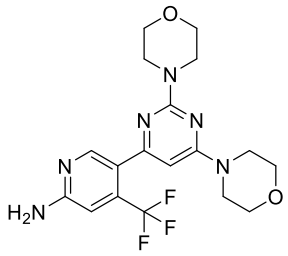
Product data sheet

MedKoo Cat#: 204690 Name: Buparlisib (BKM120) CAS#: 944396-07-0 (free base) Chemical Formula: $C_{18}H_{21}F_3N_6O_2$ Exact Mass: 410.16781 Molecular Weight: 410.39	
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:

Buparlisib, also known as BKM120, is an orally bioavailable specific oral inhibitor of the pan-class I phosphatidylinositol 3-kinase (PI3K) family of lipid kinases with potential antineoplastic activity. PI3K inhibitor BKM120 specifically inhibits class I PIK3 in the PI3K/AKT kinase (or protein kinase B) signaling pathway in an ATP-competitive manner, thereby inhibiting the production of the secondary messenger phosphatidylinositol-3,4,5-trisphosphate and activation of the PI3K signaling pathway.

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	91.0	221.74
Ethanol	82.0	199.81

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.44 mL	12.18 mL	24.37 mL
5 mM	0.49 mL	2.44 mL	4.87 mL
10 mM	0.24 mL	1.22 mL	2.44 mL
50 mM	0.05 mL	0.24 mL	0.49 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. Sadeghi S, Esmaeili S, Pourbagheri-Sigaroodi A, Safaroghli-Azar A, Bashash D. PI3K Abrogation Using Pan-PI3K Inhibitor BKM120 Gives Rise to a Significant Anticancer Effect on AML-Derived KG-1 Cells by Inducing Apoptosis and G2/M Arrest. Turk J Haematol. 2020 Aug 28;37(3):167-176. doi: 10.4274/tjh.galenos.2020.2019.0440. Epub 2020 Mar 12. PMID: 32160736; PMCID: PMC7463220.
2. Padthaisong S, Dokduang H, Yothaisong S, Techasen A, Namwat N, Yongvanit P, Khuntikeo N, Titapun A, Sangkhamanon S, Loilome W. Inhibitory effect of NVP-BKM120 on cholangiocarcinoma cell growth. Oncol Lett. 2018 Aug;16(2):1627-1633. doi: 10.3892/ol.2018.8848. Epub 2018 May 31. PMID: 30008846; PMCID: PMC6036373.

In vivo study

1. Xie S, Ni J, McFaline-Figueroa JR, Wang Y, Bronson RT, Ligon KL, Wen PY, Roberts TM, Zhao JJ. Divergent Roles of PI3K Isoforms in PTEN-Deficient Glioblastomas. Cell Rep. 2020 Sep 29;32(13):108196. doi: 10.1016/j.celrep.2020.108196. PMID: 32997991; PMCID: PMC7571617.
2. Li X, Martinez-Ledesma E, Zhang C, Gao F, Zheng S, Ding J, Wu S, Nguyen N, Clifford SC, Wen PY, Ligon KL, Yung WKA, Koul D. Tie2-FGFR1 Interaction Induces Adaptive PI3K Inhibitor Resistance by Upregulating Aurora A/PLK1/CDK1 Signaling in

Product data sheet

Glioblastoma. Cancer Res. 2019 Oct 1;79(19):5088-5101. doi: 10.1158/0008-5472.CAN-19-0325. Epub 2019 Aug 15. PMID: 31416846.

7. Bioactivity

Biological target:

Buparlisib (BKM120; NVP-BKM120) is a pan-class I PI3K inhibitor, with IC50s of 52, 166, 116 and 262 nM for p110α, p110β, p110δ and p110γ, respectively.

In vitro activity

The results demonstrated that the treatment of KG-1 with BKM120 not only inhibited proliferative capacity by reducing DNA replication and the number of viable cells but also led to an increased percentage of cells in the G2/M phase, suggesting that the antiproliferative effects of the inhibitor are mediated, at least partially, through the induction of G2/M arrest. In an investigation of the effects of PI3K suppression on multiple myeloma cells, the inhibitory effect of pan-PI3K inhibition on the survival of both KMM-1 and RPMI 8226 cells via the induction of SIRT1-mediated G2/M arrest was also highlighted. Among examples of overactivation of malignant signaling networks, and foremost of the PI3K pathway, the c-Myc oncogene is explicitly activated and subsequently leads to cell cycle progression via the inhibition of cell cycle-related genes such as p21 and p27 cyclin-dependent kinase inhibitors. Remarkably, while BKM120-induced G2/M arrest was associated with the upregulation of p21 and p27 expression, this study could find no noticeable alteration in c-Myc mRNA levels, suggesting the probable contribution of the c-Myc oncogene with less sensitivity of leukemic cells to the PI3K inhibitors. Accordingly, investigation of the effects of the small-molecule inhibitor of c-Myc revealed that 10058-F4 reduced KG-1 cell survival and sensitized the cells to lower concentrations of either BKM120 or idelalisib, supporting the hypothesis that the c-Myc inhibitors may restore leukemic cell sensitivity to PI3K inhibitors when administered as part of combination regimens.

Reference: Turk J Haematol. 2020 Sep; 37(3): 167–176. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7463220/

In vivo activity

This study next used intracranial orthotopic allografts of PP ($p53^{f/f};Pten^{f/f}$) GBM (glioblastoma) to examine BKM120 (also known as buparlisib; Table S1). BKM120 is currently the only pan-PI3K inhibitor with proven brain penetration and has been tested in the clinic for GBM patients. Treatment with BKM120 prolonged the median survival of PP-bearing mice slightly from 22 to 27 days (Figure 4A). While this result is statistically significant, it is unlikely to have a meaningful clinical impact. WB and IHC analyses of tumors harvested from experimental mice showed that BKM120 modestly reduced phosphorylation of both Akt and S6RP (Figures 4B and and4C),4C), suggesting that while BKM120 can cross the BBB, it cannot deeply suppress Akt-mammalian target of rapamycin (mTOR) signaling. Data are consistent with a recent clinical trial that showed that BKM120 does not effectively suppress S6RP phosphorylation despite adequate brain penetration and has limited efficacy in patients with GBM.

Reference: Cell Rep. 2020 Sep 29; 32(13): 108196. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7571617/