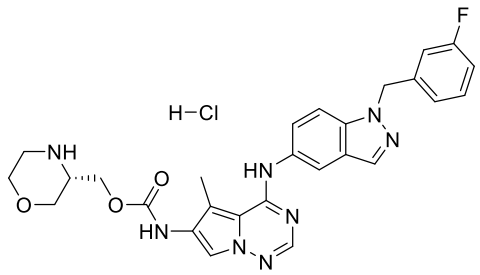
Product data sheet

MedKoo Cat#: 200078 Name: AC480 HCl CAS#: 873837-23-1 (HCl) Chemical Formula: $C_{27}H_{28}ClFN_8O_3$ Exact Mass: 566.2 Molecular Weight: 567.02	
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:

AC480, also known as BMS-599626, is an orally bioavailable inhibitor of the HER1, HER2 and HER4 tyrosine kinases (IC50 =22, 32 and 190 nM, respectively) with potential antineoplastic activity. BMS-599626 inhibits human epidermal growth factor receptors (HER) HER1, HER2 and HER4, thereby inhibiting the proliferation of tumor cells that overexpress these receptors.

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	100.0	176.36

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.76 mL	8.82 mL	17.64 mL
5 mM	0.35 mL	1.76 mL	3.53 mL
10 mM	0.18 mL	0.88 mL	1.76 mL
50 mM	0.04 mL	0.18 mL	0.35 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. Torres MA, Raju U, Molkentine D, Riesterer O, Milas L, Ang KK. AC480, formerly BMS-599626, a pan Her inhibitor, enhances radiosensitivity and radioresponse of head and neck squamous cell carcinoma cells in vitro and in vivo. Invest New Drugs. 2011 Aug;29(4):554-61. doi: 10.1007/s10637-010-9389-3. Epub 2010 Feb 2. PMID: 20119866.

In vivo study

1. Becker MA, Farzan T, Harrington SC, Krempski JW, Weroha SJ, Hou X, Kalli KR, Wong TW, Haluska P. Dual HER/VEGF receptor targeting inhibits in vivo ovarian cancer tumor growth. Mol Cancer Ther. 2013 Dec;12(12):2909-16. doi: 10.1158/1535-7163.MCT-13-0547. Epub 2013 Oct 15. PMID: 24130056; PMCID: PMC3880137.
2. Kedrin D, Wyckoff J, Boimel PJ, Coniglio SJ, Hynes NE, Arteaga CL, Segall JE. ERBB1 and ERBB2 have distinct functions in tumor cell invasion and intravasation. Clin Cancer Res. 2009 Jun 1;15(11):3733-9. doi: 10.1158/1078-0432.CCR-08-2163. Epub 2009 May 19. PMID: 19458057; PMCID: PMC2859965.

7. Bioactivity

Biological target:

BMS-599626 Hydrochloride (AC480 Hydrochloride) is a HER1 and HER2 inhibitor, with IC50s of 20 and 30 nM, respectively.

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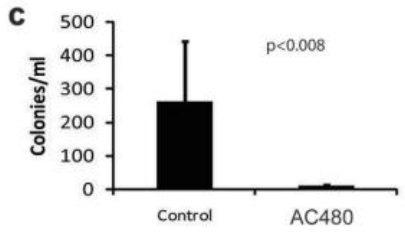
In vitro activity

Treatment with AC480 inhibited EGFR and HER2 receptor phosphorylation and downstream signaling in HN-5 cells. By immunoprecipitation analysis, the agent markedly reduced the phosphorylation of EGFR and HER2 and heterodimerization of the two receptors (Fig. 1). By western blot analysis, AC480 downregulated the expression of pEGFR (y845) (Fig. 1) but had no appreciable effect on the expression of pEGFR (y1173) or pEGFR (y992) or on the expression of pHER2 (y1248) or pHER2 (y877) (data not shown). The radiation-induced phosphorylation of MAPK, a downstream effector molecule within the EGFR pathway, was greatly reduced by AC480 (Fig. 1).

Reference: Invest New Drugs. 2011 Aug;29(4):554-61. https://pubmed.ncbi.nlm.nih.gov/20119866/

In vivo activity

Treatment with AC480 reduced EGF-induced in vivo invasion to background levels (Fig. 2A). To test the ability of AC480 to block intravasation, blood from the right atria of mice carrying MTLn3E or MDA-MB-231 xenograft tumors was collected and numbers of tumor cells per milliliter were scored. This study found that AC480 treatment resulted in a greater than 80% decrease in the number of intravasated MTLn3E (Fig. 2B) or MDA-MB-231 (Fig. 2C) cells. Cells exposed to AC480 for 3 hours showed similar survival post-treatment to DMSO controls (Fig. 2D), demonstrating that the effect of AC480 on intravasation was not due to altered cell survival. In order to confirm that the observed effects of AC480 treatment are caused by ERBB inhibition and not by off-target effects, this study treated tumor bearing animals with a different ERBB1 and ERBB2 inhibitor, lapatinib (GW572016). Lapatinib treatment also significantly reduced intravasation of tumor cells (Fig. 2B), indicating that the inhibition of intravasation reflects inhibition of ERBB signaling.



Reference: Clin Cancer Res. 2009 Jun 1; 15(11): 3733–3739. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2859965/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.