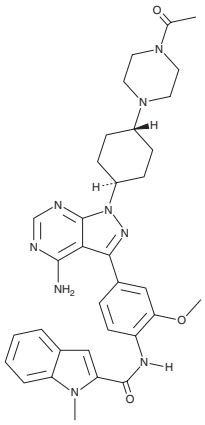
PRODUCT INFORMATION

A-770041

Item No. 32854



CAS Registry No.:	869748-10-7
Formal Name:	N-[4-[1-[*trans*-4-(4-acetyl-1-piperazinyl) cyclohexyl]-4-amino-1H-pyrazolo[3,4-d] pyrimidin-3-yl]-2-methoxyphenyl]-1-methyl-1H-indole-2-carboxamide
MF:	$C_{34}H_{39}N_9O_3$
FW:	621.7
Purity:	≥98%
Supplied as:	A 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-770041 is supplied as a solid. A stock solution may be made by dissolving the A-770041 in the solvent of choice, which should be purged with an inert gas. A-770041 is soluble in organic solvents such as ethanol, DMSO, and hydrochloric acid (0.1 M). The solubility of A-770041 in ethanol is approximately 2 mg/ml and approximately 20 mg/ml in DMSO and hydrochloric acid (0.1 M).

Description

A-770041 is an inhibitor of LCK kinase (IC_{50} = 0.147 µM).[1] It is selective for LCK over other Src family tyrosine kinases including Src, Fyn, Fgr, HCK, and Tie2 (IC_{50}s = 9.05, 44.1, 14.1, 1.22, and >50 µM, respectively). A-770041 induces dephosphorylation of LCK by SHP-1, inactivating LCK, in IgE/antigen-stimulated bone marrow-derived mast cells (BMMCs).[5] It inhibits IL-2 production induced by an anti-CD3 antibody and phorbol 12-myristate 13-acetate (PMA; Item No. 10008014) in isolated human whole blood (EC_{50} = 80 nM) and by concanavalin A (Item No. 14951) in rats.[2] A-770041 (10 mg/kg) prevents acute rejection and increases graft survival in a rat model of heterotopic heart transplantation. It also inhibits the growth of CTV-1 human acute myeloid leukemia cells (IC_{50} = 224 nM) and sensitizes $U2OS_{MR}$ and $KHOS_{R2}$ multidrug resistant human osteosarcoma cells to paclitaxel (Item No. 10461) and doxorubicin (Item No. 15007).[3,4]

References

1. Burchat, A., Borhani, D.W., Calderwood, D.J., *et al.* Discovery of A-770041, a src-family selective orally active lck inhibitor that prevents organ allograft rejection. *Bioorg. Med. Chem. Lett.* **16(1)**, 118-122 (2006).
2. Stachlewitz, R.F., Hart, M.A., Bettencourt, B., *et al.* A-770041, a novel and selective small-molecule inhibitor of Lck, prevents heart allograft rejection. *J. Pharmacol. Exp. Ther.* **315(1)**, 36-41 (2005).
3. Li, L., Cui, Y., Shen, J., *et al.* Evidence for activated Lck protein tyrosine kinase as the driver of proliferation in acute myeloid leukemia cell, CTV-1. *Leuk. Res.* **78**, 12-20 (2019).
4. Duan, Z., Zhang, J., Ye, S., *et al.* A-770041 reverses paclitaxel and doxorubicin resistance in osteosarcoma cells. *BMC Cancer* **14**, 681 (2014).
5. Chang, H.W., Kanegasaki, S., Jin, F., *et al.* A common signaling pathway leading to degranulation in mast cells and its regulation by CCR1-ligand. *Allergy* **75(6)**, 1371-1381 (2020).

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
Buyer agrees to purchase the material subject to Cayman's Terms and Conditions. Complete Terms and Conditions including Warranty and Limitation of Liability information can be found on our website.

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