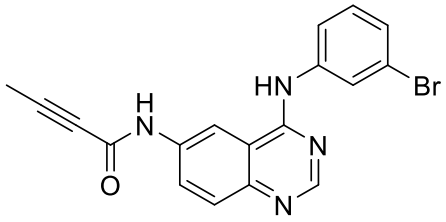
Product data sheet

MedKoo Cat#: 406106 Name: CL-387785 CAS#: 194423-06-8 Chemical Formula: $C_{18}H_{13}BrN_4O$ Exact Mass: 380.02727 Molecular Weight: 381.23	
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:

CL-387785, also known as EKI-785 , is a n irreversible inhibitor of EGF-receptor (EGFR) kinase activity in vivo (IC50 = 250-490 pM). CL-387785 covalently bound to EGF-R. It also specifically inhibited kinase activity of the protein (IC50 = 370+/-120 pM), blocked EGF-stimulated autophosphorylation of the receptor in cells (ic50 approximately 5 nM), inhibited cell proliferation (IC50 = 31-125 nM) primarily in a cytostatic manner in cell lines that overexpress EGF-R or c-erbB-2, and profoundly blocked the growth of a tumor that overexpresses EGF-R in nude mice (when given orally at 80 mg/kg/day for 10 days, daily). CL-387,785 is useful for studying the interaction of small molecules with EGF-R and may have clinical utility.

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	13.67	35.86

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.62 mL	13.12 mL	26.23 mL
5 mM	0.52 mL	2.62 mL	5.25 mL
10 mM	0.26 mL	1.31 mL	2.62 mL
50 mM	0.05 mL	0.26 mL	0.52 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. Shimamura T, Li D, Ji H, Haringsma HJ, Liniker E, Borgman CL, Lowell AM, Minami Y, McNamara K, Perera SA, Zaghlul S, Thomas RK, Greulich H, Kobayashi S, Chirieac LR, Padera RF, Kubo S, Takahashi M, Tenen DG, Meyerson M, Wong KK, Shapiro GI. Hsp90 inhibition suppresses mutant EGFR-T790M signaling and overcomes kinase inhibitor resistance. Cancer Res. 2008 Jul 15;68(14):5827-38. doi: 10.1158/0008-5472.CAN-07-5428. PMID: 18632637; PMCID: PMC3272303.

2. Zannetti A, Iommelli F, Speranza A, Salvatore M, Del Vecchio S. 3'-deoxy-3'-18F-fluorothymidine PET/CT to guide therapy with epidermal growth factor receptor antagonists and Bcl-xL inhibitors in non-small cell lung cancer. J Nucl Med. 2012 Mar;53(3):443-50. doi: 10.2967/jnumed.111.096503. Epub 2012 Feb 13. PMID: 22331221.

In vivo study

1. Sweeney WE, Chen Y, Nakanishi K, Frost P, Avner ED. Treatment of polycystic kidney disease with a novel tyrosine kinase inhibitor. Kidney Int. 2000 Jan;57(1):33-40. doi: 10.1046/j.1523-1755.2000.00829.x. PMID: 10620185.

2. Zannetti A, Iommelli F, Speranza A, Salvatore M, Del Vecchio S. 3'-deoxy-3'-18F-fluorothymidine PET/CT to guide therapy with epidermal growth factor receptor antagonists and Bcl-xL inhibitors in non-small cell lung cancer. J Nucl Med. 2012 Mar;53(3):443-50. doi: 10.2967/jnumed.111.096503. Epub 2012 Feb 13. PMID: 22331221.

7. Bioactivity

Biological target:

CL-387785 (EKI-785, WAY-EKI 785) is an irreversible, and selective EGFR inhibitor with IC50 of 370 pM.

In vitro activity

It is shown that higher concentrations of the irreversible EGFR inhibitor CL-387,785 are required to inhibit EGFR phosphorylation in T790M-expressing cells compared with EGFR mutant NSCLC cells without T790M. Additionally, CL-387,785 does not fully suppress phosphorylation of other activated receptor tyrosine kinases (RTK) in T790M-expressing cells. These deficiencies result in residual Akt and mammalian target of rapamycin (mTOR) activities. Full suppression of EGFR-mediated signaling in T790M-expressing cells requires the combination of CL-387,785 and rapamycin. In contrast, Hsp90 inhibition overcomes these limitations in vitro and depletes cells of EGFR, other RTKs, and phospho-Akt and inhibits mTOR signaling whether or not T790M is present. EGFR-T790M-expressing cells rendered resistant to CL-387,785 by a kinase switch mechanism retain sensitivity to Hsp90 inhibition. Finally, Hsp90 inhibition causes regression in murine lung adenocarcinomas driven by mutant EGFR (L858R) with or without T790M. However, efficacy in the L858R-T790M model requires a more intense treatment schedule and responses were transient.

Reference: Cancer Res. 2008 Jul 15;68(14):5827-38. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18632637/

In vivo activity

Treatment of BPK mice with EKI-785 resulted in a marked reduction of collecting tubule (CT) cystic lesions, improved renal function, decreased biliary epithelial abnormalities, and an increased life span. Untreated cystic animals died of renal failure at postnatal day 24 (P-24) with a CT cystic index of 4.8, a maximal urine osmolarity of 361 mOsm, and moderate to severe biliary abnormalities. Cystic animals treated with EKI-785 to postnatal day 48 (P-48) were alive and well with normal renal function, a reduced CT cystic index of 2.0 ($P < 0.02$), a threefold increased in maximum urinary concentrating ability ($P < 0.01$), and a significant decrease in biliary epithelial proliferation/fibrosis ($P < 0.01$).

Reference: Kidney Int. 2000 Jan;57(1):33-40. https://linkinghub.elsevier.com/retrieve/pii/S0085-2538(15)46703-1

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.