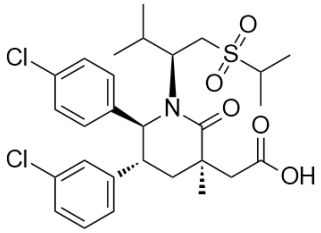
AMG 232

Cat. No.:	HY-12296
CAS No.:	1352066-68-2
Molecular Formula:	$C_{28}H_{35}Cl_2NO_5S$
Molecular Weight:	568.55
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 (87.94 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	1.7589 mL	8.7943 mL	17.5886 mL
5 mM	0.3518 mL	1.7589 mL	3.5177 mL
10 mM	0.1759 mL	0.8794 mL	1.7589 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
4. Add each solvent one by one: PBS
   Solubility: 1.5 mg/mL (2.64 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

IC50: 0.6 nM (p53-MDM2 interaction)[1]

	Kd: 0.045 nM (MDM2)[1]
In Vitro	AMG 232 (10 μM) induces p53 signaling and inhibits tumor cell proliferation in three p53 wild-type tumor cell lines[1]. AMG 232 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	AMG 232 (10, 25, 75 mg/kg, once daily, p.o.) activates p53 pathway activity in vivo[1]. AMG 232 (10, 25, 75 mg/kg, once daily, p.o.) potently inhibits growth of tumor xenografts in mice[1]. AMG 232 (10, 25, 75 mg/kg, once daily, p.o.) blocks DNA synthesis and induces apoptosis in vivo[1]. AMG 232 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

- BMC Biol. 2017 Nov 9;15(1):108.
- Cell Death Discov. 2020 Jul 6;6:57.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA