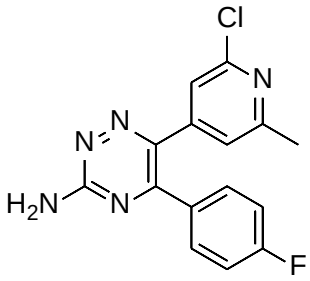
Product data sheet

MedKoo Cat#: 206930 Name: AZD4635 CAS#: 1321514-06-0 Chemical Formula: $C_{15}H_{11}ClFN_5$ Exact Mass: 315.068 Molecular Weight: 315.74	
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-4635, also known as HTL-1071, is an orally available, small molecule adenosine A2A receptor antagonist.

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	56.65	179.42
DMSO:PBS(pH 7.2) (1:3)	0.25	0.79
DMF	30.0	95.01

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.17 mL	15.84 mL	31.67 mL
5 mM	0.63 mL	3.17 mL	6.33 mL
10 mM	0.32 mL	1.58 mL	3.17 mL
50 mM	0.06 mL	0.32 mL	0.63 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. Borodovsky A, Barbon CM, Wang Y, Ye M, Prickett L, Chandra D, Shaw J, Deng N, Sachsenmeier K, Clarke JD, Linghu B, Brown GA, Brown J, Congreve M, Cheng RK, Dore AS, Hurrell E, Shao W, Woessner R, Reimer C, Drew L, Fawell S, Schuller AG, Mele DA. Small molecule AZD4635 inhibitor of A2AR signaling rescues immune cell function including CD103+ dendritic cells enhancing anti-tumor immunity. J Immunother Cancer. 2020 Jul;8(2):e000417. doi: 10.1136/jitc-2019-000417. PMID: 32727810; PMCID: PMC7394305.

In vivo study

1. Yang R, Elsaadi S, Misund K, Abdollahi P, Vandsemb EN, Moen SH, Kusnierczyk A, Slupphaug G, Standal T, Waage A, Slørdahl TS, Rø TB, Rustad E, Sundan A, Hay C, Cooper Z, Schuller AG, Woessner R, Borodovsky A, Menu E, Børset M, Sponaas AM. Conversion of ATP to adenosine by CD39 and CD73 in multiple myeloma can be successfully targeted together with adenosine receptor A2A blockade. J Immunother Cancer. 2020 May;8(1):e000610. doi: 10.1136/jitc-2020-000610. PMID: 32409420; PMCID: PMC7239696.

7. Bioactivity
Biological target: AZD4635 binds to human A2AR with a Ki of 1.7 nM and shows >30-fold selectivity over other adenosine receptors.

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In vitro activity

The A2A receptor is a member of the G-coupled receptor family with activation leading to increased intracellular levels of cAMP. The potency of AZD4635 in inhibiting A2AR signaling was determined in a cAMP accumulation assay using CHO cells stably transfected with human A2AR (figure 1D) and stimulated with adenosine (100, 10, 1 and 0.1 μM). Owing to the competitive binding mechanism of inhibition, the antagonist activity (IC50) of AZD4635 was impacted by the adenosine concentration. As the concentration of adenosine was increased, the potency of AZD4635 antagonist activity was reduced, with a linear relationship. AZD4635 demonstrated an IC50 of 0.000794, 0.0123, 0.155 and 2.69 μM at concentrations of 0.1, 1, 10 and 100 μM adenosine.

Reference: J Immunother Cancer. 2020 Jul;8(2):e000417. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7394305/

In vivo activity

C57BL/KaLwRij mice develop MM within 3 weeks of injection of 5T33MM cells. Mice were treated with inhibitors of the adenosine pathway, POM-1, anti-CD73, and AZD4635, as shown in figure 6A. The 5T33MM tumor expressed CD39 (figure 6B). In this model, tumor cells secrete M component, reside in the BM, and migrate to hematopoietic organs such as the spleen. The migration to the spleen causes up to a 20-fold increase in spleen weight, and it is, in addition to M component, used as an indicator of tumor load in the model.36 Administering AZD4635 alone had no effect on any parameter analyzed. However, mice treated with the CD39 inhibitor POM-1 in combination with anti-CD73 antibody and AZD4635 had significantly lower spleen weights (figure 6C), fewer tumor cells in the spleen (figure 6D) as well as significantly lower M component level in circulation (10.6 g/L vs 19.4) than untreated control mice (figure 6F), which suggests that the treatment reduced tumor load.

Reference: J Immunother Cancer. 2020 May;8(1):e000610. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7239696/