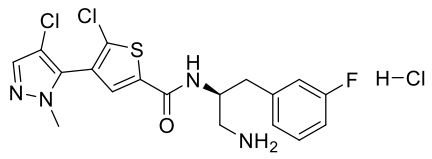
Product data sheet

MedKoo Cat#: 205478 Name: Afuresertib HCl CAS#: 1047645-82-8 (HCl) Chemical Formula: $C_{18}H_{18}Cl_3FN_4OS$ Molecular Weight: 463.78	
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:

Afuresertib, also known as GSK2110183, is an orally bioavailable inhibitor of the serine/threonine protein kinase Akt (protein kinase B) with potential antineoplastic activity. Akt inhibitor GSK2110183 binds to and inhibits the activity of Akt, which may result in inhibition of the PI3K/Akt signaling pathway and tumor cell proliferation and the induction of tumor cell apoptosis. Activation of the PI3K/Akt signaling pathway is frequently associated with tumorigenesis and dysregulated PI3K/Akt signaling may contribute to tumor resistance to a variety of antineoplastic agents.

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	65.0	140.15
DMF	50.0	107.81
Ethanol	50.0	107.81
Ethanol:PBS (pH 7.2) (1:1)	0.5	1.08

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.16 mL	10.78 mL	21.56 mL
5 mM	0.43 mL	2.16 mL	4.31 mL
10 mM	0.22 mL	1.08 mL	2.16 mL
50 mM	0.04 mL	0.22 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. Wu JH, Limmer AL, Narayanan D, Doan HQ, Simonette RA, Rady PL, Tyring SK. The novel AKT inhibitor Afuresertib suppresses human Merkel cell carcinoma MKL-1 cell growth. Clin Exp Dermatol. 2021 Jun 11. doi: 10.1111/ced.14798. Epub ahead of print. PMID: 34115902.
2. Yamaji M, Ota A, Wahiduzzaman M, Karnan S, Hyodo T, Konishi H, Tsuzuki S, Hosokawa Y, Haniuda M. Novel ATP-competitive Akt inhibitor afuresertib suppresses the proliferation of malignant pleural mesothelioma cells. Cancer Med. 2017 Nov;6(11):2646-2659. doi: 10.1002/cam4.1179. Epub 2017 Sep 27. PMID: 28960945; PMCID: PMC5673922.

In vivo study

1. Zhou H, Ning Y, Zeng G, Zhou C, Ding X. Curcumin promotes cell cycle arrest and apoptosis of acute myeloid leukemia cells by inactivating AKT. Oncol Rep. 2021 Apr;45(4):11. doi: 10.3892/or.2021.7962. Epub 2021 Mar 2. PMID: 33649826; PMCID: PMC7877002.

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7. Bioactivity

Biological target:

Afuresertib hydrochloride (GSK 2110183 hydrochloride) is an ATP-competitive pan-Akt kinase inhibitor with Kis of 0.08/2/2.6 nM for Akt1/Akt2/Akt3 respectively.

In vitro activity

This study found that afuresertib enhanced the phosphorylation of Akt at Thr308 and Ser473, which is consistent with that observed using other catalytic, ATP-competitive Akt inhibitors, including GDC-0068. Results of gene expression profiling performed in this study showed that afuresertib significantly suppresses oncogenic gene expression related to serum response, E2F1, MYC, mTOR, as well as Akt. This result suggests that afuresertib-induced hyperphosphorylation does not activate of Akt-mediated signaling. Afuresertib increased the expression of gene sets associated with inositol phosphate and/or amino acid metabolisms, including branched chain amino acids (BCAAs) and tryptophan metabolism, suggesting that these metabolic pathways are alternatively used to supply cellular energy after Akt inhibition in MPM cells. Therefore, it would be interesting to examine whether inhibition of inositol phosphate and/or BCAA metabolic pathways enhances afuresertib-induced suppression in MPM cells.

Reference: Cancer Med. 2017 Nov; 6(11): 2646–2659. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5673922/

In vivo activity

Next, the in vivo efficacy of curcumin and afuresertib for the treatment of AML was evaluated. NOD/SCID mice were intravenously injected with 1×106 ML-2 cells. Drug treatment began 15 days after injection and continued every other day for 16 days. After treatment, peripheral blood mononuclear cells (PBMCs) and bone marrow mononuclear cells (BMMCs) were isolated and evaluated for human hematopoietic (hCD45) chimerism via flow cytometry (Fig. 4). Compared with the control group (VEH), the mice treated with curcumin (CCM) or afuresertib (AFU) either alone or in combination (CCM+AFU) had fewer human CD45+ cells in the bone marrow and peripheral blood. Moreover, combination drug therapy was more effective than single drug therapy in reducing the chimerism of hCD45 (Fig. 4). These results indicated that curcumin and afuresertib synergistically suppressed the engraftment of AML cells.

Reference: Oncol Rep. 2021 Apr; 45(4): 11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7877002/

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.