Navtemadlin

Cat. No.: HY-12296

CAS No.: 1352066-68-2

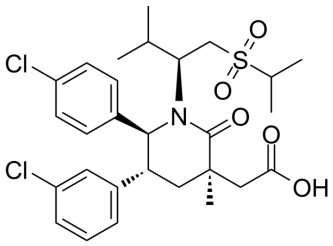
Molecular Formula: $C_{28}H_{35}Cl_2NO_5S$

Molecular Weight: 569

Target: MDM-2/p53; E1/E2/E3 Enzyme

Pathway: Apoptosis; Metabolic Enzyme/Protease

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (87.87 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7575 mL	8.7873 mL	17.5747 mL
	5 mM	0.3515 mL	1.7575 mL	3.5149 mL
	10 mM	0.1757 mL	0.8787 mL	1.7575 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (17.57 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
5. Add each solvent one by one: PBS
   Solubility: 1.5 mg/mL (2.64 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Navtemadlin (AMG 232) is a potent, selective and orally available inhibitor of p53-MDM2 interaction, with an IC_{50} of 0.6 nM. Navtemadlin binds to MDM2 with a K_d of 0.045 nM[1][2].

IC_{50} & Target	IC50: 0.6 nM (p53-MDM2 interaction)[1] Kd: 0.045 nM (MDM2)[1]
In Vitro	Navtemadlin (AMG 232) (10 μM) induces p53 signaling and inhibits tumor cell proliferation in three p53 wild-type tumor cell lines[1]. Navtemadlin potently inhibits proliferation of non-MDM2-amplified HCT116 colorectal cells (IC_{50}=10 nM)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	SJSA-1, HCT116, ACHN, NCI-H460, MOLM-13, RKO, MCF7, 22RV1, HT-29, PC-3, NCI-H82, NCI-SNU1, MG-63, NCI-H2452, SW982, C32, SK-HEP-1, A375, RT4, RPMI2650, MDA-MB-134-VI, NCI-H2347 and A427 cells.
Concentration:	0-10 μM.
Incubation Time:	72 hours.
Result:	Induced p53 signaling and inhibits tumor cell proliferation in three p53 wild-type tumor cell lines (SJSA-1, HCT116, and ACHN). Caused robust p21 mRNA induction between 9.76 and 34.9 fold with IC50 values ranging from 12.8 to 46.8 nM.

In Vivo	Navtemadlin (AMG 232) (10, 25, 75 mg/kg, once daily, p.o.) activates p53 pathway activity in vivo[1]. Navtemadlin (10, 25, 75 mg/kg, once daily, p.o.) potently inhibits growth of tumor xenografts in mice[1]. Navtemadlin (10, 25, 75 mg/kg, once daily, p.o.) blocks DNA synthesis and induces apoptosis in vivo[1]. Navtemadlin causes a dose-dependent tumor growth inhibition with an ED_{50} of 16 mg/kg[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female athymic nude mice (n=10/group) based cancer models[1].
Dosage:	10, 25, 75 mg/kg.
Administration:	Once daily by oral gavage.
Result:	Resulted in significant tumor growth inhibition across all models. SJSA-1, an MDM2 amplified osteosarcoma model, was the most sensitive to AMG 232 treatment with an ED_{50} of 9.1 mg/kg. In the highest dose group of 75 mg/kg, 10/10 tumors completely regressed and were undetectable after 10 days of treatment.

CUSTOMER VALIDATION

- Clin Transl Med. 2022 Jul;12(7):e961.
- Br J Cancer. 2023 Mar 23.
- Cell Death Discov. 2020 Jul 6;6:57.
- BMC Biol. 2017 Nov 9;15(1):108.
- Biomedicines. 2022, 10(3), 638.

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REFERENCES

[1]. Canon J, et al. The MDM2 Inhibitor AMG 232 Demonstrates Robust Antitumor Efficacy and Potentiates the Activity of p53-Inducing Cytotoxic Agents. Mol Cancer Ther. 2015 Mar;14(3):649-58.

[2]. Rew Y, et al. Discovery of a small molecule MDM2 inhibitor (AMG 232) for treating cancer. J Med Chem. 2014 Aug 14;57(15):6332-41.

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