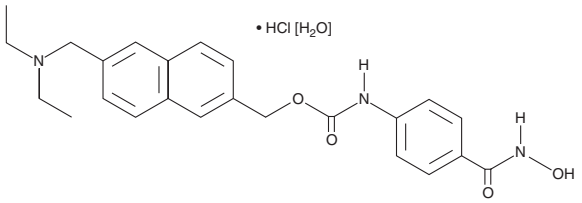
PRODUCT INFORMATION

ITF 2357

Item No. 11045

CAS Registry No.: 732302-99-7
Formal Name: N-[4-[(hydroxyamino)carbonyl]phenyl]-carbamic acid, [6-[(diethylamino)methyl]-2-naphthalenyl]methyl ester, monohydrochloride, monohydrate
Synonym: Givinostat
MF: $C_{24}H_{27}N_3O_4 \bullet HCl\ [H_2O]$
FW: 476.0
Purity: ≥98%
UV/Vis.: λ_{max}: 228, 265 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ITF 2357 is supplied as a crystalline solid. A stock solution may be made by dissolving the ITF 2357 in the solvent of choice, which should be purged with an inert gas. ITF 2357 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of ITF 2357 in ethanol is approximately 2 mg/ml and approximately 30 mg/ml in DMSO and DMF.

ITF 2357 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ITF 2357 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. ITF 2357 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

ITF 2357 is an inhibitor of class I and class II histone deacetylases (HDACs).[1] It inhibits HDAC1, -2, -3, -4, -6, and -7 in a fluorometric assay using a baculoviral system expressing the recombinant human isoforms (EC_{50}s = 28, 56, 21, 52, 27, and 163 nM, respectively). ITF 2357 (0.2 µM) reduces the viability of Raji, NAMALWA, SU-DHL-4, and DoHH2 c-Myc$^+$ B cell non-Hodgkin lymphoma (NHL) cells, as well as reduces the expression of c-Myc and induces apoptosis in the same cells.[2] It reduces tumor volume in Raji or NAMALWA mouse xenograft models when administered alone at a dose of 50 mg/kg, with an additive effect when administered in combination with cyclophosphamide (Item No. 13849). ITF 2357 decreases LPS-induced secretion of TNF-α, IL-1α, IL-1β, and IFN-γ in primary human peripheral blood mononuclear cells (PBMCs).[3] It also reduces LPS-induced increases in serum Tnf-α and Ifn-γ in mice when administered at doses ranging from 1 to 10 mg/kg. Formulations containing ITF 2357 have been used in the treatment of Duchenne muscular dystrophy (DMD).

References

1. Khan, N., Jeffers, M., Kumar, S., *et al.* Determination of the class and isoform selectivity of small-molecule histone deacetylase inhibitors. *Biochem. J.* **409(2)**, 581-589 (2008).
2. Zappasodi, R., Cavanè, A., Iorio, M.V., *et al.* Pleiotropic antitumor effects of the pan-HDAC inhibitor ITF2357 against c-Myc-overexpressing human B-cell non-Hodgkin lymphomas. *Int. J. Cancer* **135(9)**, 2034-2045 (2014).
3. Leoni, F., Fossati, G., Lewis, E.C., *et al*. The histone deacetylase inhibitor ITF2357 reduces production of pro-inflammatory cytokines *in vitro* and systemic inflammation *in vivo*. *Mol. Med*. **11(1-12)**, 1-15 (2005).

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