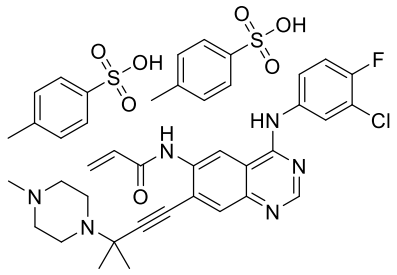
Product data sheet

MedKoo Cat#: 200944 Name: AV-412 Tosylate CAS#: 451493-31-5 (tosylate) Chemical Formula: $C_{41}H_{44}ClFN_6O_7S_2$ Molecular Weight: 850.24	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

AV-412, also known as MP-412, is a second-generation, orally bioavailable dual kinase inhibitor with potential antineoplastic activity. EGFR/HER2 inhibitor AV-412 binds to and inhibits the epidermal growth factor receptor (EGFR) and the human epidermal growth factor receptor 2 (HER2), which may result in the inhibition of tumor growth and angiogenesis, and tumor regression in EGFR/HER2-expressing tumors. This agent may be active against EGFR/HER2-expressing tumor cells that are resistant to first-generation kinase inhibitors. EGFR and HER2 are receptor tyrosine kinases that play major roles in tumor cell proliferation and tumor vascularization.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	21.5	25.29
DMSO:PBS (pH 7.2) (1:3)	0.25	0.29
DMF	15.0	17.64
Ethanol	0.25	0.29

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.18 mL	5.88 mL	11.76 mL
5 mM	0.24 mL	1.18 mL	2.35 mL
10 mM	0.12 mL	0.59 mL	1.18 mL
50 mM	0.02 mL	0.12 mL	0.24 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Suzuki T, Fujii A, Ochi H, Nakamura H. Ubiquitination and downregulation of ErbB2 and estrogen receptor-alpha by kinase inhibitor MP-412 in human breast cancer cells. J Cell Biochem. 2011 Sep;112(9):2279-86. doi: 10.1002/jcb.23147. PMID: 21503962.
2. Suzuki T, Fujii A, Ohya J, Nakamura H, Fujita F, Koike M, Fujita M. Antitumor activity of a dual epidermal growth factor receptor and ErbB2 kinase inhibitor MP-412 (AV-412) in mouse xenograft models. Cancer Sci. 2009 Aug;100(8):1526-31. doi: 10.1111/j.1349-7006.2009.01197.x. Epub 2009 May 13. PMID: 19459856.

In vivo study

1. Suzuki T, Fujii A, Ohya J, Nakamura H, Fujita F, Koike M, Fujita M. Antitumor activity of a dual epidermal growth factor receptor and ErbB2 kinase inhibitor MP-412 (AV-412) in mouse xenograft models. Cancer Sci. 2009 Aug;100(8):1526-31. doi: 10.1111/j.1349-7006.2009.01197.x. Epub 2009 May 13. PMID: 19459856.

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2. Suzuki T, Fujii A, Ohya J, Amano Y, Kitano Y, Abe D, Nakamura H. Pharmacological characterization of MP-412 (AV-412), a dual epidermal growth factor receptor and ErbB2 tyrosine kinase inhibitor. Cancer Sci. 2007 Dec;98(12):1977-84. doi: 10.1111/j.1349-7006.2007.00613.x. Epub 2007 Sep 18. PMID: 17888033.

7. Bioactivity

Biological target:

AV-412 (MP412) is an EGFR inhibitor with IC50s of 0.75, 0.5, 0.79, 2.3, 19 nM for EGFR, EGFRL858R, EGFRT790M, EGFRL858R/T790M and ErbB2, respectively.

In vitro activity

This study examined first the ability of MP-412 to inhibit phosphorylation signaling of ErbB2 in human breast cancer cell line T-47D. In western blotting, MP-412 showed complete inhibition of ErbB2 autophosphorylation as well as the consequent activation of Akt and Erk at 1 μM for only 1 h while both DMAG and PS-341 did not affect ErbB2 phosphorylation within this short period of time (Fig. 1A). This study also observed the ubiquitination and downregulation of ErbB2 by MP-412 in another cell line MCF7 (data not shown). These results indicated that MP-412 has the ability to induce ubiquitination and downregulation of ErbB2 at concentrations relatively higher than those required for kinase inhibition.

Reference: J Cell Biochem. 2011 Sep;112(9):2279-86. https://onlinelibrary-wiley-com.libproxy.lib.unc.edu/doi/10.1002/jcb.23147

In vivo activity

This study next examined the antitumor effects of four TKI (MP-412, lapatinib, erlotinib, and gefitinib) in H1650 and H1975 xenografts in nude mice. Similar to the results of the in vitro assays, MP-412 completely inhibited the tumor growth of both H1650 and H1975 xenografts (Fig. 2). In contrast, lapatinib, erlotinib, and gefitinib showed no effects on H1975 xenografts, even at their MTD, despite the fact that they significantly inhibited the tumor growth of H1650 xenografts (Fig. 2). These results indicate that MP-412 is a potent inhibitor of tumor growth in lung cancer models with T790M mutation resistant to erlotinib, gefitinib, and lapatinib.

Reference: Cancer Sci. 2009 Aug;100(8):1526-31. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1349-7006.2009.01197.x