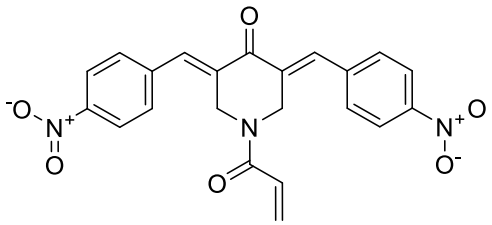
Product data sheet

MedKoo Cat#: 406452 Name: b-AP15 CAS#: 1009817-63-3 Chemical Formula: $C_{22}H_{17}N_3O_6$ Exact Mass: 419.11174 Molecular Weight: 419.39	
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:

b-AP15 is a novel inhibitor of proteasome deubiquitination. b-AP15 displays antitumor activity in several preclinical, solid tumor models. b-AP15 triggers time- and dose-dependent apoptosis of the human multiple myeloma (MM) cell lines RPMI8226 and U266, as determined by phosphatidylserine exposure. Furthermore, b-AP15 triggered processing of pro-caspase-3 and cleavage of poly (ADP-ribose) polymerase in MM cells. b-AP15 also induced caspase-independent apoptosis in primary human natural killer cells. b-AP15 may have potential for treatment of multiple myeloma patients.

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	20	47.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.38 mL	11.92 mL	23.84 mL
5 mM	0.48 mL	2.38 mL	4.77 mL
10 mM	0.24 mL	1.19 mL	2.38 mL
50 mM	0.05 mL	0.24 mL	0.48 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. D'Arcy P, Brnjic S, Olofsson MH, Fryknäs M, Lindsten K, De Cesare M, Perego P, Sadeghi B, Hassan M, Larsson R, Linder S. Inhibition of proteasome deubiquitinating activity as a new cancer therapy. Nat Med. 2011 Nov 6;17(12):1636-40. doi: 10.1038/nm.2536. PMID: 22057347.

2. Tian Z, D'Arcy P, Wang X, Ray A, Tai YT, Hu Y, Carrasco RD, Richardson P, Linder S, Chauhan D, Anderson KC. A novel small molecule inhibitor of deubiquitylating enzyme USP14 and UCHL5 induces apoptosis in multiple myeloma and overcomes bortezomib resistance. Blood. 2014 Jan 30;123(5):706-16. doi: 10.1182/blood-2013-05-500033. Epub 2013 Dec 6. PMID: 24319254; PMCID: PMC3907756.

In vivo study

1. D'Arcy P, Brnjic S, Olofsson MH, Fryknäs M, Lindsten K, De Cesare M, Perego P, Sadeghi B, Hassan M, Larsson R, Linder S. Inhibition of proteasome deubiquitinating activity as a new cancer therapy. Nat Med. 2011 Nov 6;17(12):1636-40. doi: 10.1038/nm.2536. PMID: 22057347.

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7. Bioactivity

Biological target:

b-AP15 is a specific inhibitor of the deubiquitinating enzymes UCHL5 and Usp14.

In vitro activity

Purified 19S proteasomes (5 nM) are treated with indicated concentrations of b-AP15 and DUB activity is determined by detectionof Ub-AMC cleavage. The IC50 value (2.1±0.411 μM) is determined from log concentration curves in Graph Pad Prism using non linear regression analysis. b-AP15 as a previously unidentified class of proteasome inhibitor that abrogates the deubiquitinating activity of the 19S regulatory particle. b-AP15 inhibited the activity of two 19S regulatory-particle-associated deubiquitinases, ubiquitin C-terminal hydrolase 5 (UCHL5) and ubiquitin-specific peptidase 14 (USP14), resulting in accumulation of polyubiquitin. b-AP15 induced tumor cell apoptosis that is insensitive to TP53 status and overexpression of the apoptosis inhibitor BCL2.

Reference: Nat Med. 2011 Nov 6;17(12):1636-40. https://doi.org/10.1038/nm.2536

In vivo activity

b-AP15 (2.5 mg/kg) inhibits tumor growth in syngenic mice models with less frequent administration schedules. We administered b-AP15 to C57BL/6J mice with Lewis lung carcinomas (LLCs) using a 2-d-on, 2-d-off schedule and to BALB/c mice with orthotopic breast carcinoma (4T1) using a 1-d-on, 3-d-off schedule. b-AP15 significantly inhibited tumor growth in both models, with T/C=0.16 ($P \leqslant 0.01$) for the C57BL/6J mice and T/C=0.25 ($P \leqslant 0.001$) for the BALB/c mice. A reduction in the number of pulmonary metastases also is observed in the group of mice with 4T1 breast carcinomas treated with b-AP15.

Reference: Nat Med. 2011 Nov 6;17(12):1636-40. https://doi.org/10.1038/nm.2536