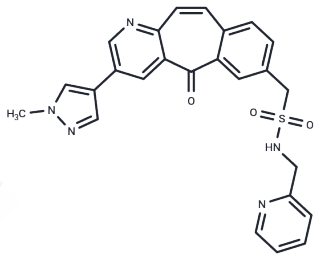
Data Sheet (Cat.No.TQ0219)

MK-8033

Chemical Properties



CAS No. : 1001917-37-8

Formula: C25H21N5O3S

Molecular Weight: 471.53

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	MK-8033 is a new and selective dual ATP competitive c-Met/Ron inhibitor (IC50: 1 nM Wt c-Met).
Targets(IC50)	c-Met/HGFR
In vitro	MK-8033 binds 3-fold more tightly to phosphorylated c-Met kinase domain (Kd: 3.2 nM) than to its unphosphorylated counterpart (Kd = 10.4 nM). Significantly, MK-8033 potently inhibits the kinase activity of three oncogenic c-Met activation loop mutants, Y1230C, Y1230H, and Y1235D (IC50s: 0.6~1 nM at 50 uM ATP) in addition to other c-Met activating mutants N1100Y and M1250T. MK-8033 potently inhibited GTL-16 proliferation (IC50: 582 nM). By contrast, the HCT116 cell line, which does not harbor basal c-Met activation, was not inhibited by MK-8033 (IC50 > 10000 nM) [1]. MK-8033 radiosensitizer the high-c-Met-expressing EBC-1 and H1993 cells but not the low-c-Met-expressing cell lines A549 and H460. However, irradiation of A549 and H460 cells increased the expression of c-Met protein at 30 minutes after the irradiation. Subsequent targeting of this up-regulated c-Met by using MK-8033 followed by a second radiation dose reduced the clonogenic survival of both A549 and H460 cells. MK-8033reduced the levels of radiation-induced phosphorylated (activated) c-Met in A549 cells [2].
In vivo	MK-8033 was orally dosed in GTL-16 tumor xenograft bearing mice. Mice were euthanized 1 h after dosing and tested for p-Met (Y1349) in tumors and MK-8033 concentrations in plasma. At 100 mg/kg, essentially complete inhibition of p-Met (Y1349) was achieved. An in vivo IC50 of 1.3 uM was deduced from the relationship between plasma MK-8033 level and Met pY1349. Dosing at 3, 10, 30, and 100 mg/kg resulted in 22, 18, 57, and 86% tumor growth inhibition, respectively, relative to the tumor from vehicle-treated mice [1].

Solubility Information

Solubility	DMSO: 45 mg/mL (95.43 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: 1 mg/mL (2.12 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one.*

In vivo Formulation	*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	2.1208 mL	10.6038 mL	21.2076 mL
5 mM	0.4242 mL	2.1208 mL	4.2415 mL
10 mM	0.2121 mL	1.0604 mL	2.1208 mL
50 mM	0.0424 mL	0.2121 mL	0.4242 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

Northrup AB, et al, Discovery of 1-[3-(1-methyl-1H-pyrazol-4-yl)-5-oxo-5H-benzo[4,5]cyclohepta[1,2-b]pyridin-7-yl]-N-(pyridin-2-ylmethyl)methanesulfonamide (MK-8033): A Specific c-Met/Ron dual kinase inhibitor with preferential affinity for the activated state of c-Met. J Med Chem. 2013 Mar 28;56(6):2294-310.
Bhardwaj V, et al. C-Met inhibitor MK-8003 radiosensitizes c-Met-expressing non-small-cell lung cancer cells with radiation-induced c-Met-expression. J Thorac Oncol. 2012 Aug;7(8):1211-7.