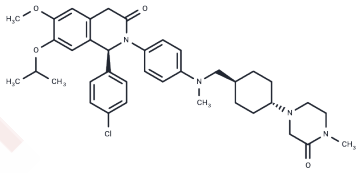
Data Sheet (Cat.No.TQ0231)

TargetMol

NVP-CGM097

Chemical Properties



CAS No. : 1313363-54-0

Formula: C38H47ClN4O4

Molecular Weight: 659.26

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	NVP-CGM097 (CGM097) is an effective and specific MDM2 inhibitor (IC50: 1.7 nM for hMDM2).
Targets(IC50)	Mdm2,E1/E2/E3 Enzyme,MDM-2/p53
In vitro	NVP-CGM097 binds to human MDM2(IC50: 1.7 nM) and shows high selectivity over MDM4 (IC50: 2000 nM). NVP-CGM097 is about four times more potent than Nutlin-3a (IC50: 8 nM). NVP-CGM097 significantly inhibits the proliferation of cells expressing wild-type p53, while sparing the p53 null cells with a 35-58-fold difference. NVP-CGM097 is able to significantly redistribute wild-type p53 into the cell nucleus with an IC50 of 0.224 μM. NVP-CGM097 significantly inhibits the proliferation of cells expressing wild-type p53, while sparing the p53 null cells with a 35-58-fold difference. NVP-CGM097 inhibits HCT116 (p53WT/WT, IC50: 454±136 nM).
In vivo	p21 mRNA levels are found to increase concomitantly with levels of NVP-CGM097 in tumor-bearing rats dosed at 30 mg/kg. The PD response is biphasic and prolonged up to 24 h. Additional p53 target genes such as MDM2 and PUMA mRNA levels are assessed in the tumor samples as well and showed similar behavior. Daily treatment with NVP-CGM097 dose-dependently and significantly inhibits SJSA-1 tumor growth in rats. It promotes stable disease at 20 mg/kg, which is associated with a plasma AUC0-24 of 163 μM?h. After iv administration, the total blood clearance (CL) of NVP-CGM097 is 5 mL/min per kg for mouse, 7 mL/min per kg for rat, 3 mL/min per kg for dog, and 4 mL/min per kg for monkey. The apparent terminal half-life (t1/2) is long in rodents and monkey (6-12 h) but is comparatively longer in dogs (20 h). After oral dosing, NVP-CGM097 is well absorbed with Tmax occurring between 1 and 4.5 h in all species tested.
Cell Research	Two pairs of cell lines are used to assess NVP-CGM097 p53-dependent antiproliferative effects: (1) an isogenic pair of HCT116 cell lines either expressing wild-type p53 or knocked-out for the p53 gene and (2) a nonisogenic pair of osteosarcoma cell lines either endogenously expressing wild-type p53 and amplified for MDM2 (SJSA-1 cells) or null for p53 (SAOS-2 cells).
Animal Research	Female athymic rats bearing subcutaneous xenotransplants of SJSA-1 tumors (n=5-12) are treated at 5, 10, 20, or 30 mg/kg or three times a week on Monday, Wednesday, and Friday (3qw M, W, F) at 30 or 70 mg/kg p.o for 14 days. Plasma AUCs are determined at the end of the study. Positive numbers indicate the percentage of tumor growth inhibition (T/C); negative numbers indicate the percentage of tumor regression.

Solubility Information

Solubility	DMSO: 48 mg/mL (72.81 mM),Sonication is recommended. H2O: Insoluble, (< 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 (3.03 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	1.5169 mL	7.5843 mL	15.1685 mL
5 mM	0.3034 mL	1.5169 mL	3.0337 mL
10 mM	0.1517 mL	0.7584 mL	1.5169 mL
50 mM	0.0303 mL	0.1517 mL	0.3034 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

Holzer P, et al. Discovery of a Dihydroisoquinolinone Derivative (NVP-CGM097): A Highly Potent and Selective MDM2 Inhibitor Undergoing Phase 1 Clinical Trials in p53wt Tumors. J Med Chem. 2015 Aug 27;58(16):6348-58