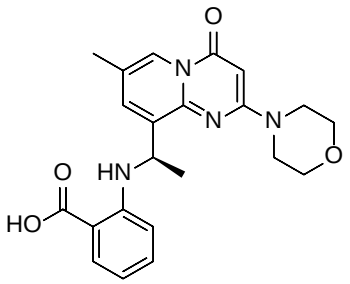
Product data sheet

MedKoo Cat#: 406268 Name: AZD6482 CAS#: 1173900-33-8 (free base) Chemical Formula: $C_{22}H_{24}N_4O_4$ Exact Mass: 408.1798 Molecular Weight: 408.45	
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:
AZD6482 is a potent, selective and ATP competitive PI3Kβ inhibitor (IC(50) 0.01 μm). AZD6482 inhibited insulin-induced human adipocyte glucose uptake in vitro (IC(50) of 4.4 μm). This is the first human target validation for PI3Kβ inhibition as anti-platelet therapy showing a mild and generalized antiplatelet effect attenuating but not completely inhibiting multiple signaling pathways with an impressive separation towards primary hemostasis. AZD6482 at 'supratherapeutic' plasma concentrations may attenuate insulin signaling, most likely through PI3Kα inhibition.

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	58.21	142.51
DMF	10.0	24.48
Ethanol	7.50	18.36

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.45 mL	12.24 mL	24.48 mL
5 mM	0.49 mL	2.45 mL	4.90 mL
10 mM	0.24 mL	1.22 mL	2.45 mL
50 mM	0.05 mL	0.24 mL	0.49 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. Xu PF, Yang JA, Liu JH, Yang X, Liao JM, Yuan FE, Liu BH, Chen QX. PI3Kβ inhibitor AZD6482 exerts antiproliferative activity and induces apoptosis in human glioblastoma cells. Oncol Rep. 2019 Jan;41(1):125-132. doi: 10.3892/or.2018.6845. Epub 2018 Nov 2. PMID: 30542720; PMCID: PMC6278584.

In vivo study

1. Zhao HF, Wu CP, Zhou XM, Diao PY, Xu YW, Liu J, Wang J, Huang XJ, Liu WL, Chen ZP, Huang GD, Li WP. Synergism between the phosphatidylinositol 3-kinase p110β isoform inhibitor AZD6482 and the mixed lineage kinase 3 inhibitor URMC-099 on the blockade of glioblastoma cell motility and focal adhesion formation. Cancer Cell Int. 2021 Jan 6;21(1):24. doi: 10.1186/s12935-020-01728-4. PMID: 33407478; PMCID: PMC7789614.

7. Bioactivity
Biological target: AZD 6482 (KIN-193) is a p110β inhibitor with an IC50 of 0.69 nM.

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In vitro activity

The effect of the PI3Kβ inhibitor AZD6482 on glioma cells was investigated. The CCK-8 assay showed dose-dependent cytotoxicity in glioma cell lines treated with AZD6482. Additionally, AZD6482 treatment was found to significantly induce apoptosis and cell cycle arrest as detected using flow cytometry. Moreover, as shown using western blot analysis, the levels of p-AKT, p-GSK-3β, Bcl-2, and cyclin D1 were decreased after AZD6482 treatment. In addition, AZD6482 inhibited the migration and invasion of glioma cells as detected by wound healing and Transwell invasion assays. These findings indicate that AZD6482 exerts an antitumour effect by inhibiting proliferation and inducing apoptosis in human glioma cells.

Reference: Oncol Rep. 2019 Jan;41(1):125-132. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6278584/

In vivo activity

To evaluate the combination effect of PI3Kβ and MLK3 inhibitors in vivo, Balb/C nude mice bearing subcutaneous U-118 MG glioblastoma xenograft were intraperitoneally injected with vehicle, AZD6482 (30 mg/kg), URMC-099 (3 mg/kg), and the combination of AZD6482 (30 mg/kg) and URMC-099 (3 mg/kg), respectively. Neither AZD6482 nor URMC-099 alone significantly suppressed U-118 MG xenograft tumor growth. However, compared with single inhibitor alone, combination of AZD6482 and URMC-099 effectively decreased tumor volume after 26-day post-administration ($p < 0.05$). Tumor weight and size were also reduced by the combination of AZD6482 and URMC-099 after sacrifice in 36-day post-administration ($p < 0.05$) (Fig. 6a, b).

Reference: Cancer Cell Int. 2021 Jan 6;21(1):24. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7789614/