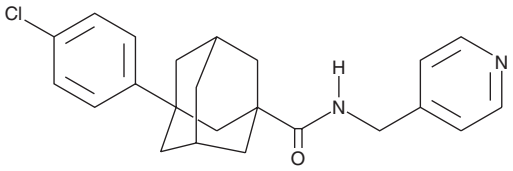
PRODUCT INFORMATION

ABC294640

Item No. 10587

CAS Registry No.:	915385-81-8
Formal Name:	3-(4-chlorophenyl)-N-(4-pyridinylmethyl)-tricyclo[3.3.1.1^{3,7}]decane-1-carboxamide
MF:	$C_{23}H_{25}ClN_2O$
FW:	380.9
Purity:	≥98%
UV/Vis.:	λ_{max}: 222, 258 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

ABC294640 is supplied as a crystalline solid. A stock solution may be made by dissolving the ABC294640 in the solvent of choice, which should be purged with an inert gas. ABC294640 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of ABC294640 in these solvents is approximately 0.16 and 16 mg/ml, respectively.

ABC294640 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ABC294640 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. ABC294640 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

ABC294640 is an inhibitor of sphingosine kinase 2 (SPHK2; K_i = 9.8 µM).[1] It inhibits SPHK2 (IC_{50} = 60 µM) without affecting SPHK1 activity up to 100 µM but does reduce SPHK1 isoform a (SPHK1a) protein levels in androgen-independent LNCaP (LNCaP-AI) cells *via* an SPHK1-indirect, proteasomal-dependent mechanism when used at concentrations ranging from 5 to 25 µM.[2] ABC294640 is inactive against a panel of 20 lipid-regulated kinases at 50 µM.[1] It decreases sphingosine-1-phosphate (S1P) production in MDA-MB-231 cells in a concentration-dependent manner. ABC294640 inhibits proliferation of a variety of cancer cells, including HepG2 liver, A-498 kidney, PANC-1 pancreas, and HT-29 colon cells (IC_{50}s = 6, 12.2, 32.8, and 48.1 µM, respectively). It reduces actin filament polymerization in, and cell migration of, A-498 cells in a scratch assay. Oral administration of ABC294640 (35 and 100 mg/kg every other day) reduces tumor growth in a mouse syngeneic model of mammary adenocarcinoma. It also reduces colonic inflammation in mouse and rat models of Crohn's disease induced by trinitrobenzene sulfonic acid (TNBS).[3]

References

1. French, K.J., Zhuang, Y., Maines, L.W., *et al*. Pharmacology and antitumor activity of ABC294640, a selective inhibitor of sphingosine kinase-2. *J. Pharmacol. Exp. Ther.* **333(1)**, 129-139 (2010).
2. McNaughton, M., Pitman, M., Pitson, S.M., *et al.* Proteasomal degradation of sphingosine kinase 1 and inhibition of dihydroceramide desaturase by the sphingosine kinase inhibitors, SKi or ABC294640, induces growth arrest in androgen-independent LNCaP-AI prostate cancer cells. *Oncotarget* **7(13)**, 16663-16675 (2016).
3. Maines, L.W., Fitzpatrick, L.R., Green, C.L., *et al*. Efficacy of a novel sphingosine kinase inhibitor in experimental Crohn's disease. *Inflammopharmacology* **18(2)**, 73-85 (2010).

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