Trametinib (DMSO solvate)

Cat. No.: HY-10999A

CAS No.: 1187431-43-1

Molecular Formula: $C_{28}H_{29}FIN_5O_5S$

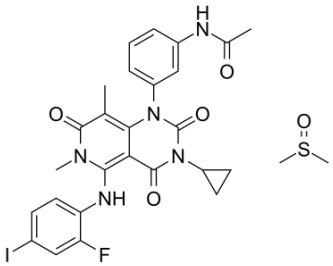
Molecular Weight: 693.53

Target: MEK; Apoptosis

Pathway: MAPK/ERK Pathway; Apoptosis

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 : 69 mg/mL (99.49 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4419 mL	7.2095 mL	14.4190 mL
	5 mM	0.2884 mL	1.4419 mL	2.8838 mL
	10 mM	0.1442 mL	0.7209 mL	1.4419 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 (3.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.60 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Trametinib (DMSO solvate) (GSK-1120212 (DMSO solvate);JTP-74057 (DMSO solvate)) is an orally active MEK inhibitor that inhibits MEK1 and MEK2 with IC_{50}s of about 2 nM. Trametinib (DMSO solvate) activates autophagy and induces apoptosis[1] [2].

IC_{50} & Target

MEK1	MEK2
2 nM (IC_{50})	2 nM (IC_{50})

In Vitro	In BRAF mutant SK-MEL-28 cells and KRAS mutant HCT116 cells, Trametinib (GSK1120212;JTP-74057) DMSO solvate causes dose-dependent inhibition of ERK1/2 phosphorylation as well as dose-dependent growth inhibition. In both SK-MEL-28 and HCT116 cells, Trametinib DMSO solvate inhibits 50% p-ERK1/2 at nearly equivalent concentrations (0.8 and 1.8 nM, respectively). However, as the slopes of the curves reflect, in SK-MEL-28 cells, Trametinib DMSO solvate inhibits 90% p-ERK1/2 at a lower concentration (3.4 nM) than in HCT116 (33.3 nM). Furthermore, in both cell lines, 50% growth inhibition is only achieved at concentrations Trametinib DMSO solvate that produces near complete ERK1/2 inhibition (85 and 90%, respectively)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Trametinib (GSK1120212;JTP-74057) DMSO solvate is evaluated in vivo in an A549 (KRAS mutant cell line) xenograft model, orally dosing daily for 21 days (qd×21). In this study, near complete tumor growth inhibition is observed at 5.0 and 2.5 mg/kg [92 and 87% tumor growth inhibition (TGI), respectively] and to a lesser degree at 0.5 and 0.1 mg/kg (62 and 58% TGI). Although 5 mg/kg is the maximally tolerated dose (MTD) in this study, 3 mg/kg is the typically observed MTD. Dose-dependent antitumor activity with Trametinib DMSO solvate treatment has been similarly reported for several other KRAS and BRAF mutant tumor models[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	SK-MEL-28, and HCT116 cell lines are plated in triplicate 96 well microtitre plates at 5000 cells per well in culture media. Trametinib dissolved in DMSO or negative control (0.1% DMSO) are added the following day and one plate is harvested with 50 µL of CellTiter-Glo for a time 0 (T=0) measurement. Remaining duplicate cell plates are typically incubated for 72 h. Cells are then lysed with 50 µL CellTiter-Glo, and chemiluminescent signal is read on the Wallac EnVision 2100 plate reader. For measurement of cellular ERK1/2 phosphorylation, cells are seeded and treated with Trametinib, and lysed after 72 h in Tris lysis buffer supplemented with phosphatase and protease inhibitors. All samples are analyzed with a phospho-ERK1/2 ELISA. Plates are read on MSD.SI6000 and curves are analyzed using the XLfit curve-fitting tool. For comparison of the growth assay curve and pERK1/2 assay curve, data are background subtracted and normalized to the vehicle treatment control[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] A549 (human non-small cell lung carcinoma) model is established from cells grown in tissue culture and harvested aseptically using a trypsin digest. Female athymic mice (strain nu/nu) are injected subcutaneously with between 5×10^6 and 10^7 cells in 50% martigel. Tumors are allowed to establish for one to four weeks before use. Trametinib is administered orally at the indicated doses in 0.2 mL/20 g by weight. Tumors are measured twice weekly using Vernier calipers. Antitumor activity is defined as tumor growth inhibition representing the % volume differential in tumor growth between the treated and control tumors at the time vehicle tumors exceeded a volume of 1000 mm^3. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2018 Aug 9;174(4):843-855.e19.
- Cancer Discov. 2020 Aug;10(8):1226-1239.
- Cancer Discov. 2018 Mar;8(3):354-369.
- Cancer Discov. 2015 Sep;5(9):960-71.
- Cancer Discov. 2012 Oct;2(10):934-47.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Yamaguchi T, et al. Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with HWA486. Inflamm Res, 2012, 61(5), 445-454.

[2]. Abe H, et al. Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO Solvate). ACS Med Chem Lett. 2011 Feb 28;2(4):320-4.

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