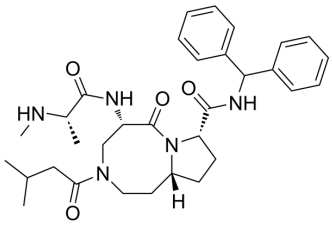
Xevinapant

Cat. No.:	HY-15454
CAS No.:	1071992-99-8
Molecular Formula:	$C_{32}H_{43}N_5O_4$
Molecular Weight:	561.71
Target:	IAP; Apoptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (178.03 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7803 mL	8.9014 mL	17.8028 mL
	5 mM	0.3561 mL	1.7803 mL	3.5606 mL
	10 mM	0.1780 mL	0.8901 mL	1.7803 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 (4.45 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Xevinapant (AT-406) is a potent and orally bioavailable Smac mimetic and an antagonist of IAPs, and it binds to XIAP, cIAP1, and cIAP2 proteins with K_i of 66.4, 1.9, and 5.1 nM, respectively.

IC_{50} & Target

cIAP1	cIAP2	XIAP
1.9 nM (Ki)	5.1 nM (Ki)	66.4 nM (Ki)

In Vitro

Xevinapant mimic closely the AVPI peptide in both hydrogen bonding and hydrophobic interactions with XIAP, with

additional hydrophobic contacts with W323 of XIAP. Xevinapant is more sensitive to these IAPs than Smac AVPI peptide with 50-100 fold binding affinities. Xevinapant (1 μM) completely restores the activity of caspase-9, which is suppressed by 500 nM XIAP BIR3 in a cell-free system. In MDA-MB-231 cell, Xevinapant induces rapid cellular cIAP1 degradation and also pulls down the cellular XIAP protein. Xevinapant effectively inhibits lots of human cancer cell lines and shows IC_{50} of 144 and 142 nM in MDA-MB-231 cell and SK-OV-3 ovarian cell, with low toxicity against normal-like human breast epithelial MCF-12F cells and primary human normal prostate epithelial cells. Xevinapant induces apoptosis in MDA-MB-231 cell by inducing activation of caspase-3 and cleavage of PARP[1]. Xevinapant displays single agent activity in ovarian cancer cell lines. The IC_{50} values of AT-406 in these ovarian cancer cells range from 0.05-0.5 μg/mL. Xevinapant exhibits anti-ovarian cancer efficacy both as a single agent and in combination with carboplatin. Xevinapant (30 μg/mL) induced degradation of XIAP in the drug sensitive ovarian cancer cell lines[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Xevinapant (AT-406) is very effective in inhibition of tumor growth in the MDA-MB-231 xenograft model, and has minimal toxicity to animals[1]. Xevinapant is evaluated for its pharmacokinetic (PK) properties in mice, rats, non-human primates and dogs[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SCID mice bearing MDA-MB-231 xenograft tumors[1]
Dosage:	30 and 100 mg/kg
Administration:	p.o.; 5 days a week for 2 weeks
Result:	Strongly inhibits tumor growth at 30 and 100 mg/kg and completely inhibits tumor growth during the treatment with 100 mg/kg.

CUSTOMER VALIDATION

- J Med Chem. 2019 Oct 24;62(20):9188-9200.
- Biochim Biophys Acta Mol Basis Dis. 2019 Jun 26;1865(10):2618-2632.
- Viruses. 2021, 13(12), 2490.
- Gene. 2023 May 18;147492.
- Research Square Preprint. 2024 Apr 15.

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REFERENCES

[1]. Cai Q, Sun H, Peng Y, et al. A potent and orally active antagonist (SM-406/AT-406) of multiple inhibitor of apoptosis proteins (IAPs) in clinical development for cancer treatment. J Med Chem. 2011;54(8):2714-2726.

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