}s of 6, 4, 15 and 1 nM, respectively.

IC_{50} & Target	VEGFR2	VEGFR3	PDGFRα	c-Kit
	6 nM (IC_{50})	4 nM (IC_{50})	15 nM (IC_{50})	1 nM (IC_{50})

In Vitro

Telatinib has low affinity for the Raf kinase pathway, epidermal growth factor receptor family, the fibroblast growth factor receptor (FGFR) family, or the Tie-2 receptor[2]. Telatinib is metabolized by various cytochrome P450 (CYP) isoforms including CYP3A4/3A5, CYP2C8, CYP2C9, and CYP2C19 as well as by uridine diphosphate glucuronosyltransferase 1A4 (UGT1A4), with the formation of the N-glucuronides of telatinib as the major biotransformation pathway in man. In vitro studies show telatinib to be a weak substrate of the adenosine triphosphate binding cassette (ABC) B1 (ABCB1) transporter

	[3]. Telatinib at 1 μM significantly enhances the intracellular accumulation of [^{3}H]-mitoxantrone (MX) in ABCG2-overexpressing cell lines. In addition, telatinib at 1 μM significantly reduces the rate of [^{3}H]-MX efflux from ABCG2-overexpressing cells. Furthermore, telatinib significantly inhibits ABCG2-mediated transport of [^{3}H]-E217βG in ABCG2 overexpressing membrane vesicles[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Telatinib causes a significant decrease in endothelium-dependent and endothelium-independent vasodilation. VEGF inhibition by itself decreases NO synthesis, which promotes vasoconstriction, increases peripheral resistance, and therefore can induce an increase in blood pressure[1]. Telatinib (15 mg/kg) with doxorubicin (1.8 mg/kg) significantly decreases the growth rate and tumor size of ABCG2 overexpressing tumors in a xenograft nude mouse model[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [4]	The vanadate (Vi)-sensitive ATPase activity of ABCG2 in the membrane of High Five insect cells is measured. Briefly, membrane (2 μg/0.06 mL) are incubated in ATPase assay buffer with or without 0.4 mM vanadate at 37°C for 5 min and then incubated with varying concentrations of telatinib at 37°C for 5 min. The ATPase reaction is started by the addition of 4 mM Mg-ATP. After incubating at 37°C for 10 min, the reactions are stopped by adding 0.05 mL of 10% SDS solution. The liberated inorganic phosphate is measured[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Mice: The mice are randomized into four groups and treated with one of the following regimens: (a) vehicle (10% N-methyl-pyrrolidinone, 90% polyethylene glycol 300) (q3d×6), (b) DOX (1.8 mg/kg, i.p., q3d×6), (c) telatinib dissolved in 10% N-methyl-pyrrolidinone, 90% polyethylene glycol 300 (15 mg/kg, p.o., every 2nd and 3rd day; total 12 times), and (d) DOX (1.8 mg/kg, i.p., q3d×6) + telatinib (15 mg/kg, p.o., every 2nd and 3rd day, given 1 h before giving DOX; total 12 times). DOX for injection is prepared by dissolving in saline. Tumor volume is measured using calipers and body weights are recorded[4]. 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.

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REFERENCES

[1]. Steeghs N, et al. Hypertension and rarefaction during treatment with telatinib, a small molecule angiogenesis inhibitor. Clin Cancer Res. 2008 Jun 1;14(11):3470-6.

[2]. Langenberg MH, et al. Phase I evaluation of telatinib, a vascular endothelial growth factor receptor tyrosine kinase inhibitor, in combination with irinotecan and capecitabine in patients with advanced solid tumors. Clin Cancer Res. 2010 Apr 1;16(7):2187-97.

[3]. Steeghs N, et al. Pharmacogenetics of telatinib, a VEGFR-2 and VEGFR-3 tyrosine kinase inhibitor, used in patients with solid tumors. Invest New Drugs. 2011 Feb;29(1):137-43.

[4]. Sodani K, et al. Telatinib reverses chemotherapeutic multidrug resistance mediated by ABCG2 efflux transporter in vitro and in vivo. Biochem Pharmacol. 2014 May 1;89(1):52-61.

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

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