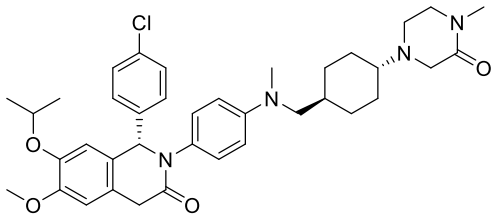
Product data sheet

MedKoo Cat#: 205957 Name: CGM097 CAS#: 1313363-54-0 Chemical Formula: $C_{38}H_{47}ClN_4O_4$ Exact Mass: 658.32858 Molecular Weight: 659.26	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

CGM097 is an orally bioavailable HDM2 (human homolog of double minute 2) antagonist with potential antineoplastic activity. Upon oral administration, p53/HDM2 interaction inhibitor CGM097 inhibits the binding of the HDM2 protein to the transcriptional activation domain of the tumor suppressor protein p53. By preventing this HDM2-p53 interaction, the proteosome-mediated enzymatic degradation of p53 is inhibited, which may result in the restoration of p53 signaling and, thus, the p53-mediated induction of tumor cell apoptosis. HDM2, a zinc finger nuclear phosphoprotein, is a negative regulator of the p53 pathway, often overexpressed in cancer cells and has been implicated in cancer cell proliferation and survival.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	50	75.84

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.52 mL	7.58 mL	15.17 mL
5 mM	0.30 mL	1.52 mL	3.03 mL
10 mM	0.15 mL	0.76 mL	1.52 mL
50 mM	0.03 mL	0.15 mL	0.30 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Holzer P, Masuya K, Furet P, Kallen J, Valat-Stachyra T, Ferretti S, Berghausen J, Bouisset-Leonard M, Buschmann N, Pissot-Soldermann C, Rynn C, Ruetz S, Stutz S, Chène P, Jeay S, Gessier F. 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. doi: 10.1021/acs.jmedchem.5b00810. Epub 2015 Aug 5. PMID: 26181851.

2. Wang Y, Kuramitsu Y, Baron B, Kitagawa T, Tokuda K, Akada J, Nakamura K. CGK733-induced LC3 II formation is positively associated with the expression of cyclin-dependent kinase inhibitor p21Waf1/Cip1 through modulation of the AMPK and PERK/CHOP signaling pathways. Oncotarget. 2015 Nov 24;6(37):39692-701. doi: 10.18632/oncotarget.5625. PMID: 26486079; PMCID: PMC4741855.

In vivo study

1. Holzer P, Masuya K, Furet P, Kallen J, Valat-Stachyra T, Ferretti S, Berghausen J, Bouisset-Leonard M, Buschmann N, Pissot-Soldermann C, Rynn C, Ruetz S, Stutz S, Chène P, Jeay S, Gessier F. Discovery of a Dihydroisoquinolinone Derivative (NVP-

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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. doi: 10.1021/acs.jmedchem.5b00810. Epub 2015 Aug 5. PMID: 26181851.

7. Bioactivity

Biological target:

NVP-CGM097 is a potent and selective MDM2 inhibitor with IC50 of 1.7±0.1 nM for hMDM2.

In vitro activity

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. In addition, NVP-CGM097 activity against the p53:MDM2 interaction is assessed in proliferation assays using either wild-type p53 or p53 null 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 inhibtis HCT116 (p53WT/WT) with IC50 of 454±136 nM.

Reference: J Med Chem. 2015 Aug 27;58(16):6348-58. https://doi.org/10.1021/acs.jmedchem.5b00810

In vivo activity

NVP-CGM097 is able to inhibit the interaction between p53 and MDM2 and reactivate the p53 pathway in vivo 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.

Reference: J Med Chem. 2015 Aug 27;58(16):6348-58. https://doi.org/10.1021/acs.jmedchem.5b00810