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产品名称：5-[(Z)-(5-氟-1,2-二氢-2-氧代-3H-吲哚-3-亚基)甲基]-N-[(2S)-2-羟基-3-(4-吗啉基)丙基]-2,4-二甲基-1H-吡咯-3-甲酰胺马来酸盐
产品别名：SU14813 maleate

生物活性：

Description	SU14813 maleate is a multi-targeted receptor tyrosine kinases inhibitor with IC50s of 50, 2, 4, 15 nM for VEGFR2, VEGFR1, PDGFRβ and KIT.			
IC_{50} & Target	VEGFR2	VEGFR1	PDGFRβ	KIT
	50 nM (IC_{50})	2 nM (IC_{50})	4 nM (IC_{50})	15 nM (IC_{50})
In Vitro	SU14813 inhibits ligand-dependent and ligand-independent proliferation, migration, and survival of endothelial cells and/or tumor cells expressing these targets. SU14813 inhibits cellular ligand-dependent phosphorylation of VEGFR-2 (transfected NIH 3T3 cells), PDGFR-β (transfected NIH 3T3 cells), KIT (Mo7e cells), and FLT3-internal tandem duplication (FLT3-ITD; MV4;11 cells) as well as FMS/CSF1R (transfected NIH 3T3 cells). SU14813 inhibits VEGFR-2, PDGFR-β, and KIT phosphorylation in porcine aorta endothelial cells overexpressing these targets, with cellular IC50 values of 5.2, 9.9, and 11.2 nM, respectively. SU14813 inhibits the growth of U-118MG with an IC50 of 50 to 100 nM[1].			
In Vivo	SU14813 inhibits VEGFR-2, PDGFR-β, and FLT3 phosphorylation in xenograft tumors in a dose- and time-dependent fashion. The plasma concentration required for in vivo target inhibition is estimated to be 100 to 200 ng/mL. Used as monotherapy, SU14813 exhibits broad and potent antitumor activity resulting in regression, growth arrest, or substantially reduced growth of various established xenografts derived from human or rat tumor cell lines. Treatment in combination with docetaxel significantly enhances both the inhibition of primary tumor growth and the survival of the tumor-bearing mice compared with administration of either agent alone[1].			

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (179.03 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7903 mL	8.9516 mL	17.9032 mL
5 mM	0.3581 mL	1.7903 mL	3.5806 mL
10 mM	0.1790 mL	0.8952 mL	1.7903 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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

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	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.48 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.48 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.48 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀
References	[1]. Patyna S, et al. SU14813: a novel multiple receptor tyrosine kinase inhibitor with potent antiangiogenic and antitumor activity. Mol Cancer Ther. 2006 Jul;5(7):1774-82.

实验参考：

Cell Assay	The effect of SU14813 on endothelial cell survival is evaluated. Passages 4 to 5 human umbilical vein endothelial cells are grown to subconfluency in EGM2 medium containing 10% FBS, endothelial cell growth supplement, and 10 μg/mL sodium heparin. The cells are seeded in 96-well plates at 10,000 per well in F12K medium and 10% FBS. The next day, cells are starved for 18 hours in F12K+1% FBS and then incubated with SU14813 in various concentrations. 45 minutes later, 20 ng/mL growth factor [VEGF or basic fibroblast growth factor (bFGF)] is introduced into the assay. Three days later, cell numbers are determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay[1].
Animal Administration	Mouse: SU14813 is evaluated for its efficacy and synergism in combination with the microtubule inhibitor docetaxel in docetaxel-resistant murine LLC model. SU14813 is administered p.o. twice daily (BID) at doses of 10, 40, 80, or 120 mg/kg beginning on day 5 after tumor implantation. Docetaxel 40 mg/kg (mouse maximum tolerated dose) is administered i.v. thrice weekly also beginning on day 5 after tumor implantation[1].
References	[1]. Patyna S, et al. SU14813: a novel multiple receptor tyrosine kinase inhibitor with potent antiangiogenic and antitumor activity. Mol Cancer Ther. 2006 Jul;5(7):1774-82.