

PRN694

Chemical Properties

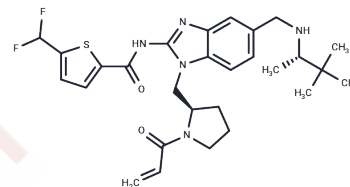
CAS No. : 1575818-46-0

Formula: C₂₈H₃₅F₂N₅O₂S

Molecular Weight: 543.67

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	PRN694 shows extended target residence time on ITK and RLK, enabling durable attenuation of effector cells in vitro and in vivo. PRN694 is an irreversible, highly selective, and effective covalent interleukin-2-inducible T-cell kinase (ITK) and resting lymphocyte kinase (RLK) dual inhibitor (IC ₅₀ s: 0.3 nM and 1.4 nM, respectively).
Targets(IC ₅₀)	Others, Tyrosine Kinases
In vitro	PRN694 obviously decreases NK cell FcR-induced killing at concentrations exceeding 0.37 μM. PRN694 inhibits TEC, BTK, BMX, BLK, JAK3 with IC ₅₀ s of 3.3, 17, 17, 125, 30 nM, respectively. Immunoblot analysis of TCR activation pathways shows that PRN694 blocks activation or nuclear translocation of NFAT1, JunB, pIκBα, and pERK. Results display inhibition of Ca ²⁺ signaling with PRN694 at all concentrations above 1 nM. Day 6 flow cytometry analysis reveals that PRN694 significantly inhibits the anti-CD3/CD28-induced proliferation of both CD4 and CD8 T-cells (p<0.01)[1].
In vivo	PRN694 treatment also causes obviously lower weights relative to the vehicle (p<0.05). Colitis studies show reduced numbers of CD4+ T cells present in the colonic epithelium of PRN694-treated mice compare with controls. The PRN694 occupancy of ITK is 98, 95, and 54% at 1, 6, and 14 h, respectively. The concentrations of PRN694 in the plasma are 2.8, 0.66, and 0.027 μM at 1, 6, and 14 h, respectively. At 14 h, the plasma level of PRN694 is over 10 fold lower than the IC ₅₀ in whole blood [1][2].

Solubility Information

Solubility	DMSO: 125 mg/mL (229.92 mM), Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 3.3 mg/mL (6.07 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8394 mL	9.1968 mL	18.3935 mL
5 mM	0.3679 mL	1.8394 mL	3.6787 mL
10 mM	0.1839 mL	0.9197 mL	1.8394 mL
50 mM	0.0368 mL	0.1839 mL	0.3679 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

Zhong Y, et al. Targeting interleukin-2-inducible T-cell kinase (ITK) and resting lymphocyte kinase (RLK) using a novel covalent inhibitor PRN694. *J Biol Chem.* 2015 Mar 6;290(10):5960-78.

Cho HS, et al. A Small Molecule Inhibitor of ITK and RLK Impairs Th1 Differentiation and Prevents Colitis Disease Progression. *J Immunol.* 2015 Nov 15;195(10):4822-31.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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