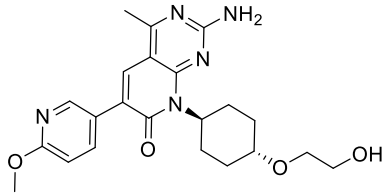
Product data sheet

MedKoo Cat#: 202226 Name: PF-04691502 CAS#: 1013101-36-4 Chemical Formula: $C_{22}H_{27}N_5O_4$ Exact Mass: 425.2063 Molecular Weight: 425.48	
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:

PF-04691502 is a PI3K/mTOR kinase inhibitor , is also an agent targeting the phosphatidylinositol 3 kinase (PI3K) and mammalian target of rapamycin (mTOR) in the PI3K/mTOR signaling pathway, with potential antineoplastic activity. PI3K/mTOR kinase inhibitor PF-04691502 inhibits both PI3K and mTOR kinases, which may result in apoptosis and growth inhibition of cancer cells overexpressing PI3K/mTOR.

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	14.0	32.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.35 mL	11.75 mL	23.50 mL
5 mM	0.47 mL	2.35 mL	4.70 mL
10 mM	0.24 mL	1.18 mL	2.35 mL
50 mM	0.05 mL	0.24 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. Chow Z, Johnson J, Chauhan A, Izumi T, Cavnar M, Weiss H, Townsend CM Jr, Anthony L, Wasilchenko C, Melton ML, Schrader J, Evers BM, Rychahou P. PI3K/mTOR Dual Inhibitor PF-04691502 Is a Schedule-Dependent Radiosensitizer for Gastroenteropancreatic Neuroendocrine Tumors. Cells. 2021 May 20;10(5):1261. doi: 10.3390/cells10051261. PMID: 34065268.
2. Yuan J, Mehta PP, Yin MJ, Sun S, Zou A, Chen J, Rafidi K, Feng Z, Nickel J, Engebretsen J, Hallin J, Blasina A, Zhang E, Nguyen L, Sun M, Vogt PK, McHarg A, Cheng H, Christensen JG, Kan JL, Bagrodia S. PF-04691502, a potent and selective oral inhibitor of PI3K and mTOR kinases with antitumor activity. Mol Cancer Ther. 2011 Nov;10(11):2189-99. doi: 10.1158/1535-7163.MCT-11-0185. Epub 2011 Jul 12. PMID: 21750219.

In vivo study

1. Bresin A, Cristofoletti C, Caprini E, Cantonetti M, Monopoli A, Russo G, Narducci MG. Preclinical Evidence for Targeting PI3K/mTOR Signaling with Dual-Inhibitors as a Therapeutic Strategy against Cutaneous T-Cell Lymphoma. J Invest Dermatol. 2020 May;140(5):1045-1053.e6. doi: 10.1016/j.jid.2019.08.454. Epub 2019 Nov 1. PMID: 31682844.
2. Blunt MD, Carter MJ, Larrayoz M, Smith LD, Aguilar-Hernandez M, Cox KL, Tipton T, Reynolds M, Murphy S, Lemm E, Dias S, Duncombe A, Strefford JC, Johnson PW, Forconi F, Stevenson FK, Packham G, Cragg MS, Steele AJ. The PI3K/mTOR inhibitor PF-

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04691502 induces apoptosis and inhibits microenvironmental signaling in CLL and the Eμ-TCL1 mouse model. Blood. 2015 Jun 25;125(26):4032-41. doi: 10.1182/blood-2014-11-610329. Epub 2015 May 8. PMID: 25957390.

7. Bioactivity

Biological target:

PF-04691502 is an inhibitor of PI3K and mTOR. PF-04691502 binds to human PI3Kα, β, δ, γ and mTOR with Kis of 1.8, 2.1, 1.6, 1.9 and 16 nM, respectively.

In vitro activity

This study treated QGP-1 and BON cells with PF-04691502 (500 nM) to test the duration of PI3K pathway inhibition (Figure 2C). The expression of pAkt was inhibited in both QGP-1 and BON cells at 24, 48 and 72 h. Similarly, expression of pS6 (Ser235/236), which is a key regulator of 40 S ribosome subunit biogenesis, was inhibited in both cell lines. Finally, this study assessed the expression of p4EBP-1 (Thr37/46), which plays a critical role in translational mRNA complex assembly and found that PF-04691502 (500 nM) inhibited expression of this protein at all time points; p4EBP-1 expression was markedly attenuated at 24 and 48 h and completely inhibited at 72 h. A single treatment with PF-04691502 not only demonstrated sustained inhibition for the 24 h period in QGP-1 and BON cells (Figure 2B), but also attenuated pAkt, pS6 and p4EBP-1 at 24 h in NT-3 cells (data not shown). Moreover, these results demonstrate that PF-04691502 can effectively inhibit PI3K/mTOR pathway components in both QGP-1 and BON cells for at least 72 h.

Reference: Cells. 2021 May 20;10(5):1261. https://pubmed.ncbi.nlm.nih.gov/34065268/

In vivo activity

Finally, this study tested the antitumor activity of PF-502 (PF-04691502) in vivo using a xenograft mouse model. HH cells were transplanted subcutaneously into the flank of nude mice. When the tumors reached a 300 mm^3 mean volume, the mice were randomized into two groups (eight mice per group): the group treated with PF-502 and the vehicle control group. Immunohistochemistry analysis of tumor specimens harvested 1 hour after PF-502 injection, confirmed the inhibition of TORC1 and TORC2 signaling compared with the control group, as measured by P-S6RP(Ser235/236) and P-AKT(Ser473) (Supplementary Figure S5). PF-502 exhibited robust antitumor activity from day 4 of treatment (Figure 5a), reaching significance on day 13 ($P < 0.005$). At the end of the treatment, the tumor size in the PF-502-treated group was 43% of the control group (400 ± 57 mm3 vs 936 ± 158 mm3, $P < 0.001$). Accordingly, the mean tumor weight in the PF-502 group was 36% of the controls (0.2 ± 0.05 g vs 0.56 ± 0.05 g, $P < 0.001$) (Figure 5b). Furthermore, the Kaplan-Meier curve revealed PF-502 treatment prolongs survival: The control group showed a median time-to-event of 19 days while all, but one, PF-502-treated mice, did not reach the predefined endpoint by the end of the experiment (day 28, $P < 0.005$, Figure 5c).

Reference: J Invest Dermatol. 2020 May;140(5):1045-1053.e6. https://pubmed.ncbi.nlm.nih.gov/31682844/

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.