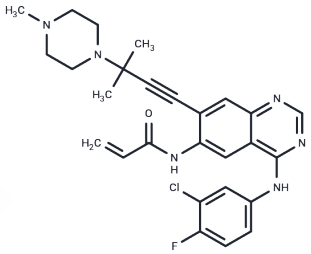
Data Sheet (Cat.No.TQ0293)

TargetMol

AV-412 free base

Chemical Properties



CAS No. : 451492-95-8

Formula: C27H28ClFN6O

Molecular Weight: 507

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AV-412 free base is an EGFR inhibitor (IC50s: 0.75, 0.79, 0.5, 2.3, 19 nM for EGFR, EGFR (T790M), EGFR(L858R), EGFR(L858R/T790M) and ErbB2).
Targets(IC50)	EGFR
In vitro	AV-412 inhibits autophosphorylation of EGFR and ErbB2 (IC50: 43 and 282 nM, respectively) and EGF-dependent cell proliferation (IC50: 100 nM). Additionally, AV-412 abrogates EGFR signaling in the gefitinib-resistant H1975 cell line, which harbors a double mutation of L858R and T790M in EGFR.
In vivo	In cancer xenograft models, AV-412 (30 mg/kg) effectively halts the growth of A431 and BT-474 cell lines, which notably overexpress EGFR and ErbB2, respectively. This compound also inhibits autophosphorylation of EGFR and ErbB2, correlating with its antitumor properties. AV-412 exhibits considerable antitumor activity across different dosing regimens, displaying significant efficacy with daily and every-other-day administrations, but not with once-weekly dosing. Additionally, it significantly combats the gefitinib-resistant, ErbB2-overexpressing breast cancer cell line KPL-4, affirming its potent antitumor effects.
Kinase Assay	Recombinant intracellular kinase domains of EGFR, EGFRL858R, EGFRT790M, EGFRL858R/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 MnCl2, 10 mM Mg acetate, 0.1 mg/mL poly(Glu, Tyr) 4:1, [γ33P-ATP], and 5-10 mU of enzyme, except that 250 μM of the GGMEDIYFEFMGGKKK peptide substrate is used for EGFRT790M. 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 filter mat. After rinsing to remove peptides bound non-specifically, the filter is scintillation counted.
Cell Research	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.
Animal Research	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

Animal Research	weighed. For evaluation of tumor phosphorylation, tumor-bearing mice are given a single administration of AV-412 and tumors are dissected 4 h later.

Solubility Information

Solubility	DMSO: 48 mg/mL (94.67 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 2 mg/mL (3.94 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0394 mL	0.1972 mL	0.3945 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.