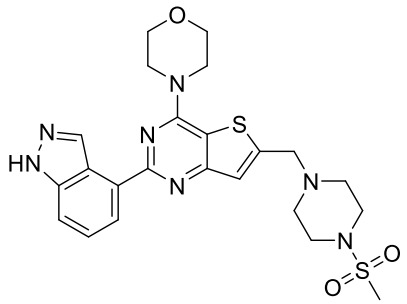
Product data sheet

MedKoo Cat#: 201395 Name: GDC-0941 (Pictilisib) CAS#: 957054-30-7 (free base) Chemical Formula: $C_{23}H_{27}N_7O_3S_2$ Exact Mass: 513.16168 Molecular Weight: 513.63	
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:
Pictilisib, also known as Pictrelisib, GDC-0941, RG7321 and GNE0941 , is an orally bioavailable, and is a potent small-molecule thieno[3,2-d]pyrimidine inhibitor of the class I phosphatidylinositol 3 kinase (PI3K) isoforms p100alpha and p100delta with potential antineoplastic activity. PI3K inhibitor GDC-0941 selectively binds to PI3K isoforms in an ATP-competitive manner, inhibiting the production of the secondary messenger phosphatidylinositol-3,4,5-trisphosphate (PIP3) and activation of the PI3K/Akt signaling pathway; inhibition of tumor cell growth, motility and survival in susceptible tumor cell populations may result.

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	100	194.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.95 mL	9.73 mL	19.47 mL
5 mM	0.39 mL	1.95 mL	3.89 mL
10 mM	0.19 mL	0.97 mL	1.95 mL
50 mM	0.04 mL	0.19 mL	0.39 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. Burrows N, Babur M, Resch J, Ridsdale S, Mejin M, Rowling EJ, Brabant G, Williams KJ. GDC-0941 inhibits metastatic characteristics of thyroid carcinomas by targeting both the phosphoinositide-3 kinase (PI3K) and hypoxia-inducible factor-1α (HIF-1α) pathways. J Clin Endocrinol Metab. 2011 Dec;96(12):E1934-43. doi: 10.1210/jc.2011-1426. Epub 2011 Oct 12. PMID: 21994956.

2. Zou ZQ, Zhang LN, Wang F, Bellenger J, Shen YZ, Zhang XH. The novel dual PI3K/mTOR inhibitor GDC-0941 synergizes with the MEK inhibitor U0126 in non-small cell lung cancer cells. Mol Med Rep. 2012 Feb;5(2):503-8. doi: 10.3892/mmr.2011.682. Epub 2011 Nov 16. PMID: 22101421.

In vivo study

1. Wullschleger S, García-Martínez JM, Duce SL. Quantitative MRI establishes the efficacy of PI3K inhibitor (GDC-0941) multi-treatments in PTEN-deficient mice lymphoma. Anticancer Res. 2012 Feb;32(2):415-20. PMID: 22287727; PMCID: PMC3292793.

2. Burrows N, Babur M, Resch J, Ridsdale S, Mejin M, Rowling EJ, Brabant G, Williams KJ. GDC-0941 inhibits metastatic characteristics of thyroid carcinomas by targeting both the phosphoinositide-3 kinase (PI3K) and hypoxia-inducible factor-1α (HIF-1α) pathways. J Clin Endocrinol Metab. 2011 Dec;96(12):E1934-43. doi: 10.1210/jc.2011-1426. Epub 2011 Oct 12. PMID: 21994956.

7. Bioactivity

Biological target:

Pictilisib (GDC-0941) is a potent inhibitor of PI3Kα/δ with an IC50 of 3 nM, with modest selectivity against p110β (11-fold) and p110γ (25-fold).

In vitro activity

The effects of the clinically relevant inhibitor GDC-0941 on pathway regulation was evaluated. Initial studies were undertaken using adenovirus-based luciferase reporter assays to evaluate the effects of GDC-0941 on HIF activity in the thyroid carcinoma cell panel. GDC-0941 at 1 μM significantly inhibited HIF-driven reporter gene expression in air, 1% O2 (hypoxia), and anoxia (Supplemental Fig. 1). Effects on protein expression were then assessed in FTC133 and 8505c cells, which have hyperactivated PI3K. Cells were exposed to GDC-0941 under varying O2 tensions and lysates Western blotted. GDC-0941 reduced PI3K pathway activity in both cell lines, illustrated by decreased pAKT. Expression of HIF-1α and the downstream target CA-9 were also reduced. Down-regulation of the HIF target lactate dehydrogenase A (LDH-A) was observed only in FTC133 cells, and reduction in glucose transporter 1 (GLUT-1) was more pronounced in 8505c rather than FTC133 cells (Fig. 1A).

Reference: J Clin Endocrinol Metab. 2011 Dec;96(12):E1934-43. https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2011-1426

In vivo activity

During treatment 1, the tumours in the GDC-0941-treated mice showed a marked non-linear shrinkage, with an average tumour regression of 52±8%. This tumour regression profile had been observed previously, with shrinkage reaching a plateaus after a month (24). When the GDC-0941 treatment ceased, the tumours in the test cohort mice grew again (off-treatment period 1) with an average linear tumour growth rate of 31.3±9.9 mm3/week (R2) (R2=0.98). R2 for individual GDC-0941 test mice are shown in Table II. After 21 days, the tumours had nearly returned to their size at the start of treatment. They grew on average nearly twice (1.9) as fast as before treatment (R2>R1); the difference was statistically significant (p=0.042). As with many molecular-targeted anticancer therapies, GDC-0941 stopped cells' proliferation but was not completely cytocidal.

Reference: Anticancer Res. 2012 Feb;32(2):415-20. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/22287727/

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.