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产品名称: **NVP-CGM097 (sulfate)**
产品别名: **CGM097 sulfate**

生物活性:					
Description	NVP-CGM097 sulfate is a potent and selective MDM2 inhibitor with IC50 of 1.7±0.1 nM for hMDM2.				
IC50 & Target	IC50 & Target: IC50: 1.7±0.1 nM (hMDM2)[1]				
In Vitro	NVP-CGM097 binds to human MDM2 with an IC50 of 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). In addition, NVP-CGM097 shows no significant activity against Bcl-2:Bak, Bcl-2:Bad, Mcl-1:Bak, Mcl-1:NOXA, XIAP:BIR3, and c-IAP:BIR3 protein-protein interactions. 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, demonstrating its ability to inhibit the p53:MDM2 interaction in living cells. 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 (p53 ^{WT/WT}) with IC50 of 454±136 nM ^[1] .				
In Vivo	NVP-CGM097 is able to inhibit the interaction between p53 and MDM2 and reactivate the p53 pathway in a MDM2-amplified SJSA-1 human tumor model, as judged by elevation of p21 mRNA levels, a pharmacodynamic (PD) indicator for p53 activity. 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 a 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 ^[1] .				
Solvent&Solubility	In Vitro: H2O : ≥ 140 mg/mL (184.86 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	Solvent / Mass Concentration	1 mg	5 mg	10 mg
		1 mM	1.3204 mL	6.6021 mL	13.2041 mL
		5 mM	0.2641 mL	1.3204 mL	2.6408 mL
		10 mM	0.1320 mL	0.6602 mL	1.3204 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限：-80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用, -20℃ 储存时，请在 1 个月内使用。				
[1]. Holzer P, et al. Discovery of a Dihydroisoquinolinone Derivative (NVP-CGM097): A Highly Potent and					



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References	Selective MDM2 Inhibitor Undergoing Phase 1 Clinical Trials in p53wt Tumors. J Med Chem. 2015 Aug 27;58(16):6348-58.
实验参考:	
Cell Assay	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)[1].
Animal Administration	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 po 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[1].
References	[1]. 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.

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