Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

PF-04691502

Catalog No: tcsc0919

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1013101-36-4

Formula:
$C_{22}H_{27}N_5O_4$

Pathway:
PI3K/Akt/mTOR;PI3K/Akt/mTOR

Target:
PI3K;mTOR

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
425.48

Product Description

PF-04691502 is a potent and selective inhibitor of **PI3K** and **mTOR** kinases with antitumor activity. PF-04691502 inhibits human and

Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

mouse PI3Kα with **K_i** of 1.8 and 1.2 nM, respectively, human PI3K isoforms β, δ, and γ with **K_i** of 2.1, 1.6, and 1.9 nM, respectively, and human mTOR with **K_i** of 16 nM.

IC50 & Target: Ki: 1.2 nM (mouse PI3Kα), 1.8 nM (human PI3Kα), 2.1 nM (human PI3Kβ), 1.6 nM (human PI3Kδ) ,1.9 nM (human PI3Kγ), 16 nM (human mTOR)[1]

In Vitro: PF-04691502 inhibits recombinant mouse PI3Kα in an ATP-competitive inhibitor. PF-04691502 potently inhibits AKT phosphorylation on S473 and T308 in all the 3 cancer cell lines with IC_{50} values of 3.8 to 20 nM and 7.5 to 47 nM, respectively. Using a 96-well plate-based P-S6RP(S235/236) ELISA assay, PF-04691502 potently inhibits mTORC1 activity with an IC_{50} of 32 nM. PF-04691502 inhibits cell proliferation of BT20, SKOV3, and U87MG with IC_{50} values of 313, 188, and 179 nM, respectively. 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[1].

In Vivo: Nude mice bearing U87MG tumors are administered orally once a day with PF-04691502 at 0.5, 1, 5, and 10 mg/kg (maximum tolerated dose, MTD). Treatment with 10 mg/kg results in a significant reduction of P-AKT(S473) levels at 1 hour postdosing, and persistent inhibition is observed for 8 hours. P-AKT(S473) recovers to above baseline 24 hours after 10 mg/kg treatment. For P-S6RP(S235/236), a similar inhibition time course is observed, but after 24 hours of treatment, P-S6RP levels remain lower than vehicle tumors. Modulation of the AKT downstream effector, P-PRAS40(T246), and mTOR downstream effector, P-4EBP1(T37/46), is observed. The PF-04691502-treated tumors are also evaluated by immunohistochemistry for levels of P-AKT(S473), total AKT, P-S6RP, and total S6RP. Phosphorylation of AKT and S6RP are significantly reduced at 4 hours after a single dose of PF-04691502 at 10 mg/kg. Dose-dependent tumor growth inhibition (TGI) is obtained in the U87MG xenograft model and approximately 73% TGI is observed at the MTD dose of 10 mg/kg[1].