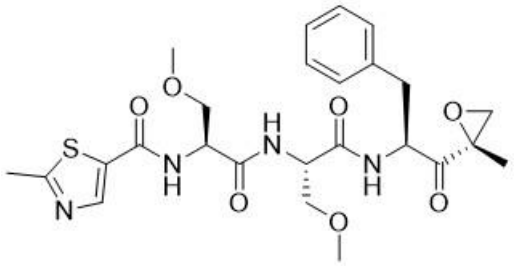
Product data sheet

MedKoo Cat#: 205565 Name: Oprozomib (ONX 0912) CAS#: 935888-69-0 Chemical Formula: $C_{25}H_{32}N_4O_7S$ Exact Mass: 532.19917 Molecular Weight: 532.61	
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:

Oprozomibm, also known as ONX 0912 and PR 047 , is a n orally bioavailable proteasome inhibitor with potential antineoplastic activity. ONX 0912 inhibits the activity of the proteasome, thereby blocking the targeted proteolysis normally performed by the proteasome; this may result in an accumulation of unwanted or misfolded proteins. Disruption of various cell signaling pathways may follow, eventually leading to the induction of apoptosis and inhibition of tumor growth. Proteasomes are large protease complexes that degrade unneeded or damaged proteins that have been ubiquitinated.

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	5.0	9.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.88	9.39	18.78
5 mM	0.38	1.88	3.76
10 mM	0.19	0.94	1.88
50 mM	0.04	0.19	0.38

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. Li QZ, Sun LP, Shi HY, Chen Y, Shen H. The new-generation proteasome inhibitor oprozomib increases the sensitivity of cervical cancer cells to cisplatin-induced apoptosis. J Biol Regul Homeost Agents. 2021 Mar-Apr;35(2):559-569. doi: 10.23812/20-504-A. PMID: 33973461.

2. Fan Y, Liang Z, Zhang J, You G. Oral Proteasomal Inhibitors Ixazomib, Oprozomib, and Delanzomib Upregulate the Function of Organic Anion Transporter 3 (OAT3): Implications in OAT3-Mediated Drug-Drug Interactions. Pharmaceutics. 2021 Feb 28;13(3):314. doi: 10.3390/pharmaceutics13030314. PMID: 33670955; PMCID: PMC7997269.

In vivo study

1. Chauhan D, Singh AV, Aujay M, Kirk CJ, Bandi M, Ciccarelli B, Raje N, Richardson P, Anderson KC. A novel orally active proteasome inhibitor ONX 0912 triggers in vitro and in vivo cytotoxicity in multiple myeloma. Blood. 2010 Dec 2;116(23):4906-15. doi: 10.1182/blood-2010-04-276626. Epub 2010 Aug 30. PMID: 20805366; PMCID: PMC3321748.

2. Semren N, Habel-Ungewitter NC, Fernandez IE, Königshoff M, Eickelberg O, Stöger T, Meiners S. Validation of the 2nd Generation Proteasome Inhibitor Oprozomib for Local Therapy of Pulmonary Fibrosis. PLoS One. 2015 Sep 4;10(9):e0136188. doi: 10.1371/journal.pone.0136188. PMID: 26340365; PMCID: PMC4560391.

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7. Bioactivity

Biological target:

Oprozomib (ONX 0912; PR047) is an inhibitor for CT-L activity of 20S proteasome β5/LMP7 with IC50 of 36 nM/82 nM and a 20S proteasome target.

In vitro activity

This study aimed to evaluate the anti-tumor effect of a new generation of protease inhibitor, oprozomib (OPZ), used alone and in combination with cisplatin, also called CDDP, on cervical cancer. Five different types of cervical cancer cell lines - HeLa, Caski, HeLa-CDDP, C33a, and SiHa - and one nontransformed cervical cell line - HaCaT -were treated with OPZ alone or in combination with cisplatin. The inhibitory effects of OPZ and cisplatin on the proliferation of cervical cancer cells were then analyzed using cytotoxicity tests, flow cytometry, and Western blotting. It was found that OPZ alone or in combination with cisplatin can reduce the proliferation of the five types of cancer cells by enhancing the lysis of caspase-3 and PARP and inducing cancer cell apoptosis. In the combined treatment, OPZ was found to inhibit the degradation of inhibitory factor κB alpha induced by cisplatin, thereby inhibiting the activation of NF-κB, which causes cisplatin resistance, and enhancing the sensitivity of the tumor cells to cisplatin. Moreover, OPZ promoted the phosphorylation of the apoptosis signaling pathway JNK that was activated by cisplatin, thereby inducing tumor cell apoptosis. These findings provide a theoretical basis for the clinical use of OPZ alone and in combination with cisplatin in the treatment of cervical cancer.

J Biol Regul Homeost Agents. Mar-Apr 2021;35(2):559-569.

In vivo activity

A marked growth inhibitory effect of ONX 0912 was observed in 2 distinct human MM xenograft mouse models. INA-6 MM cells are injected directly into human bone chips that are implanted subcutaneously in SCID mice, and MM cell growth is assessed by serial measurements of circulating levels of soluble human IL-6R in mouse serum. A more robust growth inhibition of tumor occurred in mice receiving oral doses (30 mg/kg or 50 mg/kg) of ONX 0912 than in mice injected with vehicle alone (Figure 5B). Importantly, treatment of tumor-bearing mice with ONX 0912, but not vehicle alone, significantly prolonged survival (P = .03; Figure 5C). A head-to-head analysis of carfilzomib and ONX 0912 showed equipotent antitumor activity in a human plasmacytoma xenograft mouse model. The findings are consistent with reported antitumor activity of ONX 0912 in nonHodgkin lymphoma (NHL) tumor xenograft and mouse syngeneic models. ONX 0912 is well tolerated, inhibits tumor growth, and prolongs survival in mice

Blood. 2010 Dec 2; 116(23): 4906–4915. Prepublished online 2010 Aug 30.