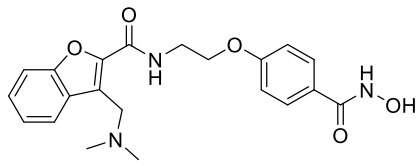
Product data sheet

MedKoo Cat#: 202170 Name: Abexinostat CAS#: 783355-60-2 (free base) Chemical Formula: $C_{21}H_{23}N_3O_5$ Exact Mass: 397.16377 Molecular Weight: 397.42	
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:

Abexinostat, also known as PCI-24781 or CRA-024781, is novel, broad-spectrum hydroxamic acid-based inhibitor of histone deacetylase (HDAC) with potential antineoplastic activity. Abexinostat inhibits several isoforms of HDAC, resulting in an accumulation of highly acetylated histones, followed by the induction of chromatin remodeling; the selective transcription of tumor suppressor genes; and the tumor suppressor protein-mediated inhibition of tumor cell division and induction of tumor cell apoptosis.

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	16.67	41.95
DMF	50.0	125.81
DMF:PBS (pH 7.2) (1:3)	0.1	0.25
Ethanol	3.0	7.55
5% TFA	3.0	7.55

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.52 mL	12.58 mL	25.16 mL
5 mM	0.50 mL	2.52 mL	5.03 mL
10 mM	0.25 mL	1.26 mL	2.52 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Ali D, Hamam R, Alfayez M, Kassem M, Aldahmash A, Alajez NM. Epigenetic Library Screen Identifies Abexinostat as Novel Regulator of Adipocytic and Osteoblastic Differentiation of Human Skeletal (Mesenchymal) Stem Cells. Stem Cells Transl Med. 2016 Aug;5(8):1036-47. doi: 10.5966/sctm.2015-0331. Epub 2016 May 18. PMID: 27194745; PMCID: PMC4954455.
2. Bhalla S, Evens AM, Prachand S, Schumacker PT, Gordon LI. Paradoxical regulation of hypoxia inducible factor-1α (HIF-1α) by histone deacetylase inhibitor in diffuse large B-cell lymphoma. PLoS One. 2013 Nov 27;8(11):e81333. doi: 10.1371/journal.pone.0081333. PMID: 24312289; PMCID: PMC3842257.

In vivo study

1. Salvador MA, Wicinski J, Cabaud O, Toiron Y, Finetti P, Josselin E, Lelièvre H, Kraus-Berthier L, Depil S, Bertucci F, Collette Y, Birnbaum D, Charafe-Jauffret E, Ginestier C. The histone deacetylase inhibitor abexinostat induces cancer stem cells differentiation in

breast cancer with low Xist expression. Clin Cancer Res. 2013 Dec 1;19(23):6520-31. doi: 10.1158/1078-0432.CCR-13-0877. Epub 2013 Oct 18. PMID: 24141629.
2. Kitamura T, Connolly K, Ruffino L, Ajiki T, Lueckgen A, DiGiovanni J, Kiguchi K. The therapeutic effect of histone deacetylase inhibitor PCI-24781 on gallbladder carcinoma in BK5.erbB2 mice. J Hepatol. 2012 Jul;57(1):84-91. doi: 10.1016/j.jhep.2012.01.018. Epub 2012 Feb 9. PMID: 22326466; PMCID: PMC3378818.

7. Bioactivity

Biological target:

Abexinostat (CRA 024781) is a pan-HDAC inhibitor mostly targeting HDAC1 with Ki of 7 nM.

In vitro activity

Abexinostat enhanced both osteoblast and adipocyte differentiation, and thus it is plausible that it targets the initial phase of commitment of hMSCs to both adipocytic and osteoblastic lineages. The previously mentioned and discussed data from DNA microarrays and ChIP-seq corroborate this hypothesis because they clearly demonstrate the induction of multiple gene and genetic pathways associated with hMSC lineage commitment. This hypothesis and its potential molecular mechanism are illustrated in the current working model (Fig. 6). Interestingly, despite marked global increase in H3K9Ac, this study observed overall fewer enriched genes in the abexinostat-treated cells compared with the control (Fig. 4D). Therefore, it seems as if abexinostat is targeting specific genomic regions, which normally have low H3K9Ac, including those related to hMSC differentiation. On the other hand, genes with high basal H3K9ac signal are not benefiting much from abexinostat. Thus, acetylation marks appear to be being diverged from genes with high basal H3K9Ac signal (such as GAPDH) to those with low basal H3K9Ac signal (such as CEBPA, PPARγ, SP7, and ALPL). Nonetheless, a plausible role for abexinostat in targeting non-H3K9 residues for acetylation or the increase in hMSC commitment could also contribute to the observed phenotype.

Reference: Stem Cells Transl Med. 2016 Aug; 5(8): 1036–1047. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4954455/

In vivo activity

An in vivo therapeutic study in BK5.erbB2 mice showed that GBCas sensitive to PCI-24781 treatment (diagnosed as PR (Partial Response)) had greatly reduced levels of p-erbB2 and total erbB2 compared to GBCas refractory to treatment (diagnosed as PG (Progressive Disease)). These results indicate that the inhibitory effect of PCI-24781 was not potent enough to reduce the levels of p-erbB2 and total erbB2 in the PG cases. This hypothesis is supported by results showing that the level of erbB2 mRNA was significantly decreased in gallbladders diagnosed as PR, but not in those diagnosed as PG (Fig. 2).

Reference: J Hepatol. 2012 Jul; 57(1): 84–91. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3378818/