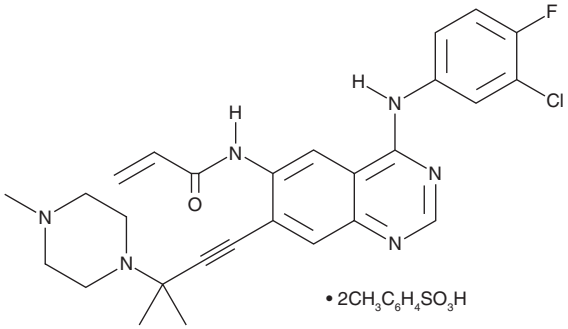
PRODUCT INFORMATION

AV-412

Item No. 29039

CAS Registry No.: 451493-31-5
Formal Name: N-[4-[(3-chloro-4-fluorophenyl) amino]-7-[3-methyl-3-(4-methyl-1-piperazinyl)-1-butyn-1-yl]-6-quinazolinyl]-2-propenamide, 4-methylbenzenesulfonate (1:2)
Synonym: MP-412
MF: $C_{27}H_{28}ClFN_6O \bullet 2C_7H_8O_3S$
FW: 851.4
Purity: ≥98%
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

AV-412 is supplied as a solid. A stock solution may be made by dissolving the AV-412 in the solvent of choice, which should be purged with an inert gas. AV-412 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of AV-412 in ethanol is approximately 0.25 mg/ml and approximately 15 mg/ml in DMSO and DMF.

AV-412 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AV-412 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AV-412 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

AV-412 is a dual inhibitor of EGFR and HER2 (IC_{50}s = 1.4, 0.51, 0.79, 2.3, and 19 nM for the EGFR, $EGFR^{L858R}$, $EGFR^{T790M}$, $EGFR^{L858R,T790M}$, and HER2 recombinant intracellular kinase domains, respectively).[1] It is selective for EGFR and HER2 over IRK, MEK1, PKA, and PKC (IC_{50}s = >10 µM) but also inhibits Abl, FLT1, and Src (IC_{50}s = 41, 920, and 2,000 nM, respectively). AV-412 (10 and 30 µM) induces ubiquitination and degradation of HER2 in SK-BR-3 cells.[2] It decreases levels of HER2 and estrogen receptor α (ERα) and increases levels of Hsp70 in MCF-7 cells when used at a concentration of 10 µM. AV-412 inhibits EGF-stimulated growth of A431 cells (IC_{50} = 0.1 µM).[1] It reduces tumor growth in an A431 mouse xenograft model when administered at doses of 10 and 30 mg/kg and in a BT-474 mouse xenograft model at 30 mg/kg.

References

1. Suzuki, T., Fujii, A., Ohya, J., *et al.* Pharmacological characterization of MP-412 (AV-412), a dual epidermal growth factor receptor and ErbB2 tyrosine kinase inhibitor. *Cancer Sci.* **98(12)**, 1977-1984 (2007).
2. Suzuki, T., Fujii, A., Ochi, H., *et al.* Ubiquitination and downregulation of ErbB2 and estrogen receptor-alpha by kinase inhibitor MP-412 in human breast cancer cells. *J. Cell. Biochem.* **112(9)**, 2279-2286 (2011).

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