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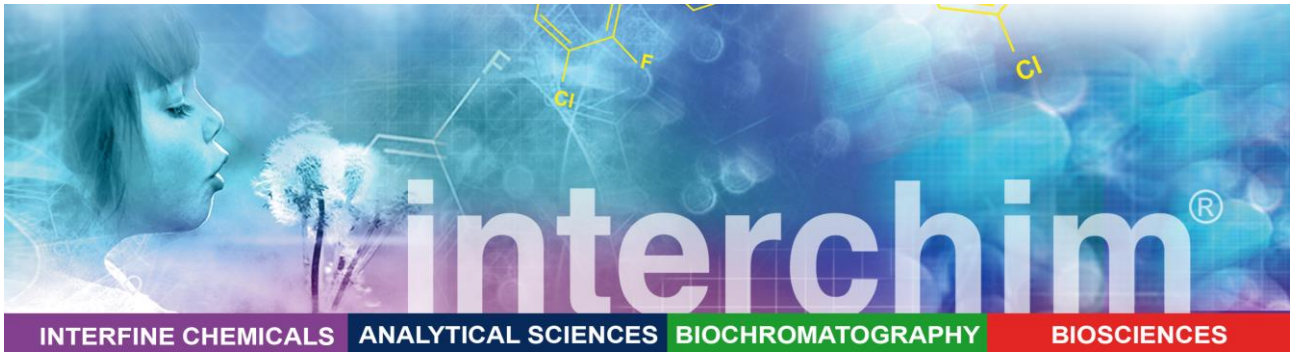
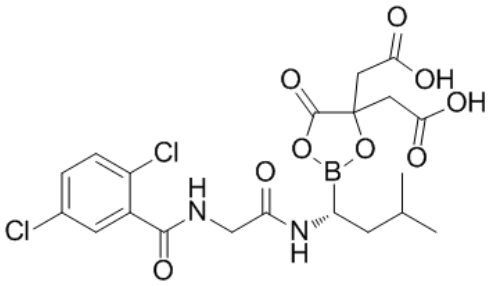


Ixazomib citrate

a reversible inhibitor of the chymotrypsin-like proteolytic β5 site of the 20S proteasome

Product Description



Catalog # : XLO200, 5mg XLO201, 10mg
XLO202, 50mg XLO203, 100mg
AX99X0, 1m at 10mM in solution

[]:

Name: **Ixazomib citrate (MLN9708)**

Syn. : 4-(carboxymethyl)-2-((R)-1-(2-(2,5-dichlorobenzamido)acetamido)-3-methylbutyl)-6-oxo-1,3,2-dioxabori nane-4-carboxylic acid ;
MLN9708 ; 1,3,2-Dioxaborolane-4,4-diacetic acid,2-((1R)-1-((2-((2,5-dichlorobenzoyl)amino)acetyl)amino)-3-methylbutyl)-5-oxo

CAS : 1239908-20-3

MW : 517.12

Solubility : Soluble in DMSO (≥ 100 mg/mL - 193.38 mM)
λmax : 282nm

Target : Serotonin Transporter; Endogenous (SSRIs)

Storage: Powder at -20°C (3 years) (M) []
In solvent -80°C (6 months) or -20°C (1 month)

Appearance:	White to off-white (Solid)
^{1}H NMR Spectrum:	Consistent with structure
Purity (NMR):	>98.0%

General information

Ixazomib citrate (MLN9708) is a reversible inhibitor of the chymotrypsin-like proteolytic β5 site of the 20S proteasome

IC50 & Target
IC50: 3.4 nM (20S proteasome β5), 31 nM (20S proteasome β1), 3500 nM (20S proteasome β2)[3].
Ki : 0.93 nM (20S proteasome).

In Vitro activity
Ixazomib citrate (MLN9708) inhibits the cell growth of both cell lines effectively in a time- and dose-dependent manner 50.20-3.20 μM°. 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

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upstream activator of PARP. Ixazomib induces eIf2-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 activity

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] .

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Directions for use - Solubilisation []

1. Add each solvent one by one: 10% DMSO 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO 40% PEG300 5% Tween-80 45% saline
   Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution

Directions dor use - Cell Assay [1]

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.

Directions for use - Animal Administration [2]

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 5.0×106 MM.1S cells in 100 µL serum-free RPMI-1640 medium, and randomized to treatment groups when tumors reach 250-300 mm3. 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 cm3.

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). Abstract .

[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. Abstract.

[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. Abstract.

Legals

Non hazardous material []

Ixazomib is sold under brand names Ninlaro amongst others.

Related Products

MLN2238 [1072833-77-2](#WOF500): a reversible inhibitor of the chymotrypsin-like proteolytic β5 site of the 20S proteasome (IC50 = 3.4 nM; Ki = 0.93 nM in cell free assays).1

Ordering information

Catalog size quantities and prices may be found at http://www.interchim.com.

Please contact InterBioTech – Interchim for any other information **Erreur ! Référence de lien hypertexte non valide.**
Hotline : +33(0)4 70 03 73 06 – Interbiotech@interchim.com

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