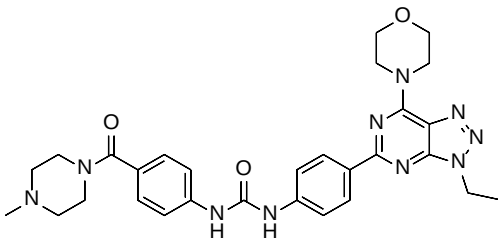
Product data sheet

MedKoo Cat#: 406324 Name: PKI-402 CAS: 1173204-81-3 Chemical Formula: $C_{29}H_{34}N_{10}O_3$ Exact Mass: 570.2815 Molecular Weight: 570.658	
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:
PKI-402 is a selective, reversible, ATP-competitive, equipotent inhibitor of class I phosphatidylinositol 3-kinases (PI3K), including PI3K-alpha mutants, and mammalian target of rapamycin (mTOR; IC(50) versus PI3K-alpha = 2 nmol/L). PKI-402 inhibited growth of human tumor cell lines derived from breast, brain (glioma), pancreas, and non-small cell lung cancer tissue and suppressed phosphorylation of PI3K and mTOR effector proteins (e.g., Akt at T308) at concentrations that matched those that inhibited cell growth.

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	2.75	4.82

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.75 mL	8.76 mL	17.52 mL
5 mM	0.35 mL	1.75 mL	3.50 mL
10 mM	0.18 mL	0.88 mL	1.75 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. Hu X, Xia M, Wang J, Yu H, Chai J, Zhang Z, Sun Y, Su J, Sun L. Dual PI3K/mTOR inhibitor PKI-402 suppresses the growth of ovarian cancer cells by degradation of Mcl-1 through autophagy. Biomed Pharmacother. 2020 Sep;129:110397. doi: 10.1016/j.biopha.2020.110397. Epub 2020 Jun 22. PMID: 32585451.
2. Yuan G, Lian Z, Liu Q, Lin X, Xie D, Song F, Wang X, Shao S, Zhou B, Li C, Li M, Yao G. Phosphatidyl inositol 3-kinase (PI3K)-mTOR inhibitor PKI-402 inhibits breast cancer induced osteolysis. Cancer Lett. 2019 Feb 28;443:135-144. doi: 10.1016/j.canlet.2018.11.038. Epub 2018 Dec 9. PMID: 30540926.

In vivo study

1. Mallon R, Hollander I, Feldberg L, Lucas J, Soloveva V, Venkatesan A, Dehnhardt C, Delos Santos E, Chen Z, Dos Santos O, Ayral-Kaloustian S, Gibbons J. Antitumor efficacy profile of PKI-402, a dual phosphatidylinositol 3-kinase/mammalian target of rapamycin inhibitor. Mol Cancer Ther. 2010 Apr;9(4):976-84. doi: 10.1158/1535-7163.MCT-09-0954. Epub 2010 Apr 6. PMID: 20371716.
2. Dehnhardt CM, Venkatesan AM, Delos Santos E, Chen Z, Santos O, Ayral-Kaloustian S, Brooijmans N, Mallon R, Hollander I, Feldberg L, Lucas J, Chaudhary I, Yu K, Gibbons J, Abraham R, Mansour TS. Lead optimization of N-3-substituted 7-

morpholinotriazolopyrimidines as dual phosphoinositide 3-kinase/mammalian target of rapamycin inhibitors: discovery of PKI-402. J Med Chem. 2010 Jan 28;53(2):798-810. doi: 10.1021/jm9014982. PMID: 19968288.

7. Bioactivity

Biological target:

PKI-402 is a selective, reversible, ATP-competitive inhibitor of PI3K, including PI3K-α mutants, and mTOR (IC50=2, 3, 7,14 and 16 nM for PI3Kα, mTOR, PI3Kβ, PI3Kδ and PI3Kγ).

In vitro activity

To investigate whether the mitochondrial apoptotic pathway is one of the apoptotic pathways induced by PI3K/AKT/mTOR pathway inhibitors, SKOV3 cells were treated with Rapamycin, BYL-719, or PKI-402 for 24 h. Then, this study detected the expressions of apoptosis-related proteins and found that cleaved caspase-3 and cleaved caspase-9 were increased, while the expression of anti-apoptotic protein Bcl-2 was decreased and that of pro-apoptotic protein Bax was increased, the ratio of Bax/Bcl-2 was increased significantly after treatment with the dual PI3K/mTOR inhibitor PKI-402 (Fig. 4A). It was worth noting that the expressions of anti-apoptotic protein Mcl-1 were decreased gradually over time when SKVO3 and A2780 cells were treated with the dual PI3K/mTOR inhibitor PKI-402 (Fig. 4B, and Fig S3B). After separation of intracellular organelles, this study found that the expression of Mcl-1 in mitochondria was decreased significantly (Fig. 4C).

Reference: Biomed Pharmacother. 2020 Sep;129:110397. https://pubmed.ncbi.nlm.nih.gov/32585451/

In vivo activity

PKI-402 is a selective, reversible, ATP-competitive, equipotent inhibitor of class I phosphatidylinositol 3-kinases (PI3K), including PI3K-alpha mutants, and mammalian target of rapamycin (mTOR; IC(50) versus PI3K-alpha = 2 nmol/L). In vivo, PKI-402 inhibited tumor growth in MDA-MB-361, glioma (U87MG), and lung (A549) mouse xenograft models. In MDA-MB-361, PKI-402 at 100 mg/kg (daily for 5 days, one round) reduced initial tumor volume of 260 mm(3) to 129 mm(3) and prevented tumor regrowth for 70 days. In MDA-MB-361 tumors, PKI-402 (100 mg/kg, single dose) suppressed Akt phosphorylation (at T308) and induced cleaved PARP. Suppression of phosphorylated Akt (p-Akt) was complete at 8 hours and still evident at 24 hours.

Reference: Mol Cancer Ther. 2010 Apr;9(4):976-84. https://pubmed.ncbi.nlm.nih.gov/20371716/

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.