Tesevatinib

Cat. No.: HY-13314

CAS No.: 781613-23-8

Molecular Formula: $C_{24}H_{25}Cl_2FN_4O_2$

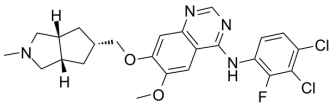
Molecular Weight: 491.39

Target: EGFR; VEGFR; Ephrin Receptor

Pathway: JAK/STAT Signaling; 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 : 100 mg/mL (203.50 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0350 mL	10.1752 mL	20.3504 mL
	5 mM	0.4070 mL	2.0350 mL	4.0701 mL
	10 mM	0.2035 mL	1.0175 mL	2.0350 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 (5.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tesevatinib (XL-647; EXEL-7647; KD-019) is an orally available, multi-target tyrosine kinase inhibitor; inhibits EGFR, ErbB2, KDR, Flt4 and EphB4 kinase with IC_{50}s of 0.3, 16, 1.5, 8.7, and 1.4 nM.

IC_{50} & Target

EGFR	ErbB2	KDR	Flt-4
0.3 nM (IC_{50})	16 nM (IC_{50})	1.5 nM (IC_{50})	8.7 nM (IC_{50})

In Vitro

Tesevatinib (XL-647) potently inhibits the EGF/ErbB2, VEGF, and ephrin RTK families. Tesevatinib (XL-647) is a reversible and ATP competitive inhibitor. Tesevatinib (XL-647) was inactive against a panel of 10 tyrosine kinases (including the insulin and the insulin-like growth factor-1 receptor) and 55 serine-threonine kinases (including cyclin-dependent kinases, stress-activated protein kinases, and protein kinase C isoforms). Tesevatinib (XL-647) inhibits cellular proliferation and EGFR

	pathway activation in the erlotinib-resistant H1975 cell line that harbors a double mutation (L858R and T790M) in the EGFR gene. In A431 cells, Tesevatinib (XL-647) reduces cell viability with IC_{50} values of 13 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tesevatinib (XL-647) shows potent and long-lived inhibition of the WT EGFR in vivo. Tesevatinib (XL-647) substantially inhibits the growth of H1975 xenograft tumors and reduces both tumor EGFR signaling and tumor vessel density[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Growth inhibition of H1975 and A431 cells by increasing concentrations of Tesevatinib (XL-647), gefitinib, or erlotinib is determined by seeding 5000 cells per well in 96-well plates. The following day, cells are washed once with low-serum RPMI 1640 (0.1% fetal bovine serum, 1% nonessential amino acids, and 1% penicillin/streptomycin), after which 90 µL of the low-serum RPMI 1640 are added. Test compounds (Tesevatinib (XL-647)) are diluted to 10 times the test concentrations and 10 µL are added to triplicate wells for a 72-h incubation. Cell viability is determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Tumor-bearing mice are given either Tesevatinib (XL-647), erlotinib, or gefitinib at 100 mg/kg and tumors are harvested 1 to 72 h later. Half an hour before respective time point, EGF (50 µg/mouse) is given via i.v. bolus injection with tumors dissected 30 min later and tumor extracts are prepared by homogenization in 10 volumes of ice-cold lysis buffer. Lysates are clarified by centrifugation and EGFR tyrosine phosphorylation levels are determined by ELISA[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep. 2023 Nov 10:113431.
- Technical University of Munich. 24.01.2018.

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REFERENCES

[1]. Gendreau SB, et al. Inhibition of the T790M gatekeeper mutant of the epidermal growth factor receptor by EXEL-7647. Clin Cancer Res. 2007 Jun 15;13(12):3713-23.

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