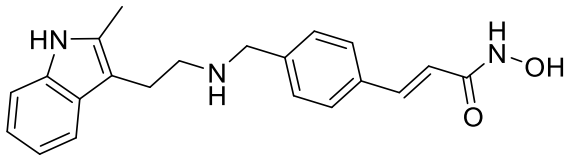
Product data sheet

MedKoo Cat#: 202151 Name: Panobinostat CAS#: 404950-80-7 (free base) Chemical Formula: $C_{21}H_{23}N_3O_2$ Exact Mass: 349.17903 Molecular Weight: 349.43	
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:

Panobinostat, also known as NVP LBH-589 or LBH-589, is a cinnamic hydroxamic acid analogue with potential antineoplastic activity. Panobinostat selectively inhibits histone deacetylase (HDAC), inducing hyperacetylation of core histone proteins, which may result in modulation of cell cycle protein expression, cell cycle arrest in the G2/M phase and apoptosis. In addition, this agent appears to modulate the expression of angiogenesis-related genes, such as hypoxia-inducible factor-1alpha (HIF-1a) and vascular endothelial growth factor (VEGF), thus impairing endothelial cell chemotaxis and invasion. On 2/23/2015, it received FDA accelerated approval for use in patients with multiple myeloma who had received at least 2 previous treatments, including bortezomib and an immunomodulatory agent.

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	33.0	94.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.86 mL	14.31 mL	28.62 mL
5 mM	0.57 mL	2.86 mL	5.72 mL
10 mM	0.29 mL	1.43 mL	2.86 mL
50 mM	0.06 mL	0.29 mL	0.57 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. Crisanti MC, Wallace AF, Kapoor V, Vandermeers F, Dowling ML, Pereira LP, Coleman K, Campling BG, Fridlender ZG, Kao GD, Albelda SM. The HDAC inhibitor panobinostat (LBH589) inhibits mesothelioma and lung cancer cells in vitro and in vivo with particular efficacy for small cell lung cancer. Mol Cancer Ther. 2009 Aug;8(8):2221-31. doi: 10.1158/1535-7163.MCT-09-0138. Epub 2009 Aug 11. PMID: 19671764; PMCID: PMC3605895.

2. Scuto A, Kirschbaum M, Kowolik C, Kretzner L, Juhasz A, Atadja P, Pullarkat V, Bhatia R, Forman S, Yen Y, Jove R. The novel histone deacetylase inhibitor, LBH589, induces expression of DNA damage response genes and apoptosis in Ph- acute lymphoblastic leukemia cells. Blood. 2008 May 15;111(10):5093-100. doi: 10.1182/blood-2007-10-117762. Epub 2008 Mar 18. PMID: 18349321; PMCID: PMC2384136.

In vivo study

Product data sheet

1. Crisanti MC, Wallace AF, Kapoor V, Vandermeers F, Dowling ML, Pereira LP, Coleman K, Campling BG, Fridlender ZG, Kao GD, Albelda SM. The HDAC inhibitor panobinostat (LBH589) inhibits mesothelioma and lung cancer cells in vitro and in vivo with particular efficacy for small cell lung cancer. Mol Cancer Ther. 2009 Aug;8(8):2221-31. doi: 10.1158/1535-7163.MCT-09-0138. Epub 2009 Aug 11. PMID: 19671764; PMCID: PMC3605895.

2. Tsai P, Wu G, Baker CE, Thayer WO, Spagnuolo RA, Sanchez R, Barrett S, Howell B, Margolis D, Hazuda DJ, Archin NM, Garcia JV. In vivo analysis of the effect of panobinostat on cell-associated HIV RNA and DNA levels and latent HIV infection. Retrovirology. 2016 May 21;13(1):36. doi: 10.1186/s12977-016-0268-7. PMID: 27206407; PMCID: PMC4875645.

7. Bioactivity

Biological target:

Panobinostat (LBH589, NVP-LBH589) is a novel broad-spectrum HDAC inhibitor with IC50 of 5 nM in a cell-free assay.

In vitro activity

Two model human Ph(-) ALL cell lines (T-cell MOLT-4 and pre-B-cell Reh) were treated with LBH589 and evaluated for biologic and gene expression responses. Low nanomolar concentrations (IC(50): 5-20 nM) of LBH589 induced cell-cycle arrest, apoptosis, and histone (H3K9 and H4K8) hyperacetylation. LBH589 treatment increased mRNA levels of proapoptosis, growth arrest, and DNA damage repair genes including FANCG, FOXO3A, GADD45A, GADD45B, and GADD45G. The most dramatically expressed gene (up to 45-fold induction) observed after treatment with LBH589 is GADD45G. LBH589 treatment was associated with increased histone acetylation at the GADD45G promoter and phosphorylation of histone H2A.X. Furthermore, treatment with LBH589 was active against cultured primary Ph(-) ALL cells, including those from a relapsed patient, inducing loss of cell viability (up to 70%) and induction of GADD45G mRNA expression (up to 35-fold). Thus, LBH589 possesses potent growth inhibitory activity against including Ph(-) ALL cells associated with up-regulation of genes critical for DNA damage response and growth arrest. These findings provide a rationale for exploring the clinical activity of LBH589 in the treatment of patients with Ph(-) ALL.

Reference: Blood. 2008 May 15;111(10):5093-100. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18349321/

In vivo activity

In lung cancer and mesothelioma animal models, panobinostat significantly decreased tumor growth by an average of 62% when compared with vehicle control. Panobinostat was equally effective in immunocompetent and severe combined immunodeficiency mice, indicating that the inhibition of tumor growth by panobinostat was not due to direct immunologic effects. Panobinostat was, however, particularly effective in small cell lung cancer (SCLC) xenografts, and the addition of the chemotherapy agent etoposide augmented antitumor effects. Protein analysis of treated tumor biopsies revealed elevated amounts of cell cycle regulators such as p21 and proapoptosis factors, such as caspase 3 and 7 and cleaved poly[ADP-ribose] polymerase, coupled with decreased levels of antiapoptotic factors such as Bcl-2 and Bcl-X(L). These studies together suggest that panobinostat may be a useful adjunct in the treatment of thoracic malignancies, especially SCLC.

Reference: Mol Cancer Ther. 2009 Aug;8(8):2221-31. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/19671764/