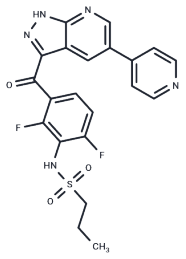
Data Sheet (Cat.No.T72956)

TargetMol

Darizmetinib

Chemical Properties



CAS No. : 2369583-33-3

Formula: C21H17F2N5O3S

Molecular Weight: 457.45

Storage: Keep away from direct sunlight,Store at low temperature
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	Darizmetinib (HRX215, HRX-0215) is a small-molecule inhibitor and an MKK4-targeted inhibitor with potent, selective, and oral activity. By enhancing MKK7 and JNK1 signaling pathways, activating ATF2 and ELK1, Darizmetinib promotes hepatocyte proliferation and regeneration, used for preventing liver failure after extensive hepatectomy or small-for-size liver transplantation.
Targets(IC50)	Antiviral,NF-κB,MAPK,JNK,p38 MAPK,MDM-2/p53
In vitro	**Methods**:Peripheral blood mononuclear cells (PBMCs) induced with exogenous lipopolysaccharide (LPS) were treated with Darizmetinib (0.3, 1, 3 μM) for 2 hours, and pMKK4 protein levels were detected. **Results**: Darizmetinib reduced LPS-induced pMKK4 levels in PBMCs. [1]
In vivo	**Methods**: In a fibrotic mouse liver partial hepatectomy model, a single oral dose of Darizmetinib (30 mg/kg) was administered for 15 minutes to 24 hours to assess hepatocyte proliferation; in a hepatectomy mouse model, a single oral dose of Darizmetinib (10 mg/kg) was administered at 2 and 9 hours to detect changes in MKK7, JNK1, ATF2, ELK1, p38, p53, NF-κB signaling pathway-related molecules, and anti-apoptotic protein Bcl-XL; in a pig hepatectomy model, Darizmetinib (5 mg/kg) was administered intravenously every 12 hours starting 24 hours before surgery to assess hepatocyte regeneration. **Results**: Darizmetinib increased hepatocyte proliferation in fibrotic mouse livers; in hepatectomized mice, activated MKK7 and JNK1 signaling pathways, downstream activation of transcription factors ATF2 and ELK1, reduced p38 and p53 activation, activated NF-κB signaling pathway, and upregulated Bcl-XL; increased hepatocyte regeneration in the pig hepatectomy model. [1]

Solubility Information

Solubility	DMSO: 180 mg/mL (393.49 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.186 mL	10.9302 mL	21.8603 mL
5 mM	0.4372 mL	2.186 mL	4.3721 mL
10 mM	0.2186 mL	1.093 mL	2.186 mL
50 mM	0.0437 mL	0.2186 mL	0.4372 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

Zwirner S, et al. First-in-class MKK4 inhibitors enhance liver regeneration and prevent liver failure. Cell. 2024 Mar 28;187(7):1666-1684. e26.
Zwirner S, et al. First-in-class MKK4 inhibitors enhance liver regeneration and prevent liver failure. Cell. 2024 Mar 28;187(7):1666-1684.e26.