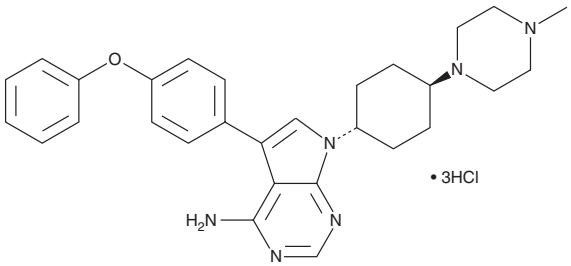
PRODUCT INFORMATION

A-419259 (hydrochloride)

Item No. 18168

CAS Registry No.: 1435934-25-0
Formal Name: 7-[*trans*-4-(4-methyl-1-piperazinyl) cyclohexyl]-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine, trihydrochloride
Synonym: RK-20449
MF: $C_{29}H_{34}N_6O$ • 3HCl
FW: 592.0
Purity: ≥95%
UV/Vis.: λ_{max}: 238, 291 nm
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

A-419259 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the A-419259 (hydrochloride) in the solvent of choice. A-419259 (hydrochloride) is soluble in the organic solvent methanol, which should be purged with an inert gas, at a concentration of approximately 1.4 mg/ml.

Description

A-419259 is an inhibitor of Src family kinases, including Src, LCK, Lyn, and Hck (IC_{50}s = 9, <3, <3, and 11.26 nM, respectively).[1,2] It is selective for these kinases over c-Abl (IC_{50} = 3,000 nM) and PKC (IC_{50} = >33 µM).[1] A-419259 inhibits growth of Philadelphia chromosome-positive (Ph^+) K-562 and Meg-01 myeloid leukemia cells (IC_{50}s = 0.1-0.3 and 0.1 µM, respectively), but not Ph^- TF-1 and HEL cells. It induces apoptosis in K-562 cells in a concentration-dependent manner. A-419259 (300 nM) inhibits differentiation of murine embryonic stem cells while maintaining pluripotency.[3] It reduces the total number of acute myeloid leukemia (AML) cells, as well as AML stem cells, in the bone marrow and spleen in mouse patient-derived xenograft (PDX) models of AML when administered at a dose of 30 mg/kg twice daily.[4]

References

1. Wilson, M.B., Schreiner, S.J., Choi, H.J., *et al.* Selective pyrrolo-pyrimidine inhibitors reveal a necessary role for Src family kinases in Bcr-Abl signal transduction and oncogenesis. *Oncogene* **21(53)**, 8075-8088 (2002).
2. Pene-Dumitrescu, T., Peterson, L.F., Donato, N.J., *et al.* An inhibitor-resistant mutant of Hck protects CML cells against the antiproliferative and apoptotic effects of the broad-spectrum Src family kinase inhibitor A-419259. *Oncogene* **27(56)**, 7055-7069 (2008).
3. Meyn, M.A., III, Schreiner, S.J., Dumitresco, T.P., *et al.* SRC family kinase activity is required for murine embryonic stem cell growth and differentiation. *Mol. Pharmacol.* **68(5)**, 1320-1330 (2005).
4. Saito, Y., Yuki, H., Kuratani, M., *et al.* A pyrrolo-pyrimidine derivative targets human primary AML stem cells *in vivo*. *Sci. Transl. Med.* **5(181)**:181ra52, (2013).

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