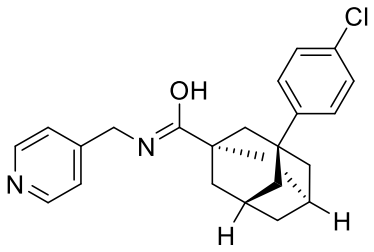
Product data sheet

MedKoo Cat#: 205806 Name: ABC294640 CAS#: 915385-81-8 (free base) Chemical Formula: $C_{23}H_{25}ClN_2O$ Exact Mass: 380.16554 Molecular Weight: 380.9104	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
ABC294640, also known as Opaganib, is an orally available, aryladamantane compound and selective inhibitor of sphingosine kinase-2 (SK2) with potential antineoplastic activity. Upon administration, ABC294640 competitively binds to and inhibits SK2, thereby preventing the phosphorylation of the pro-apoptotic amino alcohol sphingosine to sphingosine 1-phosphate (S1P), the lipid mediator that is pro-survival and critical for immunomodulation. This may eventually lead to the induction of apoptosis and may result in an inhibition of cell proliferation in cancer cells overexpressing SK2.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	76	199.52
Ethanol	28	73.51

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.63 mL	13.13 mL	26.25 mL
5 mM	0.53 mL	2.63 mL	5.25 mL
10 mM	0.26 mL	1.31 mL	2.63 mL
50 mM	0.05 mL	0.26 mL	0.53 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. French KJ, Zhuang Y, Maines LW, Gao P, Wang W, Beljanski V, Upson JJ, Green CL, Keller SN, Smith CD. Pharmacology and antitumor activity of ABC294640, a selective inhibitor of sphingosine kinase-2. J Pharmacol Exp Ther. 2010 Apr;333(1):129-39. doi: 10.1124/jpet.109.163444. Epub 2010 Jan 8. PMID: 20061445; PMCID: PMC2846016.

2. Beljanski V, Knaak C, Zhuang Y, Smith CD. Combined anticancer effects of sphingosine kinase inhibitors and sorafenib. Invest New Drugs. 2011 Dec;29(6):1132-42. doi: 10.1007/s10637-010-9452-0. Epub 2010 May 18. PMID: 20473784; PMCID: PMC3089696.

In vivo study

1. French KJ, Zhuang Y, Maines LW, Gao P, Wang W, Beljanski V, Upson JJ, Green CL, Keller SN, Smith CD. Pharmacology and antitumor activity of ABC294640, a selective inhibitor of sphingosine kinase-2. J Pharmacol Exp Ther. 2010 Apr;333(1):129-39. doi: 10.1124/jpet.109.163444. Epub 2010 Jan 8. PMID: 20061445; PMCID: PMC2846016.

2. Beljanski V, Knaak C, Zhuang Y, Smith CD. Combined anticancer effects of sphingosine kinase inhibitors and sorafenib. Invest New Drugs. 2011 Dec;29(6):1132-42. doi: 10.1007/s10637-010-9452-0. Epub 2010 May 18. PMID: 20473784; PMCID: PMC3089696.

7. Bioactivity

Biological target:

Opaganib (ABC294640) is a selective, competitive sphingosine kinase 2 (SK2) inhibitor with Ki of 9.8 μM.

In vitro activity

An aryladamantane compound, termed ABC294640 [3-(4-chlorophenyl)-adamantane-1-carboxylic acid (pyridin-4-ylmethyl)amide], was identified to selectively inhibit SK2 activity in vitro, acting as a competitive inhibitor with respect to sphingosine with a K(i) of 9.8 muM, and attenuates S1P formation in intact cells. In tissue culture, ABC294640 suppresses the proliferation of a broad panel of tumor cell lines, and inhibits tumor cell migration concomitant with loss of microfilaments. Using recombinant human SK1 and SK2, ABC294640 demonstrated dose-dependent inhibition of SK2 with an IC50 of approximately 60 μM without affecting the activity of SK1 at concentrations up to at least 100 μM (Fig. 2A). Additional studies demonstrated that ABC294640 acts as a competitive inhibitor with respect to sphingosine, making the IC50 strongly affected by the concentration of sphingosine used in the assay. Kinetic analyses of varying concentrations of ABC294640 in the presence of 2.5 to 25 μM sphingosine indicated a Ki of 9.8 ± 1.4 μM for the inhibition of SK2 (Fig. 2B). It was also important to determine the ability of ABC294640 to inhibit endogenous SK activity in an intact cell model. MDA-MB-231 cells were incubated with [3H]sphingosine at a final concentration of 1 μM to test this. In this assay, ABC294640 decreased [3H]S1P formation in a dose-dependent fashion with an IC50 value of 26 μM. The effects of ABC294640 on the proliferation of human tumor cell lines representing major tumor types were determined by use of the sulforhodamine B assay for quantifying cell number. As indicated in Table 2, ABC294640 inhibited tumor cell proliferation with IC50 values ranging from approximately 6 to 48 μM with Hep-G2 and HT-29 cells being the most and least sensitive, respectively. It is notable that the IC50 for inhibition of the proliferation of MDA-MB-231 cells closely matches the IC50 for suppression of SK activity in this cell line, i.e., 29 and 26 μM, respectively, supporting the hypotheses that the antiproliferative effects of ABC294640 are mediated by inhibition of SK activity, and that SK2, in particular, is important for cell proliferation.

Reference: J Pharmacol Exp Ther. 2010 Apr;333(1):129-39. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/20061445/

In vivo activity

The antitumor activity of ABC294640 was tested in a syngeneic tumor model that uses the mouse JC mammary adenocarcimona cell line growing subcutaneously in immunocompetent BALB/c mice. Because of the excellent oral absorption, it was determined the ability of orally delivered ABC294640 to reduce tumor growth in vivo. The SK inhibitor was administered to fasted mice on odd days at doses ranging from 3.5 to 100 mg/kg. Body weights and tumor volumes were monitored daily. As demonstrated in Fig. 7, ABC294640 caused dose-dependent reductions in the growth of the mammary adenocarcinoma xenografts. Body weights in each treatment group remained unchanged from vehicle-treated mice during the course of the study (data not shown). Comparison with the potencies in the tumor studies with the toxicity data described above reveals that ABC294640·HCl has a therapeutic index of greater than 7 (250 mg/kg nontoxic dose / 35 mg/kg antitumor activity). Thus, this SK2 inhibitor has an excellent therapeutic index.

Reference: J Pharmacol Exp Ther. 2010 Apr;333(1):129-39. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/20061445/