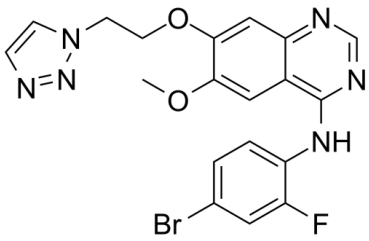
Data Sheet

Product Name:	ZD-4190
Cat. No.:	CS-6801
CAS No.:	413599-62-9
Molecular Formula:	$C_{19}H_{16}BrFN_6O_2$
Molecular Weight:	459.27
Target:	EGFR; VEGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 20.83 mg/mL (45.35 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

ZD-4190 is a potent, orally available inhibitor of the vascular endothelial cell growth factor receptor 2 (**VEGFR2**) and of epidermal growth factor receptor (**EGFR**) signalling, used for the treatment of cancer. **In Vitro:** ZD4190 exhibits cytotoxic activity against the tumor cells[2]. **In Vivo:** ZD4190 (100 mg/kg, p.o.) effectively delays MDA-MB-435 tumor growth in mice. In ZD4190-treated tumors, 18F-FPPRGD2 uptake has decreased significantly relative to baseline by 26.74±8.12% ($p<0.05$) on day 1 and by 41.19±6.63% ($p<0.01$) on day 3, then has returned to baseline on day 7. Tumor uptake of 18F-FLT has also decreased on both day 1 and day 3 after initiation of ZD4190 treatment. However, ZD4190 does not significantly change 18F-FDG uptake in tumors, compared with the control group[1]. ZD4190 (50 mg/kg, p.o.) prevents outgrowth of residual tumour in a muscle model of minimal residual carcinoma[2]. ZD4190 (12.5-100 mg/kg, p.o.) produces a dose-dependent reduction in K(trans) in PC-3 prostate tumors. At 100 mg/kg, ZD4190 reduces K(trans) in PC-3 tumors by 31% following 2 doses and by 53% following 8 doses[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]The cytotoxicity of ZD4190 for PDVC57B cells is established when 10^4 cells are exposed to 1-10 μM ZD4190 for 96 h before MTS solution is added and the optical density measured at 490 nm. Cells are also grown to 40% confluence and treated with 1-100 μM ZD4190 for 7 days and the cytopathic effect examined by staining with crystal violet. **Animal Administration:** ZD-4190 is suspended in a 1% (v/v) solution of polyoxyethylene sorbitan mono-oleate in deionized water[3]ZD4190 is suspended in a 1% (v/v) solution of polyoxyethylene sorbitan mono-oleate in deionized water and administered by oral gavage (0.1 mL/10 g body weight). In each experiment, mice are randomized to receive either vehicle or ZD4190, administered once daily using a 1 day (at 0 and 22 h) or 7 day (at 0, 24, 48, 72, 96, 120, 144, and 166 h) treatment regimen (i.e., daily administration of compound for 1 or 7 days with an additional dose given 2 h prior to the end of the treatment period) followed by DCEMRI under terminal anesthesia.

References:

[1]. Yang M, et al. PET imaging of early response to the tyrosine kinase inhibitor ZD4190. Eur J Nucl Med Mol Imaging. 2011 Jul;38(7):1237-47. doi: 10.1007/s00259-011-1742-z. Epub 2011 Mar 1.

[2]. Gaballah K, et al. The antiangiogenic agent ZD4190 prevents tumour outgrowth in a model of minimal residual carcinoma in deep tissues. Br J Cancer. 2009 Aug 4;101(3):418-23. doi: 10.1038/sj.bjc.6605092. Epub 2009 Jul 21.

[3]. Checkley D, et al. Dynamic contrast-enhanced MRI of vascular changes induced by the VEGF-signalling inhibitor ZD4190 in human tumour xenografts. Magn Reson Imaging. 2003 Jun;21(5):475-82.

CAIndexNames:

4-Quinazolinamine, N-(4-bromo-2-fluorophenyl)-6-methoxy-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]-

SMILES:

COC1=CC2=C(NC3=CC=C(Br)C=C3F)N=CN=C2C=C1OCCN4N=NC=C4

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

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