For Research Use Only

# Xevinapant

www.ptgcn.com

## Catalog Number: CM04683

### 产品信息

**Catalog Number:**
CM04683

**CAS号:**
1071992-99-8

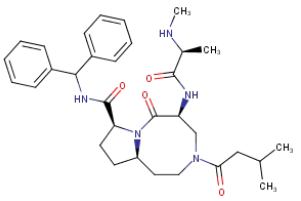
**分子式:**
$C_{32}H_{43}N_5O_4$

**主要靶点:**
IAP

**主要通路:**
凋亡

**分子量:**
561.71

**溶解度:**
H2O:<1 mg/mL,Ethanol:93 mg/mL (165.6 mM),DMSO:93 mg/mL (165.6 mM)



### 靶点活性

XIAP-BIR3:66.4 nM(Ki)|cIAP2-BIR3:5.1 nM(Ki)|cIAP1-BIR3:1.9 nM(Ki)

### 体外活性

AT-406 is a Smac mimetic and appears to mimic closely the AVPI peptide in both hydrogen bonding and hydrophobic interactions with XIAP, with additional hydrophobic contacts with W323 of XIAP. AT-406 is more sensitive to these IAPs than Smac AVPI peptide with 50-100 fold binding affinities. AT-406 (at 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, AT-406 induces rapid cellular cIAP1 degradation and also pulls down the cellular XIAP protein. AT-406 effectively inhibits lots of human cancer cell lines and shows IC50 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. AT-406 induces apoptosis in MDA-MB-231 cell by inducing activation of caspase-3 and cleavage of PARP. [1]

### 体内活性

AT-406 has good pharmacokinetic (PK) properties and oral bioavailability in mice, rats, non-human primates, and dogs. In the MDA-MB-231 xenograft, AT-406 effectively induces cIAP1 degradation and processing of procaspase-8, cleavage of PARP in tumor tissues at 100 mg/kg with well toleration even at 200 mg/kg. AT-406 induces significant tumor growth inhibition with p of 0.0012 at 100 mg/kg. [1]

### 细胞实验

Cells are seeded in 96-well flat bottom cell culture plates at a density of (3-4) × 103 cells/well with AT-406 and incubated for 4 days. The rate of cell growth inhibition after treatment with different concentrations of AT-406 is determined by assaying with (2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium monosodium salt (WST-8). WST-8 is added to each well to a final concentration of 10%, and then the plates are incubated at 37 °C for 2−3 hours. The absorbance of the samples is measured at 450 nm using a TECAN ULTRA reader. Concentration of AT-406 that inhibited cell growth by 50% (IC50) is calculated by comparing absorbance in the untreated cells and the cells treated with AT-406. (Only for Reference)

### 描述

Xevinapant (Debio-1143) is a potent Smac mimetic and an antagonist of IAP (inhibitor of apoptosis protein via E3 ubiquitin ligase), binding to XIAP-BIR3, cIAP1-BIR3 and cIAP2-BIR3 with Ki of 66.4 nM, 1.9 nM, and 5.1 nM, 50- to 100-fold higher affinities than the Smac AVPI peptide. Phase 1.

### 储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years