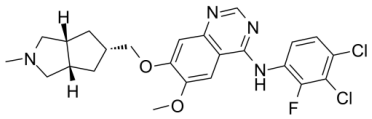
Data Sheet

Product Name:	Tesevatinib
Cat. No.:	CS-3666
CAS No.:	781613-23-8
Molecular Formula:	C24H25Cl2FN4O2
Molecular Weight:	491.39
Target:	EGFR; Ephrin Receptor; VEGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 30 mg/mL (61.05 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 0.3 nM (EGFR), 16 nM (EGFR), 1.5 nM (EGFR), 8.7 nM (EGFR), 1.4 nM (EGFR)[1] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **Animal Administration:** Tesevatinib (XL-647) is formulated for oral administration by dissolution of the dry powder in sterile filtered (0.45 µm) saline (0.9% USP) or in sterile water for injection[1].[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].

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.

CAIndexNames:

4-Quinazolinamine, N-(3,4-dichloro-2-fluorophenyl)-6-methoxy-7-[[(3aα,5β,6aα)-octahydro-2-methylcyclopenta[c]pyrrol-5-yl]methoxy]-

SMILES:

[H][C@@]12[C@@](C[C@@H](COC3=CC4=C(C(NC5=C(F)C(Cl)=C(Cl)C=C5)=NC=N4)C=C3OC)C2)([H])CN(C)C1

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