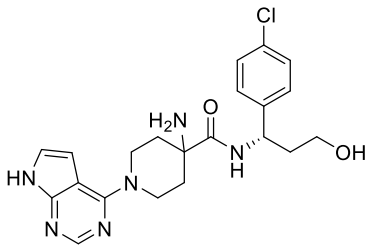
Product data sheet

MedKoo Cat#: 205669 Name: Capivasertib CAS#: 1143532-39-1 Chemical Formula: $C_{21}H_{25}ClN_6O_2$ Exact Mass: 428.17275 Molecular Weight: 428.9152	
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:
AZD5363, also known as Capivasertib, is an orally available inhibitor of the serine/threonine protein kinase AKT (protein kinase B) with potential antineoplastic activity. AKT inhibitor AZD5363 binds to and inhibits all AKT isoforms. Inhibition of AKT prevents the phosphorylation of AKT substrates that mediate cellular processes, such as cell division, apoptosis, and glucose and fatty acid metabolism. A wide range of solid and hematological malignancies show dysregulated PI3K/AKT/mTOR signaling due to mutations in multiple signaling components.

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	42.89	100.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.33 mL	11.66 mL	23.31 mL
5 mM	0.47 mL	2.33 mL	4.66 mL
10 mM	0.23 mL	1.17 mL	2.33 mL
50 mM	0.05 mL	0.23 mL	0.47 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. Zhang Y, Zheng Y, Faheem A, Sun T, Li C, Li Z, Zhao D, Wu C, Liu J. A novel AKT inhibitor, AZD5363, inhibits phosphorylation of AKT downstream molecules, and activates phosphorylation of mTOR and SMG-1 dependent on the liver cancer cell type. Oncol Lett. 2016 Mar;11(3):1685-1692. doi: 10.3892/ol.2016.4111. Epub 2016 Jan 14. PMID: 26998062; PMCID: PMC4774473.
2. Chen C, Zhang Q, Liu S, Lambrechts M, Qu Y, You Z. AZD5363 Inhibits Inflammatory Synergy between Interleukin-17 and Insulin/Insulin-Like Growth Factor 1. Front Oncol. 2014 Dec 1;4:343. doi: 10.3389/fonc.2014.00343. PMID: 25520943; PMCID: PMC4249256.

In vivo study

1. Gris-Oliver A, Palafox M, Monserrat L, Brasó-Maristany F, Òdena A, Sánchez-Guixé M, Ibrahim YH, Villacampa G, Grueso J, Parés M, Guzmán M, Rodríguez O, Bruna A, Hirst CS, Barnicle A, de Bruin EC, Reddy A, Schiavon G, Arribas J, Mills GB, Caldas C, Dienstmann R, Prat A, Nuciforo P, Razavi P, Scaltriti M, Turner NC, Saura C, Davies BR, Oliveira M, Serra V. Genetic Alterations in the PI3K/AKT Pathway and Baseline AKT Activity Define AKT Inhibitor Sensitivity in Breast Cancer Patient-derived

Xenografts. Clin Cancer Res. 2020 Jul 15;26(14):3720-3731. doi: 10.1158/1078-0432.CCR-19-3324. Epub 2020 Mar 27. PMID: 32220884; PMCID: PMC7814659.
2. De Velasco MA, Kura Y, Yoshikawa K, Nishio K, Davies BR, Uemura H. Efficacy of targeted AKT inhibition in genetically engineered mouse models of PTEN-deficient prostate cancer. Oncotarget. 2016 Mar 29;7(13):15959-76. doi: 10.18632/oncotarget.7557. PMID: 26910118; PMCID: PMC4941290.

7. Bioactivity

Biological target:

Capivasertib, a novel pyrrolopyrimidine-derived compound, inhibits all AKT isoforms with a potency of 10 nM or less.

In vitro activity

mTOR, a 289-kDa serine/threonine protein kinase, belongs to the PIKK family and is activated through the PI3K and AKT signaling pathways via phosphorylation of specific residues; once activated, mTOR mediates transcription, cytoskeleton organization, cell growth and cell survival. To investigate the effect of AZD5363 on the mTOR pathway, the phosphorylation levels of mTOR were analyzed. In contrast to the inhibited phosphorylation of AKT substrates, AZD5363 exhibited reduced activity in the mTOR pathway, as presented in panels of tumor cell lines in vitro. AZD5363 enhanced the phosphorylation of mTOR, however, this was only observed in the Huh-7 cells. This indicated that AZD5363 significantly stimulated mTOR signaling, but that this was dependent on liver cancer cell type (Fig.4 and 5; $P<0.01$).

Reference: Oncol Lett. 2016 Mar; 11(3): 1685–1692. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4774473/

In vivo activity

To further unravel the mechanism of action of AZD5363 in vivo, this study measured Ki67 and cleaved caspase 3 in short-term AZD5363-treated PDXs (patient-derived xenografts). The percentage of Ki67-positive cells in untreated tumors was lower in AZD5363-sensitive models compared to the resistant ones ($p=0.005$, Fig. 3A). In addition, treatment with AZD5363 resulted in a greater reduction of Ki67 in sensitive PDXs compared to the resistant tumors ($p<0.001$). This study also noted that AZD5363 did not induce cleaved caspase 3 across AZD5363-sensitive tumors, consistent with previous findings for this dosing schedule (Fig. S4F and (8)). Given that S6K mediates efficient cap-dependent translation of cyclin D1 and that AKT/GSK3β axis regulates cyclin D1 stability, it was posited that treatment with AZD5363 impaired cell cycle progression through the CDK4/6-cyclin D1 restriction point in sensitive models. Therefore, this study quantified cyclin D1 by IHC in PDXs before and after treatment with AZD5363. These experiments revealed that most of AZD5363-resistant PDXs expressed low levels of cyclin D1, compared to AZD5363-sensitive PDXs (Fig. 3B, S4D, 12 out of 16, 75% vs. 2 out of 8, 25%, receiver operating characteristic (ROC) curve cut-off H-score ≤ 13.3, ROC $p=0.066$), suggesting that, in AZD5363-resistant tumors, cell cycle progression was not dependent on cyclin D1. It was also observed that, although AZD5363 downregulated cyclin D1 in all the models expressing cyclin D1 (Fig. 3B), the reduction in cyclin D1 was more relevant in AZD5363-sensitive models ($p<0.001$). Altogether, these results suggest that cyclin D1 downregulation and cell cycle blockade is an important mechanism of action of AZD5363 in vivo.

Reference: Clin Cancer Res. 2020 Jul 15; 26(14): 3720–3731. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7814659/

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.