Pimasertib

Cat. No.: HY-12042

CAS No.: 1236699-92-5

Molecular Formula: $C_{15}H_{15}FIN_3O_3$

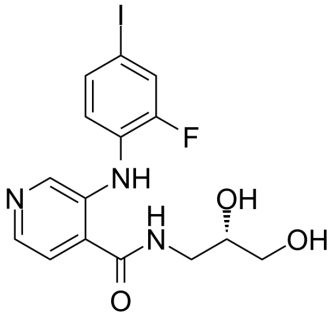
Molecular Weight: 431.2

Target: MEK

Pathway: MAPK/ERK Pathway

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (231.91 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3191 mL	11.5955 mL	23.1911 mL
5 mM	0.4638 mL	2.3191 mL	4.6382 mL
10 mM	0.2319 mL	1.1596 mL	2.3191 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pimasertib (AS703026) is a highly selective, ATP non-competitive allosteric orally available MEK1/2 inhibitor[1][2].

IC_{50} & Target

MEK1	MEK2

In Vitro

Pimasertib (5, 0.5, and 0.1 μM) specifically blocks ERK1/2 activation in MM cells, cultured alone or with BMSCs. Pimasertib inhibits the growth of MM cell lines in a dose-dependent manner, with IC_{50}s ranging from 0.005 to 2 μM. The IC_{50}s of

	Pimasertib against INA-6, U266, H929 cells are 10 nM, 5 nM, 200 nM respectively. Pimasertib induces apoptosis and modulates the cell cycle profile. Pimasertib targets MM cells in the BM microenvironment[1]. Pimasertib (10 μmol/L) inhibits ERK pathway, proliferation, and transformation in cetuximab-resistant D-MUT cells[2]. Pimasertib in combination with PLX4032 significantly induces apoptosis of RPMI-7951 cells, whereas each drug used alone does not. Pimasertib synergizes with small interfering RNA-mediated downregulation of BRAF to produce results similar to those of combined treatment with PLX4032 and Pimasertib[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pimasertib (15, 30 mg/kg) significantly inhibits the growth of tumor in the human H929 MM xenograft model in CB17 SCID mice[1]. Pimasertib (10 mg/kg, p.o.) inhibits tumor growth of cetuximab-resistant tumor attributed by K-ras mutation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The inhibitory effects of study compounds on MM cell growth and survival are assessed by both [^{3}H]thymidine incorporation and by measuring MTT dye absorbance. Cells (10^4/well for MM cell line, in triplicates and 2-5×10^5/well for patient MM cells) are cultured in 96-well plates for 3 days (MM cell lines) or 5-days (patient MM cells). For the [^{3}H]thymidine incorporation assay, cells are pulsed with 0.5 μCi (0.0185 MBq)/well [^{3}H]thymidine for 6 h (cell lines), harvested onto glass fiber filters, and counted in a β-scintillation counter. Due to low DNA synthesis of patient MM cells, they are pulsed with 2 μCi/well [^{3}H]thymidine and measured during the last 36 h of culture. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	CB17 severe combined immunodeficiency (SCID) mice are subcutaneously inoculated with H929 ($4×10^6$) cells in 100 μL RPMI-1640 medium. Mice developed palpable tumors (appr 130 mm^3) approximately 3 weeks after cell injection and are randomized to receive orally twice daily either Pimasertib (15 or 30 mg/kg) or control vehicle alone. Tumor size is measured every other day in 2 dimensions using calipers, and tumor volume is calculated. Animals are euthanized when their tumors reach 2 cm^3 in volume, when they are moribund or show paralysis or major compromise in their quality of life occurs. Tumor formation changes in mice treated with control vehicle vs. Pimasertib are plotted using the GraphPad Prism version 4.03 for Windows. Tumors are subjected to immunoblotting and immunochemistry analyses using specific monoclonal (m)Abs. Images are examined with a Leica DM LB research microscope, captured using Leica IM50 Image Manager, and processed using Adobe Photoshop Software version 7.0. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Oncogenesis. 2019 Nov 4;8(11):65.
- ACS Comb Sci. 2019 Dec 9;21(12):805-816.
- Oncotarget. 2020 Nov 3;11(44):3921-3932.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Kim K, et al. 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, 149(4), 537-549.

[2]. Yoon J, et al. 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, 71(2), 445-453.

[3]. Park SJ, et al. The MEK1/2 inhibitor AS703026 circumvents resistance to the BRAF inhibitor PLX4032 in human malignant melanoma cells. Am J Med Sci. 2013 Dec;346(6):494-8.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA