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产品名称: **Avitinib (maleate)**
产品别名: 艾维替尼马来酸盐

生物活性:				
Description	Avitinib maleate is a pyrrolopyrimidine-based irreversible epidermal growth factor receptor (EGFR) inhibitor with an IC ₅₀ of 7.68 nM.			
IC ₅₀ & Target	EGFR			
	7.68 nM (IC ₅₀)			
In Vitro	Avitinib is structurally distinct from previously reported pyrimidine-based irreversible EGFR inhibitors such as osimertinib and rociletinib. Avitinib is designed specifically to inhibit EGFR active mutations and the T790M acquired resistant mutation, while sparing wild type EGFR. Avitinib selectively inhibits EGFR active and T790M mutations with up to 298-fold increase in potency compared to wild-type EGFR. Avitinib exhibits potent inhibitory activity with IC ₅₀ value of 0.18 nM against EGFR L858R/T790M double mutations, nearly 43-fold greater potency over wild-type EGFR (IC ₅₀ =7.68 nM). Avitinib selectively inhibits mutant EGFR phosphorylation with IC ₅₀ values of 7.3 nM and 2.8 nM in NCI-H1975 and NIH/3T3_TC32T8 cells, about 115- and 298-fold more sensitive than that of the inhibition of wild type EGFR in A431 ^[1] .			
In Vivo	Oral administration of avitinib at daily dose of 500 mg/kg results in complete remission of tumors with EGFR active and T790M mutations for over 143 days with no weight loss. Three major metabolites of avitinib are tested and show no wild-type EGFR inhibition and off-target effects such as inhibition of IGF-1R. Avitinib is safe in non-small cell lung cancer (NSCLC) patients at the dose range between 50 mg and 550 mg once per day and no hyperglycemia and other severe adverse effects are detected such as grade 3 QT prolongation ^[1] .			
Solvent&Solubility	In Vitro: DMSO : ≥ 100 mg/mL (165.67 mM) * "≥" means soluble, but saturation unknown.			
		Solvent / Mass Concentration	1 mg	5 mg
	Preparing	1 mM	1.6567 mL	8.2836 mL
	Stock Solutions	5 mM	0.3313 mL	1.6567 mL
		10 mM	0.1657 mL	0.8284 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 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline			



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	<p>Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.14 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>2. 请依序添加每种溶剂: 10% DMSO \rightarrow 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.14 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>3. 请依序添加每种溶剂: 10% DMSO \rightarrow 90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.14 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。</p> <p>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。</p>
References	<p>[1]. Xu X, et al. AC0010, an Irreversible EGFR Inhibitor Selectively Targeting Mutated EGFR and Overcoming T790M-Induced Resistance in Animal Models and Lung Cancer Patients. Mol Cancer Ther. 2016 Nov;15(11):2586-2597.</p>
实验参考:	
Cell Assay	<p>Cell proliferation is assayed by a cell viability reagent, WST-1. Cells are seeded at optimal density onto 96-well plates and incubated for 24 hours, followed by avitinib treatment for 72 hours. Cell viability is then assayed by incubating cells with WST-1 reagent for 2-3 hrs^[1].</p>
Animal Administration	<p>Rats: To assess the potential skin toxicity of avitinib, a rat model is used. Rats are administrated daily with avitinib at 300 mg/kg for 4 weeks, and in control groups gefitinib at 50mg/kg or vehicle control (0.5% MC) is administrated^[1].</p> <p>Mice: NCI-H1975 tumor bearing mice are orally treated with a vehicle control (0.5% MC), avitinib at dose levels of 12.5 mg/kg and 50 mg/kg for 17 days when TV value in vehicle control group reached approximately 2000 mm³. After 17-day dosing, animals in the vehicle control group are sacrificed, whereas animals in avitinib groups are continually daily administrated with increased dose at 500 mg/kg till the test mice cannot tolerate the treatment. Mouse body weight and TV are measured twice per week. TV is then used for the calculation of tumor inhibitory rate and tumor regression rate^[1].</p>
References	<p>[1]. Xu X, et al. AC0010, an Irreversible EGFR Inhibitor Selectively Targeting Mutated EGFR and Overcoming T790M-Induced Resistance in Animal Models and Lung Cancer Patients. Mol Cancer Ther. 2016 Nov;15(11):2586-2597.</p>