上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：MLN9708
产品别名：艾沙佐米柠檬酸盐；Ixazomib citrate

生物活性：

Description	Ixazomib citrate (MLN9708) is a reversible inhibitor of the chymotrypsin-like proteolytic β5 site of the 20S proteasome with an IC50 of 3.4 nM and a Ki of 0.93 nM.
IC_{50} & Target	IC50: 3.4 nM (20S proteasome β5), 31 nM (20S proteasome β1), 3500 nM (20S proteasome β2)[3]
In Vitro	Ixazomib citrate (MLN9708; 0.20-3.20 μM) inhibits the cell growth of both cell lines effectively in a time- and dose-dependent manner. Ixazomib induces cell cycle arrest in MG-63 and Saos-2 cells. Ixazomib induces apoptosis mainly through the caspases pathway and requires the activation of both caspase8 and caspase9. Ixazomib treatment increases the levels of pro-apoptotic proteins and down regulates the anti-apoptotic proteins that control MOMP. Ixazomib treatment induces the release of Cytc, Smac, OMI from mitochondria and decreases the protein levels of XIAP. Ixazomib inhibits the invasion ability of MG-63 and Saos-2 cells and decreases both the expression and secretion levels of MMP2/9[1].Ixazomib citrate (MLN9708; 12 nM) shows inhibitory activity against C-L and T-L proteasome activities. Treatment of H929 and MM.1S MM cells with Ixazomib triggers a marked increase in proteolytic cleavage of poly(ADP) ribose polymerase (PARP), a signature event during apoptosis. Ixazomib induces cleavage of caspase-3, an upstream activator of PARP. Ixazomib induces elf2-α kinase activity and protein levels of Bip and CHOP/GADD153. Ixazomib blocks BMSCs-induced MM cell proliferation, inhibits in vitro capillary tubule formation, and target NF-κB[2].
In Vivo	Ixazomib citrate (MLN9708; 11 mg/kg) significantly inhibits MM tumor growth and prolongs survival in the human plasmacytoma MM.1S xenograft mouse model. The blood chemistry profiles of Ixazomib-treated mice show normal levels of creatinine, hemoglobin, and bilirubin. Ixazomib dramatically increases the number of cleaved-caspase-3 positive cells of the xenograft model[2].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 100 mg/mL (193.38 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9338 mL	9.6689 mL	19.3379 mL
5 mM	0.3868 mL	1.9338 mL	3.8676 mL
10 mM	0.1934 mL	0.9669 mL	1.9338 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出

	现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.83 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.83 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.83 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Liu R, et al. A New Perspective for Osteosarcoma Therapy: Proteasome Inhibition by MLN9708/2238 Successfully Induces Apoptosis and Cell Cycle Arrest and Attenuates the Invasion Ability of Osteosarcoma Cells in Vitro. Cell Physiol Biochem. 2017 Jan 27;41(2 [2]. Chauhan D, et al. In vitro and in vivo selective antitumor activity of a novel orally bioavailable proteasome inhibitor MLN9708 against multiple myeloma cells. Clin Cancer Res. 2011 Aug 15;17(16):5311-21. [3]. Kupperman E, et al. Evaluation of the proteasome inhibitor MLN9708 in preclinical models of human cancer. Cancer Res. 2010 Mar 1;70(5):1970-80.

实验参考：

Cell Assay	Cell viability is assessed using the MTT assay. Cells are trypsinized and seeded in 96-well plate at 5000 cells per well. Cells are treated with Ixazomib or DMSO in basal medium at the indicated doses and times. Cell viability is determined relative to control cells treated with vehicle alone. [1]
Animal Administration	Ixazomib is dissolved in 5% 2-hydroxypropyl-β- cyclodextrin at 2 mg/mL concentration. The human plasmacytoma xenograft tumor model is used in the assay. CB-17 SCID mice (n=21) are subcutaneously inoculated with 5.0×10^6MM.1S cells in 100 μL serum-free RPMI-1640 medium, and randomized to treatment groups when tumors reach 250-300 mm^3. Mice are treated with vehicle, bortezomib (1 mg/kg; i.v) or Ixazomib (11 mg/kg; i.v) twice weekly for 3 weeks. Animals are euthanized when their tumors reach 2 cm^3. [2]
	[1]. Liu R, et al. A New Perspective for Osteosarcoma Therapy: Proteasome Inhibition by MLN9708/2238 Successfully Induces Apoptosis and Cell Cycle Arrest and Attenuates the Invasion Ability of Osteosarcoma Cells in Vitro. Cell Physiol Biochem. 2017 Jan 27;41(2 [2]. Chauhan D, et al. In vitro and in vivo selective antitumor activity of a novel orally bioavailable

References	proteasome inhibitor MLN9708 against multiple myeloma cells. Clin Cancer Res. 2011 Aug 15;17(16):5311-21. [3]. Kupperman E, et al. Evaluation of the proteasome inhibitor MLN9708 in preclinical models of human cancer. Cancer Res. 2010 Mar 1;70(5):1970-80.