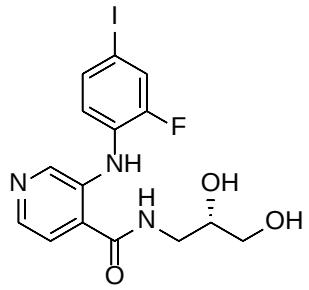
Product data sheet

MedKoo Cat#: 200297 Name: Pimasertib CAS: 1236699-92-5 (free base) Chemical Formula: $C_{15}H_{15}FIN_3O_3$ Exact Mass: 431.0142 Molecular Weight: 431.2059	
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:
Pimasertib, also known as AS703026, SAR245509, MSC1936369B, is an orally bioavailable small-molecule inhibitor of MEK1 and MEK2 (MEK1/2) with potential antineoplastic activity. MEK inhibitor AS703026 selectively binds to and inhibits the activity of MEK1/2, preventing the activation of MEK1/2-dependent effector proteins and transcription factors, which may result in the inhibition of growth factor-mediated cell signaling and tumor cell proliferation.

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	30.0	69.57
DMSO	72.0	166.97
DMSO:PBS (pH 7.2) (1:1)	0.5	1.16
Ethanol	1.0	2.32

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.32 mL	11.60 mL	23.19 mL
5 mM	0.46 mL	2.32 mL	4.64 mL
10 mM	0.23 mL	1.16 mL	2.32 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. Yoon J, Koo KH, Choi KY. MEK1/2 inhibitors AS703026 and AZD6244 may be potential therapies for KRAS mutated colorectal cancer that is resistant to EGFR monoclonal antibody therapy. Cancer Res. 2011 Jan 15;71(2):445-53. doi: 10.1158/0008-5472.CAN-10-3058. Epub 2010 Nov 30. PMID: 21118963.
2. Kim K, Kong SY, Fulciniti M, Li X, Song W, Nahar S, Burger P, Rumizen MJ, Podar K, Chauhan D, Hideshima T, Munshi NC, Richardson P, Clark A, Ogden J, Goutopoulos A, Rastelli L, Anderson KC, Tai YT. Blockade of the MEK/ERK signalling cascade by AS703026, a novel selective MEK1/2 inhibitor, induces pleiotropic anti-myeloma activity in vitro and in vivo. Br J Haematol. 2010 May;149(4):537-49. doi: 10.1111/j.1365-2141.2010.08127.x. Epub 2010 Mar 12. PMID: 20331454; PMCID: PMC3418597.

In vivo study

Product data sheet

1. Yoon J, Koo KH, Choi KY. MEK1/2 inhibitors AS703026 and AZD6244 may be potential therapies for KRAS mutated colorectal cancer that is resistant to EGFR monoclonal antibody therapy. Cancer Res. 2011 Jan 15;71(2):445-53. doi: 10.1158/0008-5472.CAN-10-3058. Epub 2010 Nov 30. PMID: 21118963.
2. Kim K, Kong SY, Fulciniti M, Li X, Song W, Nahar S, Burger P, Rumizen MJ, Podar K, Chauhan D, Hideshima T, Munshi NC, Richardson P, Clark A, Ogden J, Goutopoulos A, Rastelli L, Anderson KC, Tai YT. Blockade of the MEK/ERK signalling cascade by AS703026, a novel selective MEK1/2 inhibitor, induces pleiotropic anti-myeloma activity in vitro and in vivo. Br J Haematol. 2010 May;149(4):537-49. doi: 10.1111/j.1365-2141.2010.08127.x. Epub 2010 Mar 12. PMID: 20331454; PMCID: PMC3418597.

7. Bioactivity

Biological target:

Pimasertib (AS703026) is a highly selective, ATP non-competitive allosteric orally available MEK1/2 inhibitor.

In vitro activity

AS703026 and AZD6244 were tested in various cell-based assays and tumor xenograft studies, focusing on isogenic human colorectal tumor cell lines that expressed only WT or mutant K-Ras (D-WT or D-MUT). The EGFR mAb cetuximab inhibited the Ras-ERK pathway and proliferation of D-WT cells in vitro and in vivo, but it did not inhibit proliferation of D-MUT cells in either setting. In contrast, AS703026 and AZD6244 effectively inhibited the growth of D-MUT cells in vitro and in vivo by specific inhibition of the key MEK downstream target kinase ERK. Inhibition of MEK by AS703026 or AZD6244 also suppressed cetuximab-resistant colorectal cancer cells attributed to K-ras mutation both in vitro and in vivo.

Reference: Cancer Res. 2011 Jan 15;71(2):445-53. https://pubmed.ncbi.nlm.nih.gov/21118963/

In vivo activity

AS703026 inhibited growth and survival of MM cells and cytokine-induced osteoclast differentiation more potently (9- to 10-fold) than AZD6244. Inhibition of proliferation induced by AS703026 was mediated by G0-G1 cell cycle arrest and was accompanied by reduction of MAF oncogene expression. AS703026 further induced apoptosis via caspase 3 and Poly ADP ribose polymerase (PARP) cleavage in MM cells, both in the presence or absence of bone marrow stromal cells (BMSCs). Importantly, AS703026 sensitized MM cells to a broad spectrum of conventional (dexamethasone, melphalan), novel or emerging (lenalidomide, perifosine, bortezomib, rapamycin) anti-MM therapies. Significant tumour growth reduction in AS703026- vs. vehicle-treated mice bearing H929 MM xenograft tumours correlated with downregulated pERK1/2, induced PARP cleavage, and decreased microvessels in vivo.

Reference: Br J Haematol. 2010 May;149(4):537-49. https://pubmed.ncbi.nlm.nih.gov/20331454/

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.