

PRODUCT INFORMATION

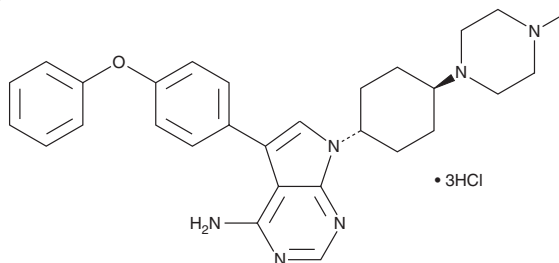


A-419259 (hydrochloride)

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: C₂₉H₃₄N₆O • 3HCl
FW: 592.0
Purity: ≥95%
UV/Vis.: λ_{max}: 238, 291 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

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, which should be purged with an inert gas. A-419259 (hydrochloride) is soluble in the organic solvent methanol 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 (IC₅₀s = 9, <3, <3, and 11.26 nM, respectively).^{1,2} It is selective for these kinases over c-Abl (IC₅₀ = 3,000 nM) and PKC (IC₅₀ = >33 μM).¹ A-419259 inhibits growth of Philadelphia chromosome-positive (Ph⁺) K-562 and Meg-01 myeloid leukemia cells (IC₅₀s = 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., Dumitrescu, 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).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

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