Cediranib maleate

Cat. No.: HY-13049

CAS No.: 857036-77-2

Molecular Formula: $C_{29}H_{31}FN_4O_7$

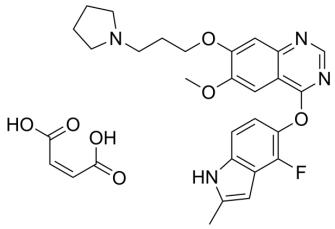
Molecular Weight: 566.58

Target: VEGFR; Autophagy; PDGFR

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (79.42 mM)

H_2O : 2 mg/mL (3.53 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.7650 mL	8.8249 mL	17.6498 mL
5 mM	0.3530 mL	1.7650 mL	3.5300 mL
10 mM	0.1765 mL	0.8825 mL	1.7650 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 2 mg/mL (3.53 mM); Clear solution; Need ultrasonic and warming and heat to 60°C

BIOLOGICAL ACTIVITY

Description

Cediranib maleate (AZD-2171 maleate) is a highly potent, orally available VEGFR 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]. 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.
- Biomaterials. 2018 Apr;161:164-178.
- Neuro Oncol. 2016 Apr;18(4):538-48.
- Sci Signal. 2015 Dec 8;8(406):ra125.

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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.

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