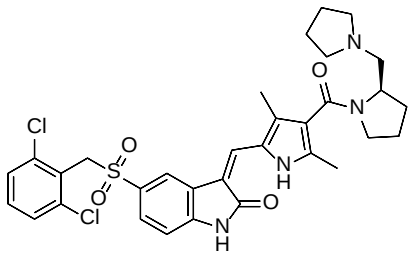
Product data sheet

MedKoo Cat#: 202231 Name: PHA-665752 CAS: 477575-56-7 Chemical Formula: $C_{32}H_{34}Cl_2N_4O_4S$ Exact Mass: 640.1678 Molecular Weight: 641.608	
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:

PHA665752 is a potent and selective inhibitor of c-Met/HGF/SF (IC50 values are 9, 68, 200, 1400, 3000, 3800 and 6000 nM for MET, Ron, Flk-1, c-abl, FGFR1, EGFR and c-src respectively). PHA-665752 suppresses the hepatocyte growth factor-induced cell proliferation and radioresistance in nasopharyngeal carcinoma cells. PHA-665752 reverses lung premalignancy induced by mutant K-ras. PHA-665752 induced apoptosis of a lung adenocarcinoma cell line derived from Kras(LA1) mice (LKR-13) and a murine lung endothelial cell line (MEC). PHA-665752 inhibited lung tumorigenesis in Kras(LA1) mice and may provide a novel therapeutic approach to the prevention of K-ras-mutant NSCLC.

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
DMF	25.0	38.96
DMF:PBS (pH 7.2) (1:1)	0.5	0.78
DMSO	56.79	88.51
Ethanol	1.0	1.56

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.56 mL	7.79 mL	15.59 mL
5 mM	0.31 mL	1.56 mL	3.12 mL
10 mM	0.16 mL	0.78 mL	1.56 mL
50 mM	0.03 mL	0.16 mL	0.31 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. Chen W, Wu S, Huang Y, Zhang T, Dong H, Zheng X, Chen T, Gong X, Liu G, Zhao X. A c-Met Inhibitor Suppresses Osteosarcoma Progression via the ERK1/2 Pathway in Human Osteosarcoma Cells. Onco Targets Ther. 2021 Sep 10;14:4791-4804. doi: 10.2147/OTT.S317122. PMID: 34531665; PMCID: PMC8440230.
2. Ma PC, Schaefer E, Christensen JG, Salgia R. A selective small molecule c-MET Inhibitor, PHA665752, cooperates with rapamycin. Clin Cancer Res. 2005 Mar 15;11(6):2312-9. doi: 10.1158/1078-0432.CCR-04-1708. PMID: 15788682.

In vivo study

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1. Puri N, Khramtsov A, Ahmed S, Nallasura V, Hetzel JT, Jagadeeswaran R, Karczmar G, Salgia R. A selective small molecule inhibitor of c-Met, PHA665752, inhibits tumorigenicity and angiogenesis in mouse lung cancer xenografts. Cancer Res. 2007 Apr 15;67(8):3529-34. doi: 10.1158/0008-5472.CAN-06-4416. PMID: 17440059.
2. Christensen JG, Schreck R, Burrows J, Kuruganti P, Chan E, Le P, Chen J, Wang X, Ruslim L, Blake R, Lipson KE, Ramphal J, Do S, Cui JJ, Cherrington JM, Mendel DB. A selective small molecule inhibitor of c-Met kinase inhibits c-Met-dependent phenotypes in vitro and exhibits cytoreductive antitumor activity in vivo. Cancer Res. 2003 Nov 1;63(21):7345-55. PMID: 14612533.

7. Bioactivity

Biological target:

PHA-665752 is a selective, ATP-competitive, and active-site inhibitor of the catalytic activity of c-Met kinase (Ki=4 nM; IC50=9 nM).

In vitro activity

The effect of PHA665752 treatment was determined on cell growth, motility and migration, apoptosis, and cell-cycle arrest of TPR-MET-transformed cells. PHA665752 specifically inhibited cell growth in BaF3. TPR-MET cells (IC(50) < 0.06 micromol/L), induced apoptosis and cell cycle arrest. Constitutive cell motility and migration of the BaF3. TPR-MET cells was also inhibited. PHA665752 inhibited specific phosphorylation of TPR-MET as well as phosphorylation of downstream targets of the mammalian target of rapamycin pathway.

Reference: Clin Cancer Res. 2005 Mar 15;11(6):2312-9. https://pubmed.ncbi.nlm.nih.gov/15788682/

In vivo activity

This study shows that treatment with PHA665752 reduced NCI-H69 (small cell lung cancer) and NCI-H441 (non-small cell lung cancer) tumorigenicity in mouse xenografts by 99% and 75%, respectively. Reduction in tumor size was also observed by magnetic resonance imaging of tumors in mice. PHA665752 inhibited c-Met phosphorylation at the autophosphorylation and c-Cbl binding sites in mouse xenografts derived from non-small cell lung cancer cell lines (NCI-H441 and A549) and small cell lung cancer cell line (NCI-H69).

Reference: Cancer Res. 2007 Apr 15;67(8):3529-34. https://pubmed.ncbi.nlm.nih.gov/17440059/

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.