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产品名称：AV-412 (free base)
产品别名：MP-412 free base

生物活性：

Description	AV-412 free base (MP-412 free base) 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.

IC$_{50}$ & Target	EGFR	ErbB2	EGFR^{L858R}	EGFR$^{L858R/T790M}$	EGFR^{T790M}
	0.75 nM (IC$_{50}$)	19 nM (IC$_{50}$)	0.51 nM (IC$_{50}$)	2.3 nM (IC$_{50}$)	0.79 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 : ≥ 50 mg/mL (98.62 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9724 mL	9.8619 mL	19.7239 mL
	5 mM	0.3945 mL	1.9724 mL	3.9448 mL
	10 mM	0.1972 mL	0.9862 mL	1.9724 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]. 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 ^{3}H-thymidine incorporation during this period is measured[1].
	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

Animal Administration	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, [γ^{33}P-ATP], and 5–10 mU of enzyme, except that 250 μM 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.