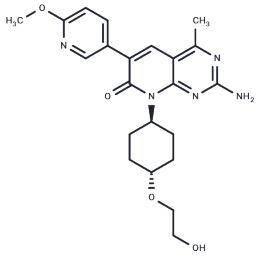
Data Sheet (Cat.No.T6251)

TargetMol

PF-04691502

Chemical Properties



CAS No. : 1013101-36-4

Formula: C22H27N5O4

Molecular Weight: 425.48

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PF-04691502 is a potent and selective inhibitor of PI3K and mTOR kinases with antitumor activity.
Targets(IC50)	Akt,Autophagy,mTOR,PI3K
In vitro	PF-04691502 potently inhibits recombinant class I PI3K and mTOR in biochemical assays and suppresses transformation of avian fibroblasts mediated by wild-type PI3K γ, δ, or mutant PI3Kα. In PIK3CA-mutant and PTEN-deleted cancer cell lines, PF-04691502 reduces phosphorylation of AKT T308 and AKT S473 (IC(50) of 7.5-47 nM and 3.8-20 nM, respectively) and inhibits cell proliferation (IC(50) of 179-313 nM). PF-04691502 inhibits mTORC1 activity in cells as measured by PI3K-independent nutrient stimulated assay, with an IC(50) of 32 nM and inhibits the activation of PI3K and mTOR downstream effectors including AKT, FKHRL1, PRAS40, p70S6K, 4EBP1, and S6RP. Short-term exposure to PF-04691502 predominantly inhibits PI3K, whereas mTOR inhibition persists for 24 to 48 hours. PF-04691502 induces cell cycle G(1) arrest, concomitant with upregulation of p27 Kip1 and reduction of Rb. [1]
In vivo	Antitumor activity of PF-04691502 is observed in U87 (PTEN null), SKOV3 (PIK3CA mutation), and gefitinib- and erlotinib-resistant non-small cell lung carcinoma xenografts. [1] PF-04691502 inhibits tumor growth at 7 days by 72%. FDG-PET imaging revealed that PF-04691502 reduces glucose metabolism dramatically. Tissue biomarkers of PI3K/mTOR pathway activity, p-AKT (S473), and p-RPS6 (S240/244), are also dramatically inhibited following PF-04691502 treatment. [2]
Kinase Assay	Kinase Assay: The fluorescence polarization assay for ATP competitive inhibition is done as follows: mPI3Kα dilution solution (90 nM) is prepared in fresh assay buffer (50 mM Hepes pH 7.4, 150 mM NaCl, 5 mM DTT, 0.05% CHAPS) and kept on ice. The enzyme reaction contains 0.5 nM mouse PI3Kα (p110α/p85α complex purified from insect cells), 30 μM PIP2, PF-04691502 (0, 1, 4, and 8 nM), 5 mM MgCl2, and 2-fold serial dilutions of ATP (0-800 μM). Final dimethyl sulfoxide is 2.5%. The reaction is initiated by the addition of ATP and terminated after 30 minutes with 10 mM EDTA. In a detection plate, 15 uL of detector/probe mixture containing 480 nM GST-Grp1PH domain and 12 nM TAMRA tagged fluorescent PIP3 in assay buffer is mixed with 15 uL of kinase reaction mixture. The plate is shaken for 3 minutes, and incubated for 35 to 40 minutes before reading on an LJL Analyst HT.

Cell Research	BT20, U87 mg, and SKOV3 cells are plated at 3,000 cell/well in 96-well culture plates in growth medium with 10% FBS. Cells are incubated overnight and treated with DMSO (0.1% final) or serial diluted compound for 3 days. Resazurin is added to 0.1 mg/mL. Plates are incubated at 37 °C in 5% CO2 for 3 hours. Fluorescence signals are read as emission at 590 nm after excitation at 530 nm. IC50 values are calculated by plotting fluorescence intensity to drug concentration in nonlinear curve(Only for Reference)

Solubility Information

Solubility	DMSO: 4.26 mg/mL (10 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3503 mL	11.7514 mL	23.5029 mL
5 mM	0.4701 mL	2.3503 mL	4.7006 mL
10 mM	0.235 mL	1.1751 mL	2.3503 mL
50 mM	0.047 mL	0.235 mL	0.4701 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Yuan J, Mol Cancer Ther, 2011, 10(11), 2189-2199
Zhou Z, Cui D, Sun M H, et al. CAFs-derived MFAP5 promotes bladder cancer malignant behavior through NOTCH2/HEY1 signaling. The FASEB Journal. 2020
Kinross KM, Mol Cancer Ther, 2011, 10(8), 1440-1449
Simmons BH, Cancer Chemother Pharmacol, 2012, 70(2), 213-220
Zhou Z, Cui D, Sun M H, et al. CAFs-derived MFAP5 promotes bladder cancer malignant behavior through NOTCH2/HEY1 signaling[J]. The FASEB Journal. 2020.