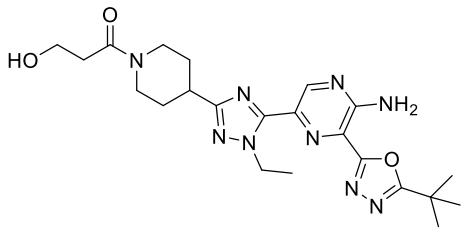
Product data sheet

MedKoo Cat#: 206479 Name: AZD8835 CAS#: 1620576-64-8 Chemical Formula: $C_{22}H_{31}N_9O_3$ Exact Mass: 469.25499 Molecular Weight: 469.55	
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:

AZD8835 is a potent and selective inhibitor of PI3Kalpha and PI3Kdelata with excellent general kinase selectivity. AZD8835 displayed low metabolic turnover and suitable physical properties for oral administration. At the enzyme level, AZD8835 is a potent mixed inhibitor of PI3Kα (IC50 0.0062 μM) and PI3Kδ (IC50 0.0057 μM), with selectivity against PI3Kβ (IC50 0.431 μM) and PI3Kγ (IC50 0.090 μM). In vivo, AZD8835 showed pharmacodynamic modulation of AKT phosphorylation and near complete inhibition of tumour growth (93% tumour growth inhibition) in a murine H1047R PI3Kalpha mutated SKOV-3 xenograft tumour model after chronic oral administration at 25 mg/kg b.i.d. AZD8835, is currently in phase I clinical trials.

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	43.0	91.58
DMSO:PBS (pH 7.2) (1:1)	0.5	1.06
DMF	16.0	34.08
Ethanol	2.0	4.26

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.13 mL	10.65 mL	21.30 mL
5 mM	0.43 mL	2.13 mL	4.26 mL
10 mM	0.21 mL	1.06 mL	2.13 mL
50 mM	0.04 mL	0.21 mL	0.43 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. Erdmann T, Klener P, Lynch JT, Grau M, Vočková P, Molinsky J, Tuskova D, Hudson K, Polanska UM, Grondine M, Mayo M, Dai B, Pfeifer M, Erdmann K, Schwammbach D, Zapukhlyak M, Staiger AM, Ott G, Berdel WE, Davies BR, Cruzalegui F, Trneny M, Lenz P, Barry ST, Lenz G. Sensitivity to PI3K and AKT inhibitors is mediated by divergent molecular mechanisms in subtypes of DLBCL. Blood. 2017 Jul 20;130(3):310-322. doi: 10.1182/blood-2016-12-758599. Epub 2017 Feb 15. PMID: 28202458.
2. Hudson K, Hancox UJ, Trigwell C, McEwen R, Polanska UM, Nikolaou M, Morentin Gutierrez P, Avivar-Valderas A, Delpuech O, Dudley P, Hanson L, Ellston R, Jones A, Cumberbatch M, Cosulich SC, Ward L, Cruzalegui F, Green S. Intermittent High-Dose Scheduling of AZD8835, a Novel Selective Inhibitor of PI3Kα and PI3Kδ, Demonstrates Treatment Strategies for PIK3CA-Dependent Breast Cancers. Mol Cancer Ther. 2016 May;15(5):877-89. doi: 10.1158/1535-7163.MCT-15-0687. Epub 2016 Feb 2. PMID: 26839307.

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In vivo study

1. Carnevalli LS, Sinclair C, Taylor MA, Gutierrez PM, Langdon S, Coenen-Stass AML, Mooney L, Hughes A, Jarvis L, Staniszewska A, Crafter C, Sidders B, Hardaker E, Hudson K, Barry ST. PI3Kα/δ inhibition promotes anti-tumor immunity through direct enhancement of effector CD8+ T-cell activity. J Immunother Cancer. 2018 Dec 27;6(1):158. doi: 10.1186/s40425-018-0457-0. PMID: 30587236; PMCID: PMC6307194.
2. Hudson K, Hancox UJ, Trigwell C, McEwen R, Polanska UM, Nikolaou M, Morentin Gutierrez P, Avivar-Valderas A, Delpuech O, Dudley P, Hanson L, Ellston R, Jones A, Cumberbatch M, Cosulich SC, Ward L, Cruzalegui F, Green S. Intermittent High-Dose Scheduling of AZD8835, a Novel Selective Inhibitor of PI3Kα and PI3Kδ, Demonstrates Treatment Strategies for PIK3CA-Dependent Breast Cancers. Mol Cancer Ther. 2016 May;15(5):877-89. doi: 10.1158/1535-7163.MCT-15-0687. Epub 2016 Feb 2. PMID: 26839307.

7. Bioactivity

Biological target:

AZD8835 is an inhibitor of PI3Kα and PI3Kδ with IC50s of 6.2 and 5.7 nM, respectively.

In vitro activity

To identify the mechanisms responsible for AZD8835-mediated cytotoxicity, induction of apoptosis was analyzed using Annexin-V/PI staining in 2 sensitive (HBL-1 and TMD8) and 1 insensitive (BJAB) model. Predominantly in HBL-1 and less pronounced in TMD8 cells, a significant increase in apoptotic cells was observed, whereas no apoptosis was detectable in BJAB cells (Figure 4B). Analyses of proliferation after AZD8835 treatment using CFSE staining showed strongly decreased proliferation in HBL-1 and TMD8 but not in BJAB cells (Figure 4C). These results suggest that PI3Kα/δ inhibition results in induction of apoptosis and inhibition of proliferation in ABC DLBCLs.

Reference: Blood. 2017 Jul 20;130(3):310-322. doi: 10.1182/blood-2016-12-758599. https://pubmed.ncbi.nlm.nih.gov/28202458/

In vivo activity

Initially, analyzing both proximal (pAKT) and downstream (pPRAS40, pS6) PI3K-pathway biomarkers in tumor tissue, this study demonstrated that pathway inhibition was both time and dose/exposure dependent (Fig. 3A). In parallel studies, this study observed glucose and insulin elevation as a transient pharmacologic response to AZD8835 in mice (Supplementary Fig. S2A and S2B), as also observed for other PI3K-inhibitors.

Reference: Mol Cancer Ther. 2016 May;15(5):877-89. https://mct.aacrjournals.org/content/15/5/877.long

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.