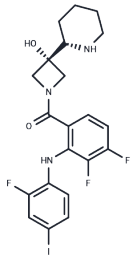
Data Sheet (Cat.No.T3623)

TargetMol

Cobimetinib

Chemical Properties



CAS No. : 934660-93-2

Formula: C21H21F3IN3O2

Molecular Weight: 531.31

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Cobimetinib (GDC-0973) is a MEK1 inhibitor (IC50=4.2 nM) with selective and oral activity. Cobimetinib exhibits antitumor activity, inhibiting tumor cell proliferation and inducing apoptosis.
Targets(IC50)	Apoptosis,MEK
In vitro	**METHODS**: A panel of BRAF-mutant, RAS-mutant, or wild-type cell lines were treated with Cobimetinib for 96 h and cell viability was measured by Cell Death Detection ELISA Plus kit. **RESULTS**: Cobimetinib showed potent cellular potency in multiple tumor types, particularly in BRAF or KRAS mutant cancer cell lines. In a subset of tumor cell lines, 80% of BRAF-mutant lines (both V600E and non-V600E mutations) were sensitive to Cobimetinib (EC50<1 μmol/L), 54% of lines harboring KRAS or NRAS-carrying mutations were sensitive, and the remaining 35% of lines were sensitive. [1] **METHODS**: NB cell lines IMR-32, SHEP, and IMR-5 were treated with Cobimetinib (1 μM) for 4 h, and target protein expression levels were measured by Western Blot. **RESULTS**: Cobimetinib treatment induced dephosphorylation of c-RAF and ERK and increased phosphorylation of MEK. [2]
In vivo	**METHODS**: To assay antitumor activity in vivo, Cobimetinib (1-10 mg/kg) was administered orally to mice bearing A375.X1 or NCI-H2122 xenografts once daily for 21 days. **RESULTS**: In the A375.X1 BRAFV600E mutant melanoma xenograft model, treatment with a dose of Cobimetinib greater than 3 mg/kg resulted in an intense TGI, and in the NCI-H2122 KRASG12C mutant NSCLC xenograft model, treatment with up to 5 mg/kg Cobimetinib resulted in a moderate TGI, and treatment with 10 mg/kg approached tumor arrest. [1]
Cell Research	Cells are plated in quadruplicate at a density of 3,000 per well in 384-well plates in normal growth medium and allowed to adhere overnight. Compounds are added in 10 concentrations based on a 3-fold dilution series. Cell viability is measured 72 h later using the CellTiter-Glo Luminescent Cell Viability Assay.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 44 mg/mL (82.81 mM),Sonication is recommended. DMSO: 84.17 mg/mL (158.42 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.76 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8821 mL	9.4107 mL	18.8214 mL
5 mM	0.3764 mL	1.8821 mL	3.7643 mL
10 mM	0.1882 mL	0.9411 mL	1.8821 mL
50 mM	0.0376 mL	0.1882 mL	0.3764 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Hoeflich KP, et al. Intermittent administration of MEK inhibitor GDC-0973 plus PI3K inhibitor GDC-0941 triggers robust apoptosis and tumor growth inhibition. Cancer Res. 2012 Jan 1;72(1):210-9.
Meng Y, Lv T, Zhang J, et al.Temporospatial inhibition of Erk signaling is required for lymphatic valve formation. Signal Transduction and Targeted Therapy.2023, 8(1): 342.
Yang Y, Suo N, Cui S, et al.Trametinib, an anti-tumor drug, promotes oligodendrocytes generation and myelin formation.Acta Pharmacologica Sinica.2024: 1-13.
Singh A, et al. Targeted inhibition of MEK1 by cobimetinib leads to differentiation and apoptosis in neuroblastoma cells. J Exp Clin Cancer Res. 2015 Sep 18;34(1):104.