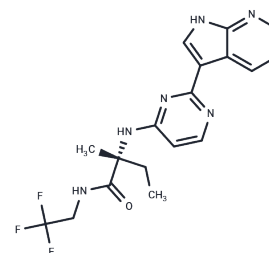


Decernotinib

Chemical Properties

CAS No. :	944842-54-0
Formula:	C ₁₈ H ₁₉ F ₃ N ₆ O
Molecular Weight:	392.38
Appearance:	no data available
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year



Biological Description

Description	Decernotinib (VRT-831509)(VX-509; VRT-831509) is a potent and selective Janus kinase 3 (JAK3) inhibitor with K_i of 2.5 nM; IC_{50} is 50-170 nM in cellular assays.
Targets(IC_{50})	Tyrosine Kinases,JAK
In vitro	In HT-2 cells, Decernotinib inhibits IL-2-stimulated HT-2 STAT-5 phosphorylation, human T-cell blast proliferation, and CD40L/IL-4-induced B-cell proliferation. [1]
In vivo	In a rat model of collagen-induced arthritis, VX-509 (50 mg/kg, p.o.) results in dose-dependent reduction in ankle swelling and paw weight and improved paw histopathology scores. In a mouse model of oxazolone-induced delayed-type hypersensitivity, VX-509 (50 mg/kg, p.o.) significantly suppresses ear edema. [1] In a rat HvG model, VX-509 (50 mg/kg, p.o.) results in dose-dependent inhibition of popliteal lymph node (PLN) hyperplasia. [2]
Kinase Assay	Kinase Activity Assays: The effect of VX-509 on JAK3 activity is assessed by measuring the residual kinase activity of the recombinantly expressed JAK3 kinase domain using a radiometric assay. The final concentrations of the components in the assay are as follows: 100 mM HEPES (pH 7.5), 10 mM MgCl ₂ , 1 mM dithiothreitol (DTT), 0.01% BSA, 0.25 nM JAK3, 0.25 mg/ml polyE4Y, and 5 μ M 33P- γ -ATP (200 μ Ci/ μ Mol). A 10 mM stock solution of VX-509 is prepared in DMSO, from which additional dilutions are prepared. A substrate mixture (100 mM HEPES, 10 mM MgCl ₂ , 0.5 mg/ml polyE4Y, and 10 μ M 33P- γ -ATP) is added and mixed with VX-509 stock solution. The reaction is initiated by the addition of an enzyme mixture [100 mM HEPES (pH 7.5), 10 mM MgCl ₂ , 2 mM DTT, 0.02% BSA, 0.5 nM JAK3]. After 15 minutes, the reaction was quenched with 20% trichloroacetic acid (TCA). The quenched reaction was transferred to the GF/B filter plates and washed three times with 5% TCA. Following the addition of Ultimate Gold scintillant (50 μ l), the samples were counted in a Packard TopCount gamma counter (PerkinElmer). In this procedure, the radioactivity trapped is a measure of the residual JAK3 kinase activity. From the activity versus concentration of VX-509 titration curve, the K_i value was determined by fitting the data to an equation for competitive tight binding inhibition kinetics using Prism software.
Cell Research	Frozen purified human B cells at thawed, washed, and resuspended in complete medium. Cells are plated onto a 96-well plate at a density of 2×10^5 cells/well. VX-509 is added, and plates are incubated for 30 minutes at 37°C, followed by stimulation with a combination of 10 ng/ml IL-4 and 1 μ g/ml CD40L. DMSO alone is added to the top two

rows, one of which is stimulated with IL-4 or CD40L (negative control) and the other of which served as a proliferation control. The plates are incubated at 37°C for 6 days. On day 6, cells are pulsed with [3H]thymidine for 7 hours and harvested onto filters for radioactive determination using a PerkinElmer-Wallace beta counter (1205 Betaplate Beta Liquid Scintillation Counter). Data are analyzed with Softmax pro software to generate an IC50 value.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 72 mg/mL (183.5 mM), Ethanol: 16 mg/mL (40.8 mM), < 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5485 mL	12.7427 mL	25.4855 mL
5 mM	0.5097 mL	2.5485 mL	5.0971 mL
10 mM	0.2549 mL	1.2743 mL	2.5485 mL
50 mM	0.051 mL	0.2549 mL	0.5097 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

Mahajan S, et al. J Pharmacol Exp Ther. 2015, 353(2), 405-414.
Farmer LJ, et al. J Med Chem. 2015, 58(18), 7195-7216.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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