

Product Data Sheet

Product Name: PF-04691502

Cat. No.: GC16417

Chemical Properties

Cas. No. 1013101-36-4

Chemical Name 2-amino-8-[4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxypyridin-3-yl)-4-methylpyrido[2,3-d]pyrimidin-7-one

SMILES CC1=C2C=C(C(=O)N(C2=NC(=N1)N)C3CCC(CC3)OCCO)C4=CN=C(C=C4)OC

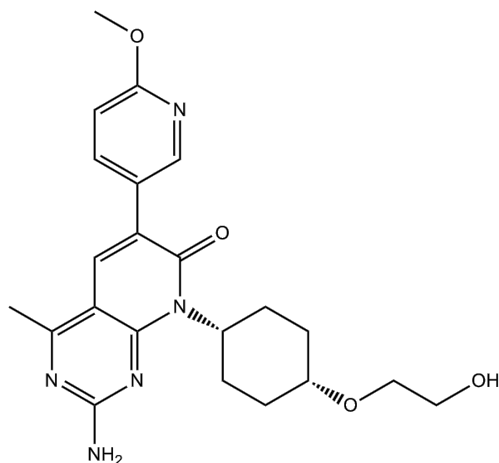
Formula $C_{22}H_{27}N_5O_4$ M.Wt 425.48

Solubility $\geq 10.625\text{mg/mL}$ in DMSO with gentle warming Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HK1 cells

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Preparation Method HK1 cells were grown in RPMI-1640 medium supplemented with 1% penicillin/streptomycin, and 10% heat-inactivated fetal bovine serum (FBS) at 37°C in an incubator with 5% CO₂. HK1 cells were cultured in 48-well plates (7000 cells per well) in culture medium. Different concentrations of PF-04691502 (0.1, 1, 10, 100, and 1000nM) were added at 24h after cell plating and incubated at 37°C with 5% CO₂ for 48h in complete medium. Cell growth inhibition was expressed as the percentage of the absorbance of control cultures measured at 570nm with a microplate reader.

Reaction Conditions 0.1, 1, 10, 100, and 1000nM; 48h

Applications PF-04691502 treatment significantly reduced growth of HK1 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models APP/PS1 mice

Preparation Method APP/PS1 mice were maintained at 22±1°C with a 12-h light/dark cycle and had free access to food and water. Mice were treated daily with PF-04691502 (1mg/kg/day) by oral administration for 12 weeks. The compound was formulated in 0.5% carboxymethylcellulose (CMC) dissolved in saline. At the end of the experimental period, the mice were sacrificed, and the whole brain was collected for downstream analyses.

Dosage form 1mg/kg/day for 12 weeks; p.o.

Applications PF-04691502 treatment reduced A β accumulation and total tau expression in the brains of APP/PS1 mice.

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References:

- [1] Wong C H, Loong H H, Hui C W C, et al. Preclinical evaluation of the PI3K-mTOR dual inhibitor PF-04691502 as a novel therapeutic drug in nasopharyngeal carcinoma[J]. Investigational new drugs, 2013, 31(6): 1399-1408.
- [2] Lanza M, Basilotta R, Caccamo A, et al. PF-04691502, a PI3K/mTOR Dual Inhibitor, Ameliorates AD-like Pathology in a Mouse Model of AD[J]. Cells, 2025, 14(18): 1474.

Background

PF-04691502 is an orally active, ATP-competitive dual inhibitor of PI3K and mTOR, with K_i values of 1.2, 2.1, 1.6, and 1.9nM for PI3K α , β , δ , and γ isoforms, respectively [1]. PF-04691502 blocks glucose transport and/or metabolism, leading to high glucose levels [2]. PF-04691502 has been widely used to inhibit the growth of various drug-resistant cancer cells and to prevent the tumor growth in mouse xenograft models[3].

In vitro, PF-04691502 treatment for 48 hours significantly inhibited the proliferation of CNE-1, CNE-2, and HK1 cells, with IC_{50} values of 222.3nM, 97nM and 181.2nM, respectively [4]. Treatment with 10 μ M PF-04691502 for 48 hours specifically targeted and eliminated the senescent cells in the NIH-3T3 cell model induced by doxorubicin[5]. 20 μ M of PF-04691502 treatment for 24 hours inhibited the phosphorylation of Akt and the expression of PTEN in HepG2 cells, suppressed cell proliferation, and induced cell cycle arrest at the G1 phase[6].

In vivo, PF-04691502 treatment via oral administration at a dose of 10mg/kg/day for 11 days significantly inhibited tumor growth in the U87MG xenograft mouse model and reduced the phosphorylation levels of AKT and S6RP in the tumor tissues[7]. Oral administration of 10mg/kg dose of PF-04691502 daily for 12 weeks significantly enhanced the cognitive function of APP/PS1 mice and significantly reduced the accumulation of insoluble A β in the brain[8].

References:

- [1] Blunt M D, Carter M J, Larrayoz M, et al. The PI3K/mTOR inhibitor PF-04691502 induces apoptosis and inhibits microenvironmental signaling in CLL and the E μ -TCL1 mouse model[J]. Blood, The Journal of the American Society of Hematology, 2015, 125(26): 4032-4041.

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- [2] Britten C D, Adjei A A, Millham R, et al. Phase I study of PF-04691502, a small-molecule, oral, dual inhibitor of PI3K and mTOR, in patients with advanced cancer[J]. Investigational new drugs, 2014, 32(3): 510-517.
- [3] Mehta P P, Walls M, Baxi S M, et al. PF-04691502, a potent and selective mTOR/PI3K dual inhibitor, demonstrates in vitro and in vivo antitumor activity in non-small cell lung carcinoma cells[J]. Cancer Research, 2010, 70(8_Supplement): 4473-4473.
- [4] Wong C H, Loong H H, Hui C W C, et al. Preclinical evaluation of the PI3K-mTOR dual inhibitor PF-04691502 as a novel therapeutic drug in nasopharyngeal carcinoma[J]. Investigational new drugs, 2013, 31(6): 1399-1408.
- [5] Fan Z, Tong Y, Yang Z, et al. Inhibitor PF-04691502 works as a senolytic to regulate cellular senescence[J]. Experimental Gerontology, 2024, 186: 112359.
- [6] Wang F Z, Yang N N, Zhao Y L, et al. PF-04691502 triggers cell cycle arrest, apoptosis and inhibits the angiogenesis in hepatocellular carcinoma cells[J]. Toxicology Letters, 2013, 220(2): 150-156.
- [7] Yuan J, Mehta P P, Yin M J, et al. PF-04691502, a potent and selective oral inhibitor of PI3K and mTOR kinases with antitumor activity[J]. Molecular cancer therapeutics, 2011, 10(11): 2189-2199.
- [8] Lanza M, Basilotta R, Caccamo A, et al. PF-04691502, a PI3K/mTOR Dual Inhibitor, Ameliorates AD-like Pathology in a Mouse Model of AD[J]. Cells, 2025, 14(18): 1474.

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