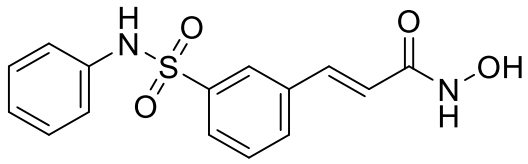
Product data sheet

MedKoo Cat#: 200460 Name: Belinostat CAS#: 866323-14-0 Chemical Formula: $C_{15}H_{14}N_2O_4S$ Exact Mass: 318.06743 Molecular Weight: 318.34	
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:
Belinostat is a novel hydroxamic acid-type histone deacetylase (HDAC) inhibitor with antineoplastic activity. Belinostat targets HDAC enzymes, thereby inhibiting tumor cell proliferation, inducing apoptosis, promoting cellular differentiation, and inhibiting angiogenesis. This agent may sensitize drug-resistant tumor cells to other antineoplastic agents, possibly through a mechanism involving the down-regulation of thymidylate synthase. Belinostat was approved in 2014 for relapsed or refractory peripheral T-cell lymphoma.

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	64	201.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.14 mL	15.71 mL	31.41 mL
5 mM	0.63 mL	3.14 mL	6.28 mL
10 mM	0.31 mL	1.57 mL	3.14 mL
50 mM	0.06 mL	0.31 mL	0.63 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. Plumb JA, Finn PW, Williams RJ, Bandara MJ, Romero MR, Watkins CJ, La Thangue NB, Brown R. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8. PMID: 12939461.

2. Plumb JA, Finn PW, Williams RJ, Bandara MJ, Romero MR, Watkins CJ, La Thangue NB, Brown R. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8. PMID: 12939461.

In vivo study

1. Plumb JA, Finn PW, Williams RJ, Bandara MJ, Romero MR, Watkins CJ, La Thangue NB, Brown R. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8. PMID: 12939461.

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2. Plumb JA, Finn PW, Williams RJ, Bandara MJ, Romero MR, Watkins CJ, La Thangue NB, Brown R. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8. PMID: 12939461.

7. Bioactivity

Biological target:

Belinostat (PXD101; PX105684) is a potent HDAC inhibitor with an IC50 of 27 nM in HeLa cell extracts.

In vitro activity

PXD101 inhibited the growth of a number of human tumor cell lines in vitro with IC50s determined by a clonogenic assay in the range 0.2–3.4 μm (Table 1). There was no effect on colony size. Sensitivity to PXD101 is not related to the total HDAC activity of the cell line or inhibition of this activity in the cell lysate. There was no correlation between sensitivity to PXD101 and sensitivity to a DNA-damaging agent, such as cisplatin (r2 = 0.01). The cisplatin- (A2780/cp70) and doxorubicin (2780AD, p-glycoprotein positive)-resistant derivatives of the human ovarian tumor cell line A2780 showed low fold cross-resistance to PXD101. PXD101 induced apoptosis as determined by measurement of PARP cleavage after drug incubation for 24 h (Fig. 3a). PARP cleavage was detected in all cell lines examined except for PC3 and 2780AD (Fig. 3a). Interestingly, these two cell lines are not the most resistant to PXD101, and the lines did not show PARP cleavage when incubated with the DNA-damaging agent cisplatin (50 μm; data not shown). The colon tumor cell line HCT116 was markedly sensitive to induction of PARP cleavage, which was observed after drug incubation for between 18 and 24 h and at a PXD101 concentration as low as 0.16 μm (Fig. 3b). Acetylation of histones H3 and H4 was also clearly apparent after incubation for 1 h with PXD101 at these concentrations.

Reference: Mol Cancer Ther. 2003 Aug;2(8):721-8. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=12939461

In vivo activity

Tumor-bearing mice were treated i.p. with PXD101 once daily for 7 days. Significant ($P < 0.01$) growth delay was observed at a dose of 10 mg/kg/day in xenografts of A2780 (Fig. 4a) and in the cisplatin derivative (A2780/cp70; Fig. 4c). For both tumors, growth delay increased with increasing dose of PXD101 up to a dose of 40 mg/kg/day. Drug treatment had no effect on the body weight of the mice (Fig. 4b), and there were no apparent signs of toxicity to the mice. Growth inhibition was also observed in xenografts of the human colon tumor cell line HCT116 (Fig. 4d). Acetylated histone H4 was detected in peripheral blood mononuclear cells at 1 and 2 h after a single i.p. injection of PXD101 (40 mg/kg) to A2780 tumor-bearing mice and had returned to baseline levels by 3 h (Fig. 5a). This effect of PXD101 on histone acetylation was dose dependent with marked acetylation apparent at doses of $\geqslant$10 mg/kg in both peripheral blood mononuclear cells (blood) and tumor (Fig. 5b). Plasma drug concentrations were determined at 0.5 and 2 h after a single i.p. injection of PXD101 (20 mg/kg) in mice. At 0.5 h, the mean drug concentration was 3.3 ± 0.7 μm (n = 3), and it had decreased to 0.042 ± 0.002 μm by 2 h.

Reference: Mol Cancer Ther. 2003 Aug;2(8):721-8. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=12939461

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.