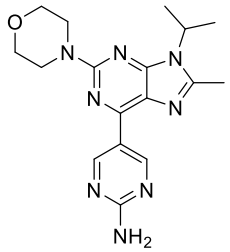
Product data sheet

MedKoo Cat#: 206109 Name: VS-5584 CAS#: 1246560-33-7 Chemical Formula: $C_{17}H_{22}N_8O$ Exact Mass: 354.19166 Molecular Weight: 354.41	
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:

VS-5584, also known as SB2343, is a potent and selective inhibitor of both phosphatidylinositol 3 kinase (PI3K) and mammalian target of rapamycin (mTOR) kinase in the PI3K/mTOR signaling pathway, with potential antineoplastic activity. PI3K/mTOR kinase inhibitor VS-5584 inhibits mTOR kinase and all class I PI3K isoforms. Consequently, this disrupts phosphorylation of substrates downstream of PI3K and mTOR and may result in apoptosis and growth inhibition in susceptible tumor cells. Activation of the PI3K/mTOR pathway promotes cell growth, survival, and resistance to chemotherapy and radiotherapy.

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	39.78	112.24
DMF	10.0	28.21
DMF:PBS (pH 7.2) (1:1)	0.5	1.41
Ethanol	3.0	8.46

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.82 mL	14.11 mL	28.22 mL
5 mM	0.56 mL	2.82 mL	5.64 mL
10 mM	0.28 mL	1.41 mL	2.82 mL
50 mM	0.06 mL	0.28 mL	0.56 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. Mustafa N, Ting Lee JX, Adina Nee HF, Bi C, Chung TH, Hart S, Chng WJ. VS-5584 mediates potent anti-myeloma activity via the upregulation of a class II tumor suppressor gene, RARRES3 and the activation of Bim. Oncotarget. 2017 Oct 20;8(60):101847-101864. doi: 10.18632/oncotarget.21988. PMID: 29254208; PMCID: PMC5731918.
2. Shao Z, Bao Q, Jiang F, Qian H, Fang Q, Hu X. VS-5584, a Novel PI3K-mTOR Dual Inhibitor, Inhibits Melanoma Cell Growth In Vitro and In Vivo. PLoS One. 2015 Jul 23;10(7):e0132655. doi: 10.1371/journal.pone.0132655. PMID: 26204252; PMCID: PMC4512677.

In vivo study

Product data sheet

1. Ning C, Liang M, Liu S, Wang G, Edwards H, Xia Y, Polin L, Dyson G, Taub JW, Mohammad RM, Azmi AS, Zhao L, Ge Y. Targeting ERK enhances the cytotoxic effect of the novel PI3K and mTOR dual inhibitor VS-5584 in preclinical models of pancreatic cancer. Oncotarget. 2017 Jul 4;8(27):44295-44311. doi: 10.18632/oncotarget.17869. PMID: 28574828; PMCID: PMC5546481.
2. Kolev VN, Wright QG, Vidal CM, Ring JE, Shapiro IM, Ricono J, Weaver DT, Padval MV, Pachter JA, Xu Q. PI3K/mTOR dual inhibitor VS-5584 preferentially targets cancer stem cells. Cancer Res. 2015 Jan 15;75(2):446-55. doi: 10.1158/0008-5472.CAN-14-1223. Epub 2014 Nov 28. PMID: 25432176.

7. Bioactivity

Biological target:

VS-5584 is a pan-PI3K/mTOR kinase inhibitor with IC50s of 16 nM, 68 nM, 42 nM, 25 nM, and 37 nM for PI3Kα, PI3Kβ, PI3Kδ, PI3Kγ and mTOR, respectively.

In vitro activity

Western blot analysis confirms the dual inhibitory activity of VS-5584. It showed that the protein levels of the substrates of (1) the PI3K pathway- phospho-Akt (Thr308) and phospho-GSKβ as well as substrate of (2) the mTORC2 pathway phospho-Akt (Ser473) and (3) mTOR/AKT substrate, phospho-S6 have been attenuated by VS-5584 treatment. Expression levels of phosphorylated Akt (Ser473) were completely abolished in H929 (hypersensitive) and reduced in OPM2 (less sensitive) (Figure (Figure1A).1A). Phospho-Akt(Thr308), phospho-GSKβ and Phospho-S6 ribosomal protein expression levels were similarly downregulated, albeit requiring a higher concentration of VS-5584. Additionally this study observes no significant change in the levels of phospho-p44/42-MAPK, thus verifying the specific targeting of VS-5584 on the PI3K/mTOR/Akt signaling pathway.

Reference: Oncotarget. 2017 Nov 24; 8(60): 101847–101864. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5731918/

In vivo activity

This study first used MDA-MB-231 triple-negative human breast cancer cells implanted orthotopically in the mouse mammary fat pad. After tumors reached a volume of approximately 200 mm^3, VS-5584 was administered orally at 25 mg/kg once daily for 9 days. Tumors were harvested and dissociated into single cells and subjected to CSC assays without further compound treatment (Fig. 3A). Results of the Aldefluor assay showed that the percentage of $Aldefluor^+$ cells was relatively low with an average of 0.7% in control tumors, VS-5584 treatment caused significant reduction of the proportion of $Aldefluor^+$ CSC to 0.2% (P = 0.015, Fig. 3B, Supplementary Fig. S5). A more rigorous and functional test for CSC is the limiting dilution assay. Accordingly, cells dissociated from either VS-5584- or vehicle-treated tumors were injected into immunodeficient mice in limiting dilutions. Cells from VS-5584–treated tumors displayed a 7-fold reduction of TIF, confirming reduction of CSC in tumors by VS-5584 treatment (Fig. 3C).

Reference: Cancer Res. 2015 Jan 15;75(2):446-55. https://cancerres.aacrjournals.org/content/75/2/446.long

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.