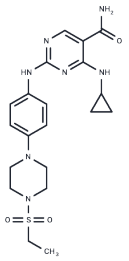
Data Sheet (Cat.No.T2487)

TargetMol

Cerdulatinib

Chemical Properties



CAS No. : 1198300-79-6

Formula: C20H27N7O3S

Molecular Weight: 445.54

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	Cerdulatinib (PRT2070) is an novel oral dual Syk/JAK inhibitor.
Targets(IC50)	Syk,JAK,Tyrosine Kinases
In vitro	Cerdulatinib effectively inhibits 60 CLL cells with IC50 values ranging between 0.37 to 10.02 μM, induces apoptosis via MCL-1 down-regulation and PARP cleavage, and overcomes microenvironmental support to trigger CLL cell death at 2 μM. It inhibits both ibrutinib-sensitive and -resistant primary CLL cell proliferation at concentrations of 250-500 nM, targets BTKC481S-transfected cell lines, halts BCR and JAK-STAT signaling, and blocks SYK and JAK leading to the downstream inhibition of AKT, ERK, and the NF-kB pathway. PRT062070, with an IC50 of 0.11 μM, limits stimulated B cell activation marker CD69 expression, demonstrating varied effectiveness against JAK/STAT pathways and induces apoptosis in BCR-signaling competent NHL cell lines at 1 or 3 μM. Cerdulatinib shows inhibitory actions on both ABC and GCB DLBCL cell subtypes, induces caspase 3 and PARP cleavage-mediated apoptosis, inhibits cell cycle progression through RB phosphorylation reduction and cyclin E down-regulation, and blocks JAK/STAT and BCR signaling. It elicits cell death in DLBCL cells under BCR stimulation and in primary human DLBCL samples, disrupts BCR-induced signaling, especially potent from 0.3 to 1 μM in IGHV-unmutated, high BCR signaling, sIgM, CD49d+, or ZAP70+ expressing samples, and neutralizes anti-IgM, IL4/CD40L, or NLC-mediated protection by preventing MCL-1 and BCL-XL upregulation, without affecting BCL-2 expression. Cerdulatinib also synergizes with venetoclax to enhance apoptosis in IL4/CD40L treated samples.
In vivo	Cerdulatinib (0.5 mg/kg) causes a nonstatistically significant trend toward reduced ankle inflammation, whereas significant reductions in inflammation are achieved with the 1.5, 3, and 5 mg/kg doses. Besides, Cerdulatinib also affects anticollagen antibody formation. Cerdulatinib (15 mg/kg) suppresses upregulation of splenic B-cell surface CD80/86 and CD69, and inhibits BCR signaling and activation in the spleen after oral dosing in mice[2].
Cell Research	Cerdulatinib is dissolved in DMSO. TMD8 cells are transfected with constructs of WT BTK or BTKC481S mutants using kit V, Program U-13 on Amaxa Nucleofector. After transfection, the cells are co-cultured with NKTert cells in a 24-well plate for 24 hrs for recovery. Ibrutinib, cerdulatinib and vehicle (DMSO) are then added into the transfected TMD8 cells and cellular viability is determined with MuseTM Count & Viability kit using

Cell Research	Muse Cell Analyzer. The cell survival is determined by flow cytometry using the Annexin V/7-AAD Apoptosis Detection Kit I on freshly isolated CLL cells.

Solubility Information

Solubility	DMSO: 250 mg/mL (561.12 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 10 mg/mL (22.44 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (22.44 mM),Solution. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2445 mL	11.2223 mL	22.4447 mL
5 mM	0.4489 mL	2.2445 mL	4.4889 mL
10 mM	0.2244 mL	1.1222 mL	2.2445 mL
50 mM	0.0449 mL	0.2244 mL	0.4489 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

Guo A, et al. Dual SYK/JAK inhibition overcomes ibrutinib resistance in chronic lymphocytic leukemia: Cerdulatinib, but not ibrutinib, induces apoptosis of tumor cells protected by the microenvironment. Oncotarget. 2017 Feb 21;8 (8):12953-12967.

Coffey G, et al. The novel kinase inhibitor PRT062070 (Cerdulatinib) demonstrates efficacy in models of autoimmunity and B-cell cancer. J Pharmacol Exp Ther. 2014 Dec;351(3):538-48.

Ma J, et al. Cerdulatinib, a novel dual SYK/JAK kinase inhibitor, has broad anti-tumor activity in both ABC and GCB types of diffuse large B cell lymphoma. Oncotarget. 2015 Dec 22;6(41):43881-96.

Blunt MD, et al. The Dual Syk/JAK Inhibitor Cerdulatinib Antagonizes B-cell Receptor and Microenvironmental Signaling in Chronic Lymphocytic Leukemia. Clin Cancer Res. 2017 May 1;23(9):2313-2324.

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