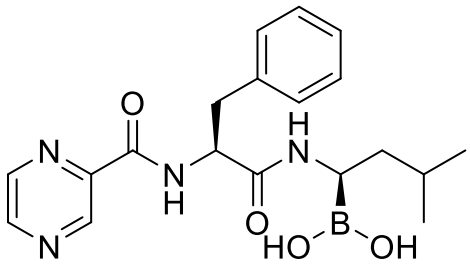
Product data sheet

MedKoo Cat#: 100100 Name: Bortezomib CAS#: 179324-69-7 Chemical Formula: $C_{19}H_{25}BN_4O_4$ Exact Mass: 384.19689 Molecular Weight: 384.24	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Bortezomib is a dipeptide boronic acid analogue with antineoplastic activity. Bortezomib reversibly inhibits the 26S proteasome, a large protease complex that degrades ubiquinated proteins. By blocking the targeted proteolysis normally performed by the proteasome, bortezomib disrupts various cell signaling pathways, leading to cell cycle arrest, apoptosis, and inhibition of angiogenesis. Specifically, the agent inhibits nuclear factor (NF)-kappaB, a protein that is constitutively activated in some cancers, thereby interfering with NF-kappaB-mediated cell survival, tumor growth, and angiogenesis. In vivo, bortezomib delays tumor growth and enhances the cytotoxic effects of radiation and chemotherapy.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	76	197.79

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.60 mL	13.01 mL	26.03 mL
5 mM	0.52 mL	2.60 mL	5.21 mL
10 mM	0.26 mL	1.30 mL	2.60 mL
50 mM	0.05 mL	0.26 mL	0.52 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Adams J, Palombella VJ, Sausville EA, Johnson J, Destree A, Lazarus DD, Maas J, Pien CS, Prakash S, Elliott PJ. Proteasome inhibitors: a novel class of potent and effective antitumor agents. Cancer Res. 1999 Jun 1;59(11):2615-22. PMID: 10363983.

2. Pérez-Galán P, Roué G, Villamor N, Montserrat E, Campo E, Colomer D. 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. doi: 10.1182/blood-2005-05-2091. Epub 2005 Sep 15. PMID: 16166592.

In vivo study

1. Adams J, Palombella VJ, Sausville EA, Johnson J, Destree A, Lazarus DD, Maas J, Pien CS, Prakash S, Elliott PJ. Proteasome inhibitors: a novel class of potent and effective antitumor agents. Cancer Res. 1999 Jun 1;59(11):2615-22. PMID: 10363983.

7. Bioactivity
Biological target:

Product data sheet

Bortezomib (PS-341, Velcade, LDP-341, MLM341, NSC 681239) is a potent 20S proteasome inhibitor with Ki of 0.6 nM.

In vitro activity

The average growth inhibition of 50% (GI50) value for PS-341 across the entire NCI cell panel was 7 nm. Moreover, when 13 dipeptide proteasome inhibitors from the boronate series were examined, a strong correlation (Pearson coefficient, r2 = 0.92) was noted after plotting Ki versus GI50 values (Fig. 1). This finding associates the intrinsic potency of this class of compounds with their antiproliferative activity in cell culture assays, confirming their activity through a biological target, the proteasome. Using the NCI's algorithm COMPARE (16) , we compared the "fingerprint" for PS-341-induced cytotoxicity to the historical file of 60,000 compounds and found it to be unique, with little correlation to other "standard" or investigational agents. In addition, PS-341 was shown to penetrate into cells and inhibit proteasome-mediated intracellular proteolysis of long-lived proteins with a concentration that inhibited 50% of the proteolysis (IC50) of ~0.1 μm (data not shown). In the in vitro screen the prostate tumor PC-3 cell line (22) was shown to be sensitive to the antiproliferative effects of PS-341. To examine the potential mechanism(s) of proteasome inhibitor-induced cytotoxicity, PS-341 was studied in detail in this prostate cell line. Numerous proteins control cell cycle progression, including the tumor suppressor p53 and the CDK inhibitors p21 and p27 (12) . PC-3 cells are p53 null (23) , and hence, this protein is not required for PS-341-induced cytotoxicity in this cell line. In fact, PS-341 was demonstrated to be cytotoxic in multiple cell lines in the NCI screen, independent of p53 status (data not shown). Protein levels of p21 were measured to exemplify the activity of PS-341 in cells. Although very little p21 protein was detected in untreated cells, levels were significantly increased with 10 nm PS-341 (Fig. 2A) occurring 24 h after drug addition. The increase in p21 protein levels could be detected 4 h after PS-341 treatment (data not shown). The increase in p21 led to an inhibition in the activity but not the levels of CDK-4 after 8 h (data not shown).

Reference: Cancer Res. 1999 Jun 1;59(11):2615-22. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=10363983

In vivo activity

Initial activity of bortezomib (PS-341) was examined in vivo with a hollow fiber assay (29), which recorded very good activity for PS-341 and a series of analogues (data not shown). This gave impetus to examine antitumor activity for PS-341 in human xenografts. For example, s.c. implantation of human PC-3 tumor cells into nude mice elicits a large tumor that is eventually lethal. PS-341 was administered to mice injected with PC-3 cells when the tumors became palpable (>300 mm3). Two studies were undertaken. First, mice bearing PC-3 tumors were injected with PS-341 (0.3 or 1.0 mg/kg) i.v. once weekly for 4 weeks, and tumor volumes were recorded. Weekly i.v. treatment with PS-341 (1.0 mg/kg) resulted in a significant decrease in tumor growth ~60% ($P < 0.05$), as determined by measurement of tumor volume. The lower dose of PS-341 (0.3 mg/kg) produced a 16% decrease in tumor volume but did not reach significance (Fig. 4A). PS-341 significantly decreased the tumor volume although distribution of the compound to the skin is limited (see below). To further explore the anticancer utility of PS-341, the drug was administered directly into PC-3 tumors in a second study. On 4 consecutive days, PS-341 (1.0 mg/kg) was administered (in 10 μl) into established PC-3 tumors, and results clearly showed a dramatic decrease in tumor burden (Fig. 4B). In addition to the large decrease in tumor volume (70%), two of five mice (40%) had no detectable tumors at the end of the study. At well-tolerated doses, treatment with PS-341 clearly suppressed tumor growth. These data highlight the full antitumor potential of PS-341. Similar effects have been observed in other murine tumors and human xenograft tumors (data not shown). No adverse effects of drug treatment were noted during any of these studies.

Reference: Cancer Res. 1999 Jun 1;59(11):2615-22. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=10363983