# **Product data sheet**



MedKoo Cat#: 206559				
Name: GDC-0084				
CAS#: 1382979-44-3				
Chemical Formula: C <sub>18</sub> H <sub>22</sub> N <sub>8</sub> O <sub>2</sub>				
Exact Mass: 382.1866				
Molecular Weight: 382.428				
Product supplied as:	Powder			
Purity (by HPLC):	$\geq 98\%$			
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:

GDC-0084, also known as RG7666 and Paxalisib, is a phosphatidylinositol 3-kinase (PI3K) inhibitor with potential antineoplastic activity. PI3K inhibitor GDC-0084 specifically inhibits PI3K in the PI3K/AKT kinase (or protein kinase B) signaling pathway, thereby inhibiting the activation of the PI3K signaling pathway. This may result in the inhibition of both cell growth and survival in susceptible tumor cell populations. Activation of the PI3K signaling pathway is frequently associated with tumorigenesis.

# 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

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Solvent	Max Conc. mg/mL	Max Conc. mM		
DMSO	7.0	18.30		

# 4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.61 mL	13.07 mL	26.15 mL
5 mM	0.52 mL	2.61 mL	5.23 mL
10 mM	0.26 mL	1.31 mL	2.61 mL
50 mM	0.05 mL	0.26 mL	0.52 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

Ippen FM, Alvarez-Breckenridge CA, Kuter BM, Fink AL, Bihun IV, Lastrapes M, Penson T, Schmidt SP, Wojtkiewicz GR, Ning J, Subramanian M, Giobbie-Hurder A, Martinez-Lage M, Carter SL, Cahill DP, Wakimoto H, Brastianos PK. The Dual PI3K/mTOR Pathway Inhibitor GDC-0084 Achieves Antitumor Activity in PIK3CA-Mutant Breast Cancer Brain Metastases. Clin Cancer Res. 2019 Jun 1;25(11):3374-3383. doi: 10.1158/1078-0432.CCR-18-3049. Epub 2019 Feb 22. PMID: 30796030; PMCID: PMC6685218.
Ding LT, Zhao P, Yang ML, Lv GZ, Zhao TL. GDC-0084 inhibits cutaneous squamous cell carcinoma cell growth. Biochem Biophys Res Commun. 2018 Sep 10;503(3):1941-1948. doi: 10.1016/j.bbrc.2018.07.139. Epub 2018 Jul 30. PMID: 30072096.

# In vivo study

Ippen FM, Alvarez-Breckenridge CA, Kuter BM, Fink AL, Bihun IV, Lastrapes M, Penson T, Schmidt SP, Wojtkiewicz GR, Ning J, Subramanian M, Giobbie-Hurder A, Martinez-Lage M, Carter SL, Cahill DP, Wakimoto H, Brastianos PK. The Dual PI3K/mTOR Pathway Inhibitor GDC-0084 Achieves Antitumor Activity in PIK3CA-Mutant Breast Cancer Brain Metastases. Clin Cancer Res. 2019 Jun 1;25(11):3374-3383. doi: 10.1158/1078-0432.CCR-18-3049. Epub 2019 Feb 22. PMID: 30796030; PMCID: PMC6685218.
Salphati L, Alicke B, Heffron TP, Shahidi-Latham S, Nishimura M, Cao T, Carano RA, Cheong J, Greve J, Koeppen H, Lau S, Lee LB, Nannini-Pepe M, Pang J, Plise EG, Quiason C, Rangell L, Zhang X, Gould SE, Phillips HS, Olivero AG. Brain Distribution and

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Efficacy of the Brain Penetrant PI3K Inhibitor GDC-0084 in Orthotopic Mouse Models of Human Glioblastoma. Drug Metab Dispos. 2016 Dec;44(12):1881-1889. doi: 10.1124/dmd.116.071423. Epub 2016 Sep 16. PMID: 27638506.

# 7. Bioactivity

Biological target:

Paxalisib (GDC-0084) is a brain penetrant inhibitor of PI3K and mTOR, with Kis of 2 nM, 46 nM, 3 nM, 10 nM and 70 nM for PI3K  $\alpha$  PI3K $\beta$ , PI3K $\delta$ , PI3K $\delta$ , PI3K $\gamma$  and mTOR, respectively.

# In vitro activity

PI3K-Akt-mTOR signaling is overactivated in cSCC cells, representing a valuable therapeutic target. GDC-0084 is a novel PI3K/mTOR dual inhibitor. Its effect in cSCC cells was studied. Three established cSCC cell lines, A431, SCC-13 and SCL-1, were tested. By performing the CCK-8 assay, this study showed that GDC-0084 inhibited survival of all cSCC cells (Fig. 1A). The PI3K/mTOR dual inhibitor displayed a dose-dependent activity in inhibiting cSCC cell survival (Fig. 1A). At the lowest concentration (10 nM) it was however ineffective (Fig. 1A). Among the tested cell lines A431 cells were most sensitive to GDC-0084, showing the lowest IC-50 ( $186.51 \pm 11.31$  nM) (Fig. 1A).

Reference: Biochem Biophys Res Commun. 2018 Sep 10;503(3):1941-1948. https://pubmed.ncbi.nlm.nih.gov/30072096/

#### In vivo activity

In a patient-derived brain metastasis mouse model, 15mg/kg/day of GDC-0084 administered orally significantly inhibited tumor growth in a trastuzumab-resistant, PIK3CA-MT cell line model and not a PIK3CA-WT cell line model. PI3K-pathway inhibition within the brain was confirmed with immunohistochemistry by reduction in signal intensity for pAkt and pS6 ribosomal protein in the PIK3CA-MT tumors treated with GDC-0084.

Reference: Clin Cancer Res. 2019 Jun 1; 25(11): 3374–3383. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6685218/

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.