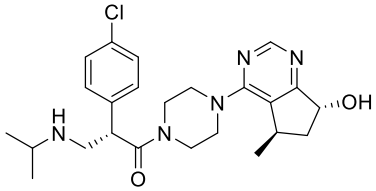
Product data sheet

MedKoo Cat#: 205467 Name: Ipatasertib (GDC-0068) CAS#: 1001264-89-6 (free base) Chemical Formula: $C_{24}H_{32}ClN_5O_2$ Exact Mass: 457.22445 Molecular Weight: 458.0	
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:
Ipatasertib, also known as GDC-0068, is an orally bioavailable inhibitor of the serine/threonine protein kinase Akt (protein kinase B) with potential antineoplastic activity. Akt inhibitor GDC-0068 binds to and inhibits the activity of Akt in a non-ATP-competitive manner, which may result in the inhibition of the PI3K/Akt signaling pathway and tumor cell proliferation and the induction of tumor cell apoptosis.

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	45.0	98.25
DMF	25.0	54.59
DMF:PBS (pH 7.2) (1:1)	0.5	1.09
Ethanol	56.0	122.27
Water	10.0	21.83

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.18 mL	10.92 mL	21.83 mL
5 mM	0.44 mL	2.18 mL	4.37 mL
10 mM	0.22 mL	1.09 mL	2.18 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Adelaiye-Ogala R, Gryder BE, Nguyen YTM, Alilin AN, Grayson AR, Bajwa W, Jansson KH, Beshiri ML, Agarwal S, Rodriguez-Nieves JA, Capaldo B, Kelly K, VanderWeele DJ. Targeting the PI3K/AKT Pathway Overcomes Enzalutamide Resistance by Inhibiting Induction of the Glucocorticoid Receptor. Mol Cancer Ther. 2020 Jul;19(7):1436-1447. doi: 10.1158/1535-7163.MCT-19-0936. Epub 2020 May 5. PMID: 32371590.
2. Sun L, Huang Y, Liu Y, Zhao Y, He X, Zhang L, Wang F, Zhang Y. Ipatasertib, a novel Akt inhibitor, induces transcription factor FoxO3a and NF-κB directly regulates PUMA-dependent apoptosis. Cell Death Dis. 2018 Sep 5;9(9):911. doi: 10.1038/s41419-018-0943-9. PMID: 30185800; PMCID: PMC6125489.

In vivo study

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1. Ippen FM, Grosch JK, Subramanian M, Kuter BM, Liederer BM, Plise EG, Mora JL, Nayyar N, Schmidt SP, Giobbie-Hurder A, Martinez-Lage M, Carter SL, Cahill DP, Wakimoto H, Brastianos PK. Targeting the PI3K/Akt/mTOR pathway with the pan-Akt inhibitor GDC-0068 in PIK3CA-mutant breast cancer brain metastases. Neuro Oncol. 2019 Nov 4;21(11):1401-1411. doi: 10.1093/neuonc/noz105. PMID: 31173106; PMCID: PMC6827829.
2. Lin J, Sampath D, Nannini MA, Lee BB, Degtyarev M, Oeh J, Savage H, Guan Z, Hong R, Kassees R, Lee LB, Risom T, Gross S, Liederer BM, Koeppen H, Skelton NJ, Wallin JJ, Belvin M, Punnoose E, Friedman LS, Lin K. Targeting activated Akt with GDC-0068, a novel selective Akt inhibitor that is efficacious in multiple tumor models. Clin Cancer Res. 2013 Apr 1;19(7):1760-72. doi: 10.1158/1078-0432.CCR-12-3072. Epub 2013 Jan 3. PMID: 23287563.

7. Bioactivity

Biological target:

Ipatasertib (GDC-0068) is an ATP-competitive pan-Akt inhibitor with IC50s of 5, 18 and 8 nM for Akt1, Akt2 and Akt3, respectively.

In vitro activity

Consistent with its mechanism of action, the effect of ipatasertib on cell viability correlated with inhibition of AKT signaling, which is manifest as an increase in AKT phosphorylation (due to its ability to protect against phosphatases) and decrease in phosphorylation of downstream targets (Fig. 1B). As expected, enzalutamide decreased AR activity, demonstrated by decreased expression of canonical AR targets PSA and NKX3 in C4-2 and LREX cells, though not in 22RV1 cells, which express the AR variant AR-V7. Interestingly, C4-2 and LREX had increased expression of these canonical AR targets in the presence of ipatasertib. To determine whether ipatasertib has an anticancer effect in hormone-sensitive prostate cancer (HSPC), this study tested its effect in the well-characterized HSPC cell lines LNCaP and LAPC4. Both models of HSPC were more sensitive to ipatasertib than to androgen withdrawal (Supplementary Fig. S1A).

Reference: Mol Cancer Ther. 2020 Jul;19(7):1436-1447. https://mct.aacrjournals.org/content/19/7/1436.long

In vivo activity

In the PIK3CA-MT MDA-MB-361 BCBM tumor model, GDC-0068 resulted in a significant inhibition of tumor growth measured by BLI in treated mice, whereas in contrast, sham-treated tumors continued to grow more rapidly (Figure 4A–C). No differences in tumor growth and survival were detected in MDA-MB-231 BrM2 intracranial tumors over the course of treatment (Supplementary Figure 2). Treatment with GDC-0068 led to a significant inhibition in the MDA-MB-361 tumor bearing mice compared with sham (mixed effect model, effect of treatment at day 77: $P < 0.0001$) (Figure 4B). Furthermore, treatment with GDC-0068 resulted in a significant survival benefit (log-rank test, $P = 0.0008$), with a median survival of 109 days in treated mice versus 82.5 days in mice receiving sham treatment (Figure 4D). To evaluate GDC-0068–induced phosphorylation inhibition of PI3K/Akt/mTOR pathway downstream targets, expression of p-PRAS40 and p-S6 ribosomal protein was analyzed with immunohistochemistry. In accordance with the previous in vitro and in vivo results, GDC-0068 treated tumors in MDA-MB-361 tumor bearing mice revealed reduced immunostaining of p-S6 ribosomal protein compared with tumors of the sham cohort (Figure 4E), but no such effect was seen in the PIK3CA-mutant cell line MDA-MB-231 BrM2 (Supplementary Figure 2).

Reference: Neuro Oncol. 2019 Nov; 21(11): 1401–1411. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6827829/

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.