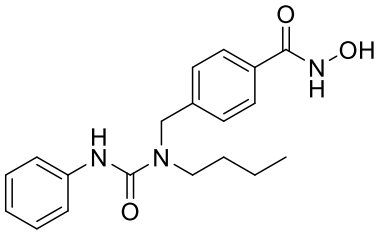
Product data sheet

MedKoo Cat#: 406549 Name: Nexturastat A CAS#: 1403783-31-2 Chemical Formula: $C_{19}H_{23}N_3O_3$ Exact Mass: 341.17394 Molecular Weight: 341.4	
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:
Nexturastat A is an aryl urea derivative that acts as a potent and highly selective inhibitor of histone deacetylase 6 (HDAC6) (IC50= 5.02 +/- 0.60 nM). Nexturastat A possesses antiproliferative effects against melanoma cells. Histone deacetylases (HDACs) mediate regulation of gene expression via changes in nucleosome conformation. Dysregulation of histone acetylation can lead to the development of cancers. There is renewed interest in capitalizing new breakthroughs in epigenetic research to address oncology therapy.

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	15.0	43.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.93 mL	14.65 mL	29.29 mL
5 mM	0.59 mL	2.93 mL	5.86 mL
10 mM	0.29 mL	1.46 mL	2.93 mL
50 mM	0.06 mL	0.29 mL	0.59 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. Sun X, Xie Y, Sun X, Yao Y, Li H, Li Z, Yao R, Xu K. The selective HDAC6 inhibitor Nexturastat A induces apoptosis, overcomes drug resistance and inhibits tumor growth in multiple myeloma. Biosci Rep. 2019 Mar 22;39(3):BSR20181916. doi: 10.1042/BSR20181916. PMID: 30782785; PMCID: PMC6430725.

In vivo study

1. Knox T, Sahakian E, Banik D, Hadley M, Palmer E, Noonepalle S, Kim J, Powers J, Gracia-Hernandez M, Oliveira V, Cheng F, Chen J, Barinka C, Pinilla-Ibarz J, Lee NH, Kozikowski A, Villagra A. Selective HDAC6 inhibitors improve anti-PD-1 immune checkpoint blockade therapy by decreasing the anti-inflammatory phenotype of macrophages and down-regulation of immunosuppressive proteins in tumor cells. Sci Rep. 2019 Apr 16;9(1):6136. doi: 10.1038/s41598-019-42237-3. Erratum in: Sci Rep. 2019 Oct 10;9(1):14824. PMID: 30992475; PMCID: PMC6467894.

7. Bioactivity
Biological target:
Nexturastat A is a HDAC6 inhibitor with IC50 of 5 nM.

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In vitro activity

To figure out the internal molecular mechanism of NexA (Nexturastat A)-inducing apoptosis of MM (multiple myeloma) cells, the expression levels of apoptosis-related factors were estimated utilizing real-time PCR. The results showed that the p21 mRNA levels were higher in RPMI-8226 and U266 cells treated for 48 h (Figure 4A,B). Then Western blot assay manifested that NexA treatment also resulted in evident increases in p21 protein levels in both cell lines (Figure 4C). After which this study carried out p21 luciferase reporter gene assays to determine whether NexA could enhance the promoter activity of p21 accordingly. The data indicated the enhanced activity of p21 with 5 and 10 μM NexA for both cell lines (Figure 4D,E). This study also evaluated p21 induction in RPMI8226/BTZ100 cells. As shown in Figure 4C, F, p21 mRNA and protein levels increased after cells were treated with 20 μM NexA. This study observed enhanced p21 promoter activity in RPMI8226/BTZ100 cells treated with 3 and 5 μM NexA (Figure 4G).

Reference: Biosci Rep. 2019 Mar 29; 39(3): BSR20181916. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6430725/

In vivo activity

This study observed a slight increase in the tumor infiltration of NK cells upon treatment with NextA (Nexturastat A) across all in vivo experiments. Therefore, this study wanted to investigate whether the inhibition of HDAC6 was able to modify the phenotype of these immune cells. Fresh NK cells were harvested from non-tumor bearing wild type C57BL/6 mice and treated with NextA to investigate the reported markers for NK cell activity and cytotoxicity, such as Granzyme B, TRAIL, and Fas ligand. Although this study observed an enhanced tumor infiltration of NK cells in all in vivo conditions using NextA, the aforementioned activation markers were minimally affected in isolated NK cells treated with this drug (Fig. 5A), suggesting that the enhanced NK infiltration observed after NextA treatment could be mediated by other indirect mechanisms.

Reference: Sci Rep. 2019; 9: 6136. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6467894/