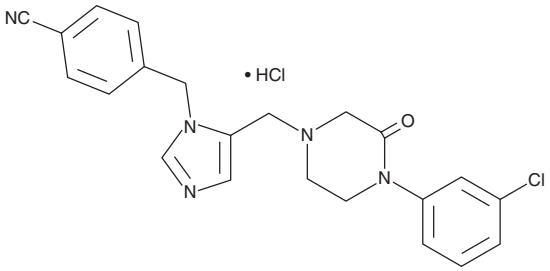
PRODUCT INFORMATION

L-778,123 (hydrochloride)

Item No. 22940

CAS Registry No.: 253863-00-2
Formal Name: 4-[[5-[[4-(3-chlorophenyl)-3-oxo-1-piperazinyl]methyl]-1H-imidazol-1-yl]methyl]-benzonitrile, monohydrochloride, trifluoroacetate salt
MF: $C_{22}H_{20}ClN_5O \bullet HCl$
FW: 442.3
Purity: ≥98%
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years



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

Laboratory Procedures

L-778,123 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the L-778,123 (hydrochloride) in the solvent of choice. L-778,123 (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of L-778,123 (hydrochloride) is approximately 10 mg/ml in ethanol and approximately 12.5 mg/ml in DMSO and DMF.

Description

L-778,123 (hydrochloride) is a dual inhibitor of farnesyl transferase (FTase; IC_{50} = 2 nM) and geranylgeranyl transferase type I (GGTase I; IC_{50} = 98 nM).[1] It inhibits prenylation of the FTase and GGTase I substrates HDJ2 and RAP1A in PSN-1 pancreatic tumor cells (EC_{50}s = 92 and 6,760 nM, respectively). L-778,123 (hydrochloride) (1-300 µM) also inhibits prenylation of the oncogenic protein KI-RAS in PSN-1 cells in a concentration-dependent manner. *Ex vivo*, L-778,123 (hydrochloride) (35-50 mg/kg per day) reduces HDJ2 and RAP1A prenylation in dog peripheral blood mononuclear cells (PBMCs) but has no effect on KI-RAS prenylation in patient-derived PBMCs. L-778,123 (hydrochloride) inhibits lectin-induced expression of the T cell activation markers CD71 and CD25 on human PMBCs (IC_{50}s = 6.48 and 84.1 µM, respectively) and inhibits IL-2-induced proliferation of CTLL-2 cells (IC_{50} = 0.81 µM).[2]

References

1. Lobell, R.B., Liu, D., Buser, C.A., *et al.* Preclinical and clinical pharmacodynamic assessment of L-778,123, a dual inhibitor of farnesyl:protein transferase and geranylgeranyl:protein transferase type-I. *Mol. Cancer Ther.* **1(9)**, 747-758 (2002).
2. Si, M.-S., Reitz, B.A., and Borie, D.C. Inhibition of lymphocyte activation and function by the prenylation inhibitor L-778,123. *Invest New Drugs* **23(1)**, 21-29 (2005).

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