Cediranib

Cat. No.: HY-10205

CAS No.: 288383-20-0

Molecular Formula: $C_{25}H_{27}FN_4O_3$

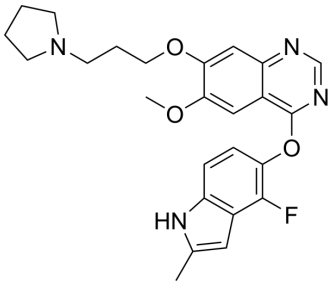
Molecular Weight: 450.51

Target: VEGFR; Autophagy; PDGFR

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (44.39 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2197 mL	11.0985 mL	22.1971 mL
	5 mM	0.4439 mL	2.2197 mL	4.4394 mL
	10 mM	0.2220 mL	1.1099 mL	2.2197 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 mg/mL (4.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (4.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cediranib (AZD2171) is a highly potent, orally available VEGFR tyrosine kinase inhibitor with IC_{50}s of <1, <3, 5, 5, 36, 2 nM for Flt1, KDR, Flt4, PDGFRα, PDGFRβ, c-Kit, respectively.

IC_{50} & Target

Flt-1 5 nM (IC_{50})	KDR 1 nM (IC_{50})	Flt-4 3 nM (IC_{50})	PDGFRα 36 nM (IC_{50})
PDGFRβ 5 nM (IC_{50})	c-Kit 2 nM (IC_{50})		

In Vitro

In human umbilical vein endothelial cells, Cediranib inhibits VEGF-stimulated proliferation and KDR phosphorylation with IC

	$_{50}$ values of 0.4 and 0.5 nM, respectively. In a fibroblast/endothelial cell coculture model of vessel sprouting, Cediranib also reduces vessel area, length, and branching at subnanomolar concentrations[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Once-daily oral administration of Cediranib ablates experimental (VEGF-induced) angiogenesis and inhibits endochondral ossification in bone or corpora luteal development in ovary; physiologic processes that are highly dependent upon neovascularization. The growth of established human tumor xenografts (colon, lung, prostate, breast, and ovary) in athymic mice is inhibited dose-dependently by Cediranib, with chronic administration of 1.5 mg per kg per day producing statistically significant inhibition in all models. A histologic analysis of Calu-6 lung tumors treated with Cediranib reveals a reduction in microvessel density within 52 hours that becomes progressively greater with the duration of treatment. These changes are indicative of vascular regression within tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The inhibitory activity of Cediranib is determined against a range of recombinant tyrosine kinases [KDR, Flt-1, Flt-4, c-Kit, PDGFR-α, PDGFR-β, CSF-1R, Flt-3, FGFR1, Src, Abl, epidermal growth factor receptor (EGFR), ErbB2, Aur-A, and Aur-B] using ELISA methodology[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Proliferation of MG63 osteosarcoma cells is induced by PDGF-AA, which selectively activates PDGFR-α homodimer signaling. Cells are cultured in DMEM without phenol red containing 1% charcoal stripped FCS, 2 mM glutamine, and 1% nonessential amino acids for 24 hours. Cediranib or vehicle is added with PDGF-AA ligand (50 ng/mL) and plates reincubated for 72 hours. Cellular proliferation is determined using a bromodeoxyuridine[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: Young female Alderley Park rats (6 weeks of age, Wistar derived, n=5) are dosed orally, once daily for 28 days with Cediranib (1.25-5 mg per kg per day) or vehicle. Additional rats (five per group) are treated with Cediranib (5 mg per kg per day) or vehicle for 28 days and maintained for a further 28 days without treatment, to examine the effect of compound withdrawal. Histologic paraffin wax sections of the femorotibial joints and ovaries are stained with H&E. Morphometric image analysis of femorotibial sections is done, with growth plate areas from both the femur and tibia in each joint being combined for an analysis of the effect of compound treatment. The area of corpora lutea in H&E-stained ovary sections is similarly determined by morphometric analysis[1]. Mice: Mice bearing established Calu-6 human lung tumor xenografts (0.2±0.01 cm^3) are selected (day 0) and treated chronically with Cediranib (6 mg per kg per day, p.o.) or vehicle. Tumors are collected (6-15 per group) 4 hours after the last dose of Cediranib or vehicle, on days 1, 2, 7, 14, and 21. CD31 is then detected in sections using a chromagen end point or fluorescent immunostaining[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Stem Cell. 2019 Sep 5;25(3):373-387.e9.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Neuro Oncol. 2016 Apr;18(4):538-48.
- Biomaterials. 2018 Apr;161:164-178.
- J Med Chem. 2023 Dec 13.

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REFERENCES

[1]. Wedge SR, et al. AZD2171: a highly potent, orally bioavailable, vascular endothelial growth factor receptor-2 tyrosine kinase inhibitor for the treatment of cancer. Cancer Res, 2005, 65(10), 4389-4400.

[2]. Zhang L, et al. Pleiotrophin promotes vascular abnormalization in gliomas and correlates with poor survival in patients with astrocytomas. Sci Signal. 2015 Dec 8;8(406):ra125.

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