AV-412

Cat. No.: HY-10346

CAS No.: 451493-31-5

Molecular Formula: $C_{41}H_{44}ClFN_6O_7S_2$

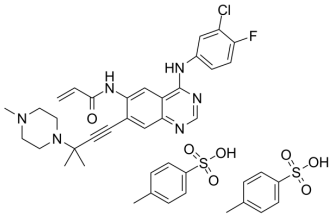
Molecular Weight: 851.41

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 28 mg/mL (32.89 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.44 mM); Clear solution

BIOLOGICAL ACTIVITY

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.

IC_{50} & Target

EGFR	$EGFR^{L858R}$	$EGFR^{T790M}$	$EGFR^{L858R/T790M}$
0.75 nM (IC_{50})	0.5 nM (IC_{50})	0.79 nM (IC_{50})	2.3 nM (IC_{50})

ErbB2
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [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 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2996-3005.

See more customer validations on www.MedChemExpress.com

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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA