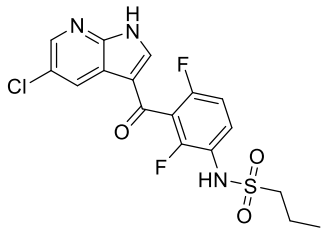
Product data sheet

MedKoo Cat#: 202272 Name: PLX4720 CAS#: 918505-84-7 Chemical Formula: $C_{17}H_{14}ClF_2N_3O_3S$ Exact Mass: 413.04125 Molecular Weight: 413.82	
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:
PLX4720 is a 7-azaindole derivative that inhibits B-Raf(V600E) with an IC(50) of 13 nM, defines a class of kinase inhibitor with marked selectivity in both biochemical and cellular assays. PLX4720 preferentially inhibits the active B-Raf(V600E) kinase compared with a broad spectrum of other kinases, and potent cytotoxic effects are also exclusive to cells bearing the V600E allele.

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	30.0	72.5

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.29 mL	11.44 mL	22.89 mL
5 mM	0.46 mL	2.29 mL	4.58 mL
10 mM	0.23 mL	1.14 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Tsai J, Lee JT, Wang W, Zhang J, Cho H, Mamo S, Bremer R, Gillette S, Kong J, Haass NK, Sproesser K, Li L, Smalley KS, Fong D, Zhu YL, Marimuthu A, Nguyen H, Lam B, Liu J, Cheung I, Rice J, Suzuki Y, Luu C, Settachatgul C, Shellooe R, Cantwell J, Kim SH, Schlessinger J, Zhang KY, West BL, Powell B, Habets G, Zhang C, Ibrahim PN, Hirth P, Artis DR, Herlyn M, Bollag G. Discovery of a selective inhibitor of oncogenic B-Raf kinase with potent antimelanoma activity. Proc Natl Acad Sci U S A. 2008 Feb 26;105(8):3041-6. doi: 10.1073/pnas.0711741105. Epub 2008 Feb 19. PMID: 18287029; PMCID: PMC2268581.

2. Paraiso KH, Xiang Y, Rebecca VW, Abel EV, Chen YA, Munko AC, Wood E, Fedorenko IV, Sondak VK, Anderson AR, Ribas A, Palma MD, Nathanson KL, Koomen JM, Messina JL, Smalley KS. PTEN loss confers BRAF inhibitor resistance to melanoma cells through the suppression of BIM expression. Cancer Res. 2011 Apr 1;71(7):2750-60. doi: 10.1158/0008-5472.CAN-10-2954. Epub 2011 Feb 11. PMID: 21317224; PMCID: PMC3070772.

In vivo study

1. Tsai J, Lee JT, Wang W, Zhang J, Cho H, Mamo S, Bremer R, Gillette S, Kong J, Haass NK, Sproesser K, Li L, Smalley KS, Fong D, Zhu YL, Marimuthu A, Nguyen H, Lam B, Liu J, Cheung I, Rice J, Suzuki Y, Luu C, Settachatgul C, Shellooe R, Cantwell J, Kim SH, Schlessinger J, Zhang KY, West BL, Powell B, Habets G, Zhang C, Ibrahim PN, Hirth P, Artis DR, Herlyn M, Bollag G.

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Discovery of a selective inhibitor of oncogenic B-Raf kinase with potent antimelanoma activity. Proc Natl Acad Sci U S A. 2008 Feb 26;105(8):3041-6. doi: 10.1073/pnas.0711741105. Epub 2008 Feb 19. PMID: 18287029; PMCID: PMC2268581.

2. Nucera C, Porrello A, Antonello ZA, Mekel M, Nehs MA, Giordano TJ, Gerald D, Benjamin LE, Priolo C, Puxeddu E, Finn S, Jarzab B, Hodin RA, Pontecorvi A, Nose V, Lawler J, Parangi S. B-Raf(V600E) and thrombospondin-1 promote thyroid cancer progression. Proc Natl Acad Sci U S A. 2010 Jun 8;107(23):10649-54. doi: 10.1073/pnas.1004934107. Epub 2010 May 24. PMID: 20498063; PMCID: PMC2890809.

7. Bioactivity

Biological target:

PLX-4720 is a potent and selective inhibitor of B-RafV600E with IC50 of 13 nM in a cell-free assay, equally potent to c-Raf-1(Y340D and Y341D mutations), and 10-fold selectivity for B-RafV600E than wild-type B-Raf.

In vitro activity

PLX-4720 displays >10 times selectivity against wild type B-Raf, and >100 times selectivity over other kinases such as Frk, Src, Fak, FGFR, and Aurora A with IC50 of 1.3-3.4 μM. PLX-4720 significantly inhibits the ERK phosphorylation in cell lines bearing B-RafV600E with IC50 of 14-46 nM, but not the cells with wild-type B-Raf. PLX-4720 significantly inhibits the growth of tumor cell lines bearing the B-RafV600E oncogene, such as COLO205, A375, WM2664, and COLO829 with GI50 of 0.31 μM, 0.50 μM, 1.5 μM, and 1.7 μM, respectively. In addition, PLX-4720 treatment at 1 μM induces cell cycle arrest and apoptosis exclusively in the B-RafV600E-positive 1205Lu cells, but not in the B-Raf wild-type C8161 cells.

Reference: Proc Natl Acad Sci U S A. 2008 Feb 26;105(8):3041-6. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18287029/

In vivo activity

Oral administration of PLX-4720 at 20 mg/kg/day induces significant tumor growth delays and regressions in B-RafV600E-dependent COLO205 tumor xenografts, without obvious adverse effects in mice even at dose of 1 g/kg. PLX-4720 at 100 mg/kg twice daily almost completely eliminates the 1205Lu xenografts bearing B-RafV600E, while has no activity against C8161 xenografts bearing wild-type B-Raf. The anti-tumor effects of PLX-4720 correlate with the blockade of MAPK pathway in those cells harboring the V600E mutation.

Reference: Proc Natl Acad Sci U S A. 2008 Feb 26;105(8):3041-6. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18287029/

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.