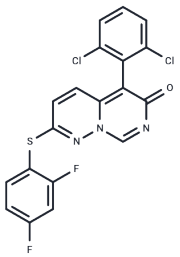
Data Sheet (Cat.No.T6089)

TargetMol

Neflamapimod

Chemical Properties



CAS No. : 209410-46-8

Formula: C19H9Cl2F2N3OS

Molecular Weight: 436.26

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Neflamapimod (VX-745) , a specific and effective inhibitor of p38α(IC50=10 nM), is 22-fold greater specificity against p38β and no inhibition activity to p38γ.
Targets(IC50)	Autophagy,p38 MAPK
In vitro	Neflamapimod selectively inhibits p38α and p38β MAPK with IC50 of 10 nM and 220 nM, respectively, but not p38γ MAPK and a large panel of other kinases, with IC50 larger than 20 μM. In a human peripheral blood mononuclear cell (PBMC) assay, Neflamapimod provides IC50 of 56 and 52 nM for IL-1β and TNFα, respectively. Neflamapimod blocks IL-6 and IL-8 production induced by IL-1 and TNFα, and COX-2 synthesis mediated by LPS and IL-1β. [1-3] Neflamapimod (60 nM-20 μM) inhibits IL-6 and VEGF secretion in bone marrow stromal cells (BMSCs), without affecting their viability. Neflamapimod also inhibits TNF-α-induced IL-6 secretion in BMSCs. Neflamapimod inhibits both multiple myeloma (MM) cell proliferation and IL-6 secretion in BMSCs triggered by adherence of MM cells to BMSCs, suggesting that Neflamapimod can inhibit paracrine multiple myeloma (MM) cell growth in the BM milieu and overcome cell adhesion-related drug resistance. [4]
In vivo	Neflamapimod is effective against adjuvant-induced arthritis (AA) in the rat with ED50 of 5 mg/kg. Histological scores for Neflamapimod in AA rats are 93% inhibition of bone resorption and 56% inhibition of inflammation. In the classical cartilage-induced arthritis model, Neflamapimod exhibits a dose-responsive decrease in severity score. [1-3] In a type II collagen-induced arthritis (CIA) mice model, Neflamapimod (2.5, 5, and 10 mg/kg) has 27%, 31%, and 44% improvement in the inflammatory scores, respectively, when compared to vehicle-treated mice. In addition, histological scores show a 32-39% protection of bone and cartilage erosion by Neflamapimod. [5]
Kinase Assay	Spectrophotometric coupled-enzyme assay: The IC50 for the inhibition of p38α and p38β homologs are obtained by a spectrophotometric coupled-enzyme assay. A fixed concentration of enzyme (15 nM of p38α or p38β) is incubated with VX-745 in DMSO for 10 min. at 30 °C in 0.1 M HEPES buffer, pH 7.5, containing 10% glycerol, 10 mM MgCl2, 2.5 mM phosphoenolpyruvate, 200 μM NADH, 150 μg/mL pyruvate kinase, 50 μg/mL lactate dehydrogenase, and 200 μM EGF receptor peptide (KRELVEPLTPSGEAPNQALLR). The reaction is initiated with 100 μM and 70 μM ATP for p38α and p38β assays, respectively. The decrease of absorbance at 340 nm is monitored to follow the rate of the reaction. IC50 is evaluated from the rate data as a function of the inhibitor

Kinase Assay	concentration.
Cell Research	BMSCs (5 × 104 cells/well) or MM cells (3 × 104 cells/well) are incubated in 96-well culture plates in the presence or absence of VX-745 for 48 hours at 37 °C. DNA synthesis is measured by [3H]-thymidine ([3H]TdR) uptake. Cells are pulsed with [3H]TdR (0.5 μCi/well [.0185 MBq]) during the last 8 hours of 48-hour cultures. Growth inhibition of both MM cells and BMSCs by VX-745 is also assessed by measuring 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) dye absorbance.(Only for Reference)

Solubility Information

Solubility	DMSO: 16.7 mg/mL (38.28 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2922 mL	11.4611 mL	22.9221 mL
5 mM	0.4584 mL	2.2922 mL	4.5844 mL
10 mM	0.2292 mL	1.1461 mL	2.2922 mL
50 mM	0.0458 mL	0.2292 mL	0.4584 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Decicco C, et al. American Chemical Society, 2000, IDDB3.
Haddad JJ, Curr Opin Investig Drugs, 2001, 2(8), 1070-1076.
Salituro FG, et al. 27th National Medicinal Chemistry Symposium, 2000, June 16.
Hideshima T, et al. Blood, 2003, 101(2), 703-705.
Duffy JP, et al. ACS Med Chem Lett, 2011, 2(10), 758-763.
Pradal J, et al. Intra-articular bioactivity of a p38 MAPK inhibitor and development of an extended-release system. Eur J Pharm Biopharm. 2015 Jun;93:110-7.
Alam JJ. Selective Brain-Targeted Antagonism of p38 MAPKα Reduces Hippocampal IL-1β Levels and Improves Morris Water Maze Performance in Aged Rats. J Alzheimers Dis. 2015;48(1):219-27.