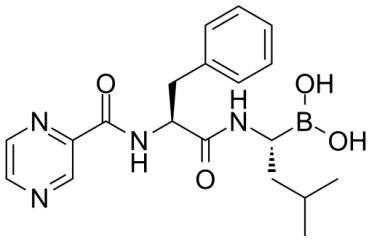
Data Sheet

Product Name:	Bortezomib
Cat. No.:	CS-1039
CAS No.:	179324-69-7
Molecular Formula:	C19H25BN4O4
Molecular Weight:	384.24
Target:	Apoptosis; Autophagy; Proteasome
Pathway:	Apoptosis; Autophagy; Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 83.3 mg/mL (216.79 mM)



BIOLOGICAL ACTIVITY:

Bortezomib (PS-341) is a cell-permeable, reversible, and selective **proteasome** inhibitor, and potently inhibits **20S proteasome** (K_i=0.6 nM) by targeting a threonine residue. Bortezomib (PS-341) disrupts the cell cycle, induces apoptosis, and inhibits **NF-κB**. Bortezomib (PS-341) is an anti-cancer drug and the first therapeutic proteasome inhibitor to be used in humans[1][2]. IC50 & Target: Ki: 0.6 nM (20S proteasome)[1]

In Vitro: Bortezomib (PS-341) (100 nM; 8 hours) results in the accumulation of cells in G2-M, with a corresponding decrease in the number of cells in G1[1].

Bortezomib (PS-341) (5-100 nM; 20 hours) induces apoptosis in mantle-cell lymphoma (MCL) cell lines[3].

Bortezomib (PS-341) (20 nM; 1-14 hours) induces Noxa up-regulation in both MCL cell lines[3].

The IC_{50} of Bortezomib (PS-341) is found to be 2.46 nM for 26S proteasome in the B16F10 cells[4].

Bortezomib (PS-341) suppresses several anti-apoptotic proteins (e.g., Bcl-XL, Bcl-2, and STAT-3)[5]. **In Vivo:** Bortezomib (PS-341) (0.3-1 mg/kg; i.v.; once weekly for 4 weeks) inhibits PC-3 Tumor Growth in Nude Mice[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Bortezomib is dissolved in DMSO and stored, and then diluted with appropriate media (DMSO 0.1%) before use[1].[1]The human PC-3 prostate tumor cells are treated with Bortezomib (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM, 10 μM) for 24-48 h in complete medium. Cytotoxicity is measured using a MTT assay[1]. **Animal Administration:** Bortezomib is prepared in 98% saline (0.9%), 2% ethanol, and 0.1% ascorbic acid (Mice)[1].;Bortezomib is dissolved in 5% DMSO solution (Rats)[4].[1][4]Mice[1]

Male nude mice (18-20 g; n=51) are used. Bortezomib (0.3 or 1.0 mg/kg) is administered in vehicle i.v. using a dose volume of 100 μL per mouse or directly into the tumor in a 10 μL volume. Due to the comparatively high levels of Bortezomib in the prostate, after i.v. dosing of radiolabeled drug, it is decided to examine the effects of this novel compound in the prostate, PC-3, xenograft tumor model. Animals are treated when the tumors become palpable (>300 mm^3). Male nude mice (18-20 g; n=51) are used. Bortezomib (0.3 or 1.0 mg/kg) is administered in vehicle i.v. using a dose volume of 100 μL per mouse or directly into the tumor in a 10 μL volume. Due to the comparatively high levels of Bortezomib in the prostate, after i.v. dosing of radiolabeled drug, it is decided to examine the effects of this novel compound in the prostate, PC-3, xenograft tumor model. Animals are treated when the tumors become palpable (>300 mm^3).

Rats[4]

Male Sprague-Dawley rats weighing 200-250 g are used. Bortezomib (0.05, 0.1, or 0.2 mg/kg) or vehicle (5% DMSO solution) is administered intraperitoneally (i.p.) twice a week for 2 weeks (on days 1, 4, 8, and 11). The administration schedule and doses of Bortezomib are determined based on clinical treatment (1.3 mg/m^2 of Bortezomib on days 1, 4, 8, and 11).

References:

[1]. Adams J, et al. Proteasome inhibitors: a novel class of potent and effective antitumor agents. Cancer Res. 1999 Jun 1;59(11):2615-22.

[2]. Shahshahan MA, et al. Potential usage of proteasome inhibitor bortezomib (Velcade, PS-341) in the treatment of metastaticmelanoma: basic and clinical aspects. Am J Cancer Res. 2011;1(7):913-24.

[3]. Pérez-Galán P, et al. The proteasome inhibitor bortezomib induces apoptosis in mantle-cell lymphoma through generation of ROS and Noxa activation independent of p53 status. Blood. 2006 Jan 1;107(1):257-64.

[4]. Yerlikaya A, et al. Combined effects of the proteasome inhibitor bortezomib and Hsp70 inhibitors on the B16F10 melanoma cell line. Mol Med Rep. 2010 Mar-Apr;3(2):333-9.

[5]. Mujtaba T, et al. Advances in the understanding of mechanisms and therapeutic use of bortezomib. Discov Med. 2011 Dec;12(67):471-80.

[6]. Fernández Y, et al. Chemical blockage of the proteasome inhibitory function of bortezomib: impact on tumor cell death. J Biol Chem. 2006 Jan 13;281(2):1107-18.

CAIndexNames:

Boronic acid, B-[(1R)-3-methyl-1-[[(2S)-1-oxo-3-phenyl-2-[(2-pyrazinylcarbonyl)amino]propyl]amino]butyl]-

SMILES:

OB(O)[C@H](CC(C)C)NC([C@@H](NC(C1=NC=CN=C1)=O)CC2=CC=CC=C2)=O

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