

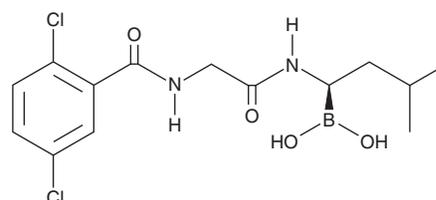
PRODUCT INFORMATION



MLN2238

Item No. 18385

CAS Registry No.: 1072833-77-2
Formal Name: B-[(1R)-1-[[2-[(2,5-dichlorobenzoyl)amino]acetyl]amino]-3-methylbutyl]-boronic acid
MF: C₁₄H₁₉BCl₂N₂O₄
FW: 361.0
Purity: ≥95%
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

MLN2238 is supplied as a crystalline solid. A stock solution may be made by dissolving the MLN2238 in the solvent of choice. MLN2238 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of MLN2238 in these solvents is approximately 25, 20, and 30 mg/ml, respectively.

MLN2238 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, MLN2238 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. MLN2238 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

MLN2238 is an inhibitor of the $\beta 5$ subunit of the 20S proteasome ($IC_{50} = 3.4$ nM in a cell-free assay) and an active metabolite of MLN9708 (Item No. 18386).^{1,2} It is formed from MLN9708 via hydrolysis in plasma.¹ MLN2238 is selective for the chymotrypsin-like $\beta 5$ subunit over the caspase-like $\beta 1$ and trypsin-like $\beta 2$ subunits (IC_{50} s = 31 and 3,500 nM, respectively). It also binds caseinolytic protease P ($K_d = 5,700$ nM) and prevents hemolysis of isolated ovine erythrocytes induced by methicillin-resistant *S. aureus* (MRSA; $EC_{50} = 3,600$ nM).³ MLN2238 inhibits the proliferation of A375 and H460 lung and HCT116 and HT-29 colon cancer cells (IC_{50} s = 20, 58, 19, and 52 nM, respectively) as well as osteoclastogenesis in peripheral blood mononuclear cells (PBMCs) isolated from patients with multiple myeloma ($IC_{50} = 4.8$ nM).^{1,2} It reduces tumor growth in a CWR22 prostate cancer mouse xenograft model when administered at a dose of 14 mg/kg. Formulations containing MLN2238 have been used in the treatment of multiple myeloma.

References

1. Kupperman, E., Lee, E.C., Cao, Y., *et al.* Evaluation of the proteasome inhibitor MLN9708 in preclinical models of human cancer. *Cancer Research* **70**(5), 1970-1980 (2010).
2. Garcia-Gomez, A., Quwaider, D., Canavese, M., *et al.* Preclinical activity of the oral proteasome inhibitor MLN9708 in Myeloma bone disease. *Clinical Cancer Research* **20**(6), 1542-1554 (2014).
3. Ju, Y., He, L., Zhou, Y., *et al.* Discovery of novel peptidomimetic boronate ClpP inhibitors with noncanonical enzyme mechanism as potent virulence blockers *in vitro* and *in vivo*. *J. Med. Chem.* **63**(6), 3104-3119 (2020).

WARNING
THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA
This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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