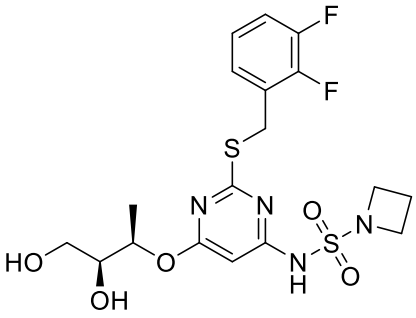
Product data sheet

MedKoo Cat#: 206473 Name: AZD-5069 CAS#: 878385-84-3 Chemical Formula: $C_{18}H_{22}F_2N_4O_5S_2$ Exact Mass: 476.09997 Molecular Weight: 476.51	
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: AZD-5069 is a potent and selective CXCR2 antagonist with the potential to inhibit neutrophil migration into the airways in patients with COPD. AZD-5069 was shown to inhibit binding of radiolabeled CXCL8 to human CXCR2 with a pIC50 value of 9.1. Furthermore, AZD5069 inhibited neutrophil chemotaxis, with a pA2 of approximately 9.6, and adhesion molecule expression, with a pA2 of 6.9, in response to CXCL1. AZD5069 was a slowly reversible antagonist of CXCR2 with effects of time and temperature evident on the pharmacology and binding kinetics. AZD-5069 is also potential useful for patient in inflammatory conditions.

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	90	188.87
Ethanol	7	14.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.10 mL	10.49 mL	20.99 mL
5 mM	0.42 mL	2.10 mL	4.20 mL
10 mM	0.21 mL	1.05 mL	2.10 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Nicholls DJ, Wiley K, Dainty I, MacIntosh F, Phillips C, Gaw A, Mårdh CK. Pharmacological characterization of AZD5069, a slowly reversible CXC chemokine receptor 2 antagonist. J Pharmacol Exp Ther. 2015 May;353(2):340-50. doi: 10.1124/jpet.114.221358. Epub 2015 Mar 3. PMID: 25736418.

2. Armstrong CWD, Coulter JA, Ong CW, Maxwell PJ, Walker S, Butterworth KT, Lyubomska O, Berlingeri S, Gallagher R, O'Sullivan JM, Jain S, Mills IG, Prise KM, Bristow RG, LaBonte MJ, Waugh DJJ. Clinical and functional characterization of CXCR1/CXCR2 biology in the relapse and radiotherapy resistance of primary PTEN-deficient prostate carcinoma. NAR Cancer. 2020 Sep;2(3):zcaa012. doi: 10.1093/narcan/zcaa012. Epub 2020 Jul 3. PMID: 32743555; PMCID: PMC7380483.

In vivo study

1. Uddin M, Betts C, Robinson I, Malmgren A, Humfrey C. The chemokine CXCR2 antagonist (AZD5069) preserves neutrophil-mediated host immunity in non-human primates. Haematologica. 2017 Feb;102(2):e65-e68. doi: 10.3324/haematol.2016.152371. Epub 2016 Oct 14. PMID: 27742769; PMCID: PMC5286957.

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2. Sody S, Uddin M, Grüneboom A, Görgens A, Giebel B, Gunzer M, Brandau S. Distinct Spatio-Temporal Dynamics of Tumor-Associated Neutrophils in Small Tumor Lesions. Front Immunol. 2019 Jun 25;10:1419. doi: 10.3389/fimmu.2019.01419. PMID: 31293583; PMCID: PMC6603174.

7. Bioactivity

Biological target: AZD 5069 is an antagonist of chemokine receptor 2 (CXCR2; IC50 = 0.79 nM in a radioligand binding assay).

In vitro activity

AZD5069 (3 nM) produced a concentration-dependent inhibition of calcium flux induced by CXCL8 (Fig. 5B). The inhibition of functional responses to CXCL8 by AZD5069 was reversible after compound was removed by washing cells. Although the washing procedure used to remove compound from the system was able to demonstrate that inhibition by AZD5069 was reversible, complete restoration of the CXCL8-mediated calcium response to control levels was not observed. AZD5069 produced a concentration-dependent inhibition of PMN chemotaxis induced by CXCL1 (Fig. 6A). Agonist response curves appeared to collapse in the presence of AZD5069. Although response to a gradient of chemokine is not a simple equilibrium-driven system, the pA2 for AZD5069 was estimated to be approximately 9.6 (range 9.2–9.9). The integrin CD11b is upregulated on neutrophils in response to a variety of inflammatory mediators. AZD5069 produced clear inhibition of CXCL1-mediated CD11b expression with a rightward shift of the concentration effect curve to CXCL1 (Fig. 6B), with a pA2 of 6.9 6 0.13 (mean 6 S.E.M., n 5 8). CXCL1 agonist response curves also appeared to collapse in the presence of AZD5069 (Fig. 6B). When several agonists inducing CD11b expression on neutrophils were investigated, a high concentration of AZD5069 was found to specifically inhibit only the CXCL1-driven response with no significant inhibition observed for neutrophils stimulated by C5a, N-formyl-methionyl-leucylphenylalanine, or leukotriene B4 (Fig. 7).

Reference: J Pharmacol Exp Ther. 2015 May;353(2):340-50. https://jpet-aspetjournals-org.libproxy.lib.unc.edu/content/jpet/353/2/340.full.pdf

In vivo activity

Analysis of the general toxicological data from 39 weeks of treatment revealed that dosing regimens of up to 525 mg/kg/day were well tolerated in cynomolgus monkeys. AZD5069 had no significant impact on most of the measured parameters. However, an increase in circulating globulin and a decrease in albumin (with a consequent reduction in the albumin/globulin ratio) was seen in a reciprocal manner, that was not dose-related. Furthermore, AZD5069-related histopathological findings were limited to the bone marrow consisting of a dose-related increment in the myeloid/erythroid ratio, with an associated increase in segmented granulocytes at all dose levels. Notably, no compound-related changes in baseline circulating neutrophil numbers were evident (data not shown), despite an apparently similar expression pattern of CXCR2 receptors to humans,10 which indicated that AZD5069 did not affect the neutrophil mobilization from the bone marrow into the peripheral circulation under homeostatic conditions. The sparing effect of AZD5069 treatment on circulating neutrophils is particularly noteworthy in this context, since there was no increased risk of infection in animals chronically treated with AZD5069 over the 39 week interval in vivo, which is reflective of the preserved pathogen-initiated phagocytic and oxidative responses observed in the high percentage of neutrophils responding normally ex vivo.

Reference: Haematologica. 2017 Feb; 102(2): e65–e68. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5286957/