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产品名称: **AV-412**
产品别名: **MP412**

生物活性:					
Description	AV-412 (MP412) is an EGFR inhibitor with IC ₅₀ s of 0.75, 0.5, 0.79, 2.3, 19 nM for EGFR, EGFR ^{L858R} , EGFR ^{T790M} , EGFR ^{L858R/T790M} and ErbB2, respectively.				
IC₅₀ & Target	EGFR	EGFR ^{L858R}	EGFR ^{T790M}	EGFR ^{L858R/T790M}	ErbB2
	0.75 nM (IC ₅₀)	0.5 nM (IC ₅₀)	0.79 nM (IC ₅₀)	2.3 nM (IC ₅₀)	19 nM (IC ₅₀)
In Vitro	AV-412 inhibits autophosphorylation of EGFR and ErbB2 with IC ₅₀ of 43 and 282 nM, respectively. AV-412 also inhibits epidermal growth factor (EGF)-dependent cell proliferation with an IC ₅₀ of 100 nM. AV-412 abrogates EGFR signaling in the gefitinib-resistant H1975 cell line, which harbors a double mutation of L858R and T790M in EGFR[1].				
In Vivo	In animal studies using cancer xenograft models, AV-412 (30 mg/kg) demonstrates complete inhibition of tumor growth of the A431 and BT-474 cell lines, which overexpress EGFR and ErbB2, respectively. AV-412 suppresses autophosphorylation of EGFR and ErbB2 at the dose corresponding to its antitumor efficacy. When various dosing schedules are applied, AV-412 shows significant effects with daily and every-other-day schedules, but not with a once-weekly schedule, suggesting that frequent dosing is preferable for this compound. Furthermore, AV-412 shows a significant antitumor effect on the ErbB2-overexpressing breast cancer KPL-4 cell line, which is resistant to gefitinib[1].				
Solvent&Solubility	In Vitro: DMSO : ≥ 28 mg/mL (32.89 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg
		Concentration			
		1 mM	1.1745 mL	5.8726 mL	11.7452 mL
		5 mM	0.2349 mL	1.1745 mL	2.3490 mL
		10 mM	0.1175 mL	0.5873 mL	1.1745 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℃, 6 months; -20℃, 1 month。-80℃ 储存时, 请在 6 个月内使用, -20℃ 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 Solubility: ≥ 2.5 mg/mL (2.94 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (2.94 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				



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	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$\rightarrow$ 90% (20% SBE-β-CD in saline) Solubility: $\geq$ 2.5 mg/mL (2.94 mM); Clear solution 此方案可获得 $\geq$ 2.5 mg/mL (2.94 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。
References	[1]. Suzuki T, et al. Pharmacological characterization of MP-412 (AV-412), a dual epidermal growth factor receptorand ErbB2 tyrosine kinase inhibitor. Cancer Sci. 2007 Dec;98(12):1977-84.
实验参考:	
Cell Assay	To test the effects of AV-412 on growth factor-dependent cell proliferation, A431 and A7r5 cells are cultured for 24 h at 37°C in the presence of 1 ng/mL epidermal growth factor and 50 ng/mL platelet-derived growth factor, respectively. The 3H-thymidine incorporation during this period is measured[1].
Animal Administration	Mice: For studies examining the dosing schedule in relation to efficacy against TE-8 tumors, AV-412 is administered either once daily, every other day, or once per week for 2 weeks. Mice are killed 1 day after the final treatment, and the tumors are dissected and weighed. For evaluation of tumor phosphorylation, tumor-bearing mice are given a single administration of AV-412 and tumors are dissected 4 h later[1].
Kinase Assay	Recombinant intracellular kinase domains of EGFR, EGFR ^{L858R} , EGFR ^{T790M} , EGFR ^{L858R/T790M} , and purified EGFR from A431 cell membranes are used. Kinase reactions are carried out in 8 mM MOPS (pH 7.0), 0.2 mM ethylenediaminetetraacetic acid (EDTA), 10 mM MnCl ₂ , 10 mM Mg acetate, 0.1 mg/mL poly(Glu, Tyr) 4:1, [³³ P-ATP], and 5–10 mU of enzyme, except that 250 μ M of the GGMEDIYFEFMGGKKK peptide substrate is used for EGFR ^{T790M} . Phosphorylation is initiated by the addition of ATP and is allowed to proceed for 40 min at room temperature. The reaction is stopped by the addition of 3% phosphoric acid, then aliquots of the reaction mixture are spotted onto a filtermat. After rinsing to remove peptides bound non-specifically, the filter is scintillation counted[1].
References	[1]. Suzuki T, et al. Pharmacological characterization of MP-412 (AV-412), a dual epidermal growth factor receptorand ErbB2 tyrosine kinase inhibitor. Cancer Sci. 2007 Dec;98(12):1977-84.