产品名称：西地尼布马来酸盐

产品别名： **AZD-2171 maleate；Cediranib maleate**

生物活性：

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

In Vitro	In human umbilical vein endothelial cells, Cediranib inhibits VEGF-stimulated proliferation and KDR phosphorylation with IC50 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].
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].

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	Solvent / Mass / Concentration	**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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

Cell Assay	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].
	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

Animal Administration	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].
Kinase Assay	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].
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.