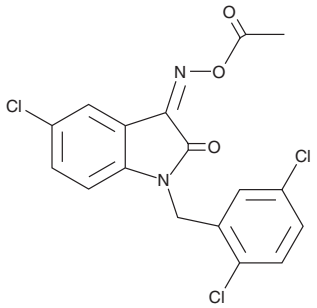
PRODUCT INFORMATION

LDN-57444

Item No. 15396

CAS Registry No.:	668467-91-2
Formal Name:	5-chloro-1-[(2,5-dichlorophenyl) methyl]-1H-indole-2,3-dione 3-(O-acetyloxime)
Synonyms:	Ubiquitin C-terminal Hydrolase L1 Inhibitor, UCH-L1 Inhibitor
MF:	$C_{17}H_{11}Cl_3N_2O_3$
FW:	397.6
Purity:	≥95%
UV/Vis.:	λ_{max}: 226, 254 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

LDN-57444 is supplied as a crystalline solid. A stock solution may be made by dissolving the LDN-57444 in the solvent of choice. LDN-57444 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of LDN-57444 in these solvents is approximately 3 and 16 mg/ml, respectively.

LDN-57444 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, LDN-57444 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. LDN-57444 has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The ubiquitin C-terminal hydrolase L1 (UCH-L1) is a member of a family of de-ubiquitinating enzymes that can generate free ubiquitin from ubiquitin precursors *via* its ubiquitin ligase activity. By associating with free ubiquitin, it also prevents its degradation. Neuronal UCH-L1 has been linked to Parkinson's disease, the development of tumors, and neuropathic pain.[1] LDN-57444 is an inhibitor of UCH-L1 activity (IC_{50} = 0.88, K_i = 0.4 µM) that demonstrates selectivity for UCH-L1 compared to UCH-L3 (IC_{50} = 25 µM).[2] Loss of UCH-L1 activity causes cell death through the apoptosis pathway due to an impaired ubiquitin-proteasome pathway. LDN-57444-induced reduction of free ubiquitin has been shown to create dramatic alterations in synaptic structure and function, increasing spine size while decreasing spine density in hippocampal neurons.[1]

References

1. Cartier, A.E., Djakovic, S.N., Salehi, A., *et al.* Regulation of synaptic structure by the ubiquitin C-terminal hydrolase UCH-L1. *J. Neurosci.* **29(24)**, 7857-7868 (2009).
2. Liu, Y., Lashuel, H.A., Choi, S., *et al.* Discovery of inhibitors that elucidate the role of UCH-L1 activity in the H1299 lung cancer cell line. *Chem. Biol.* **10(9)**, 837-846 (2003).

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