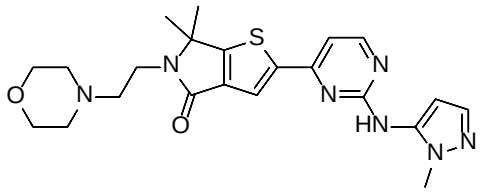
Product data sheet

MedKoo Cat#: 206821 Name: LY-3214996 CAS#: 1951483-29-6 Chemical Formula: $C_{22}H_{27}N_7O_2S$ Exact Mass: 453.1947 Molecular Weight: 453.57	
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:
LY-3214996 is a otent and selective, orally available inhibitor of extracellular signal-regulated kinase (ERK) 1 and 2, with potential antineoplastic activity. Upon oral administration, LY3214996 inhibits both ERK 1 and 2, thereby preventing the activation of mitogen-activated protein kinase (MAPK)/ERK-mediated signal transduction pathways. This results in the inhibition of ERK-dependent tumor cell proliferation and survival.

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	23.50	51.81
Ethanol	16.0	35.28

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.20 mL	11.02 mL	22.05 mL
5 mM	0.44 mL	2.20 mL	4.41 mL
10 mM	0.22 mL	1.10 mL	2.20 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Bhagwat SV, McMillen WT, Cai S, Zhao B, Whitesell M, Shen W, Kindler L, Flack RS, Wu W, Anderson B, Zhai Y, Yuan XJ, Pogue M, Van Horn RD, Rao X, McCann D, Dropsey AJ, Manro J, Walgren J, Yuen E, Rodriguez MJ, Plowman GD, Tiu RV, Joseph S, Peng SB. ERK Inhibitor LY3214996 Targets ERK Pathway-Driven Cancers: A Therapeutic Approach Toward Precision Medicine. Mol Cancer Ther. 2020 Feb;19(2):325-336. doi: 10.1158/1535-7163.MCT-19-0183. Epub 2019 Nov 19. PMID: 31744895.

In vivo study

1. Bhagwat SV, McMillen WT, Cai S, Zhao B, Whitesell M, Shen W, Kindler L, Flack RS, Wu W, Anderson B, Zhai Y, Yuan XJ, Pogue M, Van Horn RD, Rao X, McCann D, Dropsey AJ, Manro J, Walgren J, Yuen E, Rodriguez MJ, Plowman GD, Tiu RV, Joseph S, Peng SB. ERK Inhibitor LY3214996 Targets ERK Pathway-Driven Cancers: A Therapeutic Approach Toward Precision Medicine. Mol Cancer Ther. 2020 Feb;19(2):325-336. doi: 10.1158/1535-7163.MCT-19-0183. Epub 2019 Nov 19. PMID: 31744895.

7. Bioactivity
Biological target: LY3214996 is an inhibitor of ERK1 and ERK2 with IC50s of 5 nM for both enzymes in biochemical assays.

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In vitro activity

To determine the effect of LY3214996 on cell-cycle regulation, KRAS-mutant HCT116 cells were treated with increasing concentrations of LY3214996 for 24, 48, and 72 hours and subjected to cell-cycle analysis by flow cytometry. LY3214996 arrested cells in the G1 phase of the cell cycle and induced apoptosis in a dose- and time-dependent manner as demonstrated by an increasing percentage of cells in the sub-G1 phase at 24, 48, and 72 hours after treatment (Fig. 2A and B; Supplementary Fig. S1).

Reference: Mol Cancer Ther. 2020 Feb;19(2):325-336. https://mct.aacrjournals.org/content/19/2/325.long

In vivo activity

The in vivo efficacy of LY3214996 was assessed in subcutaneous xenograft models derived from several colorectal cancer (KRAS-mutant HCT116, BRAF-mutant Colo205, and MEK1-mutant SW48), melanoma (NRAS-mutant SK-MEL-30), pancreatic cancer (KRAS-mutant MiaPaCa-2), and NSCLC (KRAS-mutant Calu6) models as representative examples of RAS/ERK pathway alterations. LY3214996 treatment resulted in significant tumor regression of HCT116 (31%), Colo205 (76%), MiaPaCa-2 (66%), and Calu-6 (54%) xenograft tumors in mice (Fig. 5A, B, E, and F; Supplementary Table S3).

Reference: Mol Cancer Ther. 2020 Feb;19(2):325-336. https://mct.aacrjournals.org/content/19/2/325.long