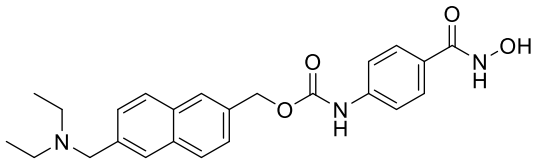
Product data sheet

MedKoo Cat#: 205774 Name: Givinostat free base CAS#: 497833-27-9 (free base) Chemical Formula: $C_{24}H_{27}N_3O_4$ Exact Mass: 421.20016 Molecular Weight: 421.497	
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:

Givinostat or gavinostat, aslo known as ITF2357, is a potent and orally active histone deacetylase inhibitor with potential anti-inflammatory, anti-angiogenic, and antineoplastic activities. It is a hydroxamate used in the form of its hydrochloride. Inhibition of HDAC activity by ITF2357 ameliorates joint inflammation and prevents cartilage and bone destruction in experimental arthritis.ITF2357 reduces cytokines and protects islet β cells in vivo and in vitro. ITF2357 decreases surface CXCR4 and CCR5 expression on CD4(+) T-cells and monocytes and is superior to valproic acid for latent HIV-1 expression in vitro.

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
TBD	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.37 mL	11.86 mL	23.72 mL
5 mM	0.47 mL	2.37 mL	4.74 mL
10 mM	0.24 mL	1.19 mL	2.37 mL
50 mM	0.05 mL	0.24 mL	0.47 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. Wang YG, Xu L, Wang T, Wei J, Meng WY, Wang N, Shi M. Givinostat inhibition of hepatic stellate cell proliferation and protein acetylation. World J Gastroenterol. 2015 Jul 21;21(27):8326-39. doi: 10.3748/wjg.v21.i27.8326. PMID: 26217084; PMCID: PMC4507102.

2. Leoni F, Fossati G, Lewis EC, Lee JK, Porro G, Pagani P, Modena D, Moras ML, Pozzi P, Reznikov LL, Siegmund B, Fantuzzi G, Dinarello CA, Mascagni P. The histone deacetylase inhibitor ITF2357 reduces production of pro-inflammatory cytokines in vitro and systemic inflammation in vivo. Mol Med. 2005 Jan-Dec;11(1-12):1-15. doi: 10.2119/2006-00005.Dinarello. PMID: 16557334; PMCID: PMC1449516.

In vivo study

1. Leoni F, Fossati G, Lewis EC, Lee JK, Porro G, Pagani P, Modena D, Moras ML, Pozzi P, Reznikov LL, Siegmund B, Fantuzzi G, Dinarello CA, Mascagni P. The histone deacetylase inhibitor ITF2357 reduces production of pro-inflammatory cytokines in vitro and systemic inflammation in vivo. Mol Med. 2005 Jan-Dec;11(1-12):1-15. doi: 10.2119/2006-00005.Dinarello. PMID: 16557334; PMCID: PMC1449516.

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7. Bioactivity

Biological target:

Givinostat (ITF-2357) is a HDAC inhibitor with an IC50 of 198 and 157 nM for HDAC1 and HDAC3, respectively.

In vitro activity

Givinostat significantly inhibited JS-1 cell proliferation and promoted cell apoptosis, leading to cell cycle arrest in G0/G1 phases. Treatment with givinostat downregulated protein expression of CDK4, CDK6, and cyclin D1, whereas expression of p21 and p57 was significantly increased. The givinostat-induced apoptosis of hepatic stellate cells was mainly mediated through p38 and extracellular signal-regulated kinase 1/2. Givinostat treatment increased intracellular reactive oxygen species production, decreased mitochondrial membrane potential, and promoted mitochondrial permeability transition pore opening. Acetylation of superoxide dismutase (acetyl K68) and nuclear factor-κB p65 (acetyl K310) was upregulated, while there was no change in protein expression. Moreover, the notable beneficial effect of givinostat on liver fibrosis was also confirmed in the mouse models.

Reference: World J Gastroenterol. 2015 Jul 21;21(27):8326-39. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26217084/

In vivo activity

Mice were given 100 μL water or ITF2357 (5 mg/kg) by gavage and, after 1 h, injected intravenously with 200 μg/mouse of ConA. Control mice received an intravenous injection of saline. Mice were bled 24 h later for evaluation of serum ALT levels as described previously (33,34). As shown in Figure 15, ALT levels were reduced by more than 80% by ITF2357 pretreatment. In another experiment, a comparison was made between 1 and 10 mg/kg of oral ITF2357. As shown in Figure 16, a dose of 1 mg/kg ITF2357 was as effective as a dose of 10 mg/kg in reducing ConA hepatitis as measured by ALT levels.

Reference: Mol Med. 2005 Jan-Dec;11(1-12):1-15. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/16557334/

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.