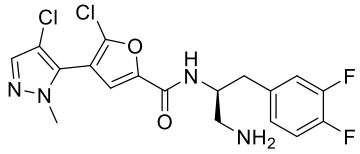
Product data sheet

MedKoo Cat#: 205481 Name: Uprosertib CAS#: 1047634-65-0 Chemical Formula: $C_{18}H_{16}Cl_2F_2N_4O_2$ Exact Mass: 428.06184 Molecular Weight: 429.25	
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:

Uprosertib, also known as GSK2141795 and GSK795, is an orally bioavailable inhibitor of the serine/threonine protein kinase Akt (protein kinase B) with potential antineoplastic activity. Akt inhibitor GSK2141795 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	45.33	105.60
DMF	1.0	2.33
Ethanol	85.0	198.02

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.33 mL	11.65 mL	23.30 mL
5 mM	0.47 mL	2.33 mL	4.66 mL
10 mM	0.23 mL	1.16 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. Datta J, Damodaran S, Parks H, Ocrainiciuc C, Miya J, Yu L, Gardner EP, Samorodnitsky E, Wing MR, Bhatt D, Hays J, Reeser JW, Roychowdhury S. Akt Activation Mediates Acquired Resistance to Fibroblast Growth Factor Receptor Inhibitor BGJ398. Mol Cancer Ther. 2017 Apr;16(4):614-624. doi: 10.1158/1535-7163.MCT-15-1010. Epub 2017 Mar 2. PMID: 28255027; PMCID: PMC5539948.

2. Dumble M, Crouthamel MC, Zhang SY, Schaber M, Levy D, Robell K, Liu Q, Figueroa DJ, Minthorn EA, Seefeld MA, Rouse MB, Rabindran SK, Heerding DA, Kumar R. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination with the MEK inhibitor. PLoS One. 2014 Jun 30;9(6):e100880. doi: 10.1371/journal.pone.0100880. PMID: 24978597; PMCID: PMC4076210.

In vivo study

1. Dumble M, Crouthamel MC, Zhang SY, Schaber M, Levy D, Robell K, Liu Q, Figueroa DJ, Minthorn EA, Seefeld MA, Rouse MB, Rabindran SK, Heerding DA, Kumar R. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination

with the MEK inhibitor. PLoS One. 2014 Jun 30;9(6):e100880. doi: 10.1371/journal.pone.0100880. PMID: 24978597; PMCID: PMC4076210.
2. Sohn SH, Sul HJ, Kim B, Kim HS, Kim BJ, Lim H, Kang HS, Soh JS, Kim KC, Cho JW, Seo J, Koh Y, Zang DY. RNF43 and PWWP2B inhibit cancer cell proliferation and are predictive or prognostic biomarker for FDA-approved drugs in patients with advanced gastric cancer. J Cancer. 2021 Jun 1;12(15):4616-4625. doi: 10.7150/jca.56014. PMID: 34149925; PMCID: PMC8210561.

7. Bioactivity

Biological target:

Uprosertib (GSK2141795) is a pan-Akt inhibitor with IC50 values of 180/328/38 nM for Akt1/Akt2/Akt3, respectively.

In vitro activity

Treatment of DMS114-R cell line with GSK2141795 alone resulted in a significant decrease in cell viability with dose as little as 100nmol/L. Though, increasing doses reduced cell viability further, with 80% decrease noticed at 3μmol/L concentration of GSK2141795 (Figure 4A). Low doses of GSK2141795 had no effect on cell viability in the DMS114 control cell line, while a high dose (3μmol/L) had a mild effect. While the combination of BGJ398 (100nmol/L) with GSK2141795 (100nmol/L) produced a significant reduction in cell viability, this effect was not significant compared to the use of GSK2141795 as a single agent, indicating that treatment of Akt inhibitor alone is sufficient to inhibit the viability of BGJ398 resistant DMS114 cells (Figure 4A). Thus, Akt signaling pathway is highly activated in the BGJ398 resistant DMS114 cell line and treatment with GSK2141795 inhibits cell viability.

Reference: Mol Cancer Ther. 2017 Apr; 16(4): 614–624. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539948/

In vivo activity

Mice bearing BT474 tumors were dosed orally with either vehicle or GSK2141795. After 20 days of treatment with 10, 20 and 30 mg/kg of GSK2141795, tumor growth inhibition (TGI) of 28, 57 and 98%, respectively, was observed relative to vehicle control (Figure 6A). Minimal body weight loss of 3–8% was reported on day 6 of dosing which recovered by the end of study (data not shown).

Reference: PLoS One. 2014; 9(6): e100880. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4076210/

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.