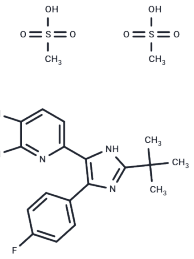
Data Sheet (Cat.No.T6047)

TargetMol

Ralimetinib dimesylate

Chemical Properties



CAS No. : 862507-23-1

Formula: C24H29FN6·2CH4O3S

Molecular Weight: 612.74

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	Ralimetinib dimesylate (LY2228820 dimesylate) is the dimesylate salt form of LY2228820, a tri-substituted imidazole derivative and orally available p38 mitogen-activated protein kinase (MAPK) inhibitor with potential anti-inflammatory and antineoplastic activities.
Targets(IC50)	Apoptosis,Autophagy,p38 MAPK
In vitro	Ralimetinib inhibits p38α, as well as the level of phosphoMAPKAPK-2 (pMK2) in RAW 264.7 cells, with IC50 values of 7 nM and 34.3 nM, respectively. Furthermore, Ralimetinib inhibits lipopolysaccharide (LPS)-induced TNFα formation in murine peritoneal macrophages, with IC50 of 5.2 nM. [1] In multiple myeloma (MM) cells, including INA6, RPMI-8226, U266, and RPMI-Dox40, Ralimetinib (200 nM-800 nM) significantly blocks p38MAPK signaling, as revealed by its inhibition on phosphorylation of HSP27, a downstream target of p38MAPK, without affecting the expression level of HSP27. Ralimetinib (200 nM-400 nM) enhances bortezomib-induced cytotoxicity and apoptosis, but Ralimetinib alone doesn't inhibit the growth of MM.1S cells. Ralimetinib (200 nM-800 nM) also inhibits secretion of IL-6 and MIP-1α in long-term BM stromal cells (LT-BMSCs), BM mononuclear cells (BMMNCs), peripheral blood (PB) CD138+, CD138 or PB CD14+ cells. Ralimetinib (400 nM-800 nM) also blocks osteoclastogenesis from CD14+ cells. [2]
In vivo	In LPS-induced mice, Ralimetinib effectively inhibits the formation of TNFα with a threshold minimum 50% effective dose (TMED50) less than 1 mg/kg. In a rat model of collagen-inducedarthritis (CIA), Ralimetinib displays potent effects on paw swelling, bone erosion, and cartilage destruction, with a threshold minimum 50% effective dose (TMED50)of 1.5 mg/kg. [1]
Kinase Assay	Inhibition of p38α: Inhibition of p38α is determined using recombinant human p38α in a standard filter binding protocol using ATP[γ-33P] and EGFR 21-mer peptide as substrate. Functional inhibition of TNFα in murine peritoneal macrophages is determined using LPS stimulation in the presence of LY2228820. To assess p38α activity in cells more directly, RAW 264.7 cells are treated with LY2228820 and then stimulated with anisomycin. The level of p38α activity is detected using a phosphoMAPKAPK-2 (pMK2) (Thr 334) antibody which reacts with a residue specifically phosphorylated by p38α.
Cell Research	MTT assays and APO 2.7 staining are performed to assess cellular proliferation and induction of apoptosis, respectively. Viability is expressed as percent viable cells. Apoptosis in cells is evaluated by APO 2.7 staining. For detection of mitochondrial membrane protein 7A6 expressed in apoptotic cells, cells are incubated with APO 2.7

Cell Research	reagent for 20 min. Expression of APO 2.7 is determined using an EPICS XL flow cytometer.(Only for Reference)

Solubility Information

Solubility	DMSO: 27.5 mg/mL (44.88 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.26 mM),Sonication is recommended. *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	1.632 mL	8.1601 mL	16.3201 mL
5 mM	0.3264 mL	1.632 mL	3.264 mL
10 mM	0.1632 mL	0.816 mL	1.632 mL
50 mM	0.0326 mL	0.1632 mL	0.3264 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

Mader M, et al. Bioorg Med Chem Lett, 2008, 18(1), 179-183.
Chiang C, Zhang M, Wang D, et al. Therapeutic potential of targeting MKK3-p38 axis with Capsaicin for Nasopharyngeal Carcinoma. Theranostics. 2020, 10(17): 7906.
Dong W, Xie W, Liu Y, et al. Receptor tyrosine kinase inhibitors block proliferation of TGEV mainly through p38 mitogen-activated protein kinase pathways. Antiviral Research. 2020, 173: 104651
Ishitsuka K, et al. Br J Haematol, 2008, 141(5), 598-606.
Ishitsuka K, et al. Oncogene, 2005, 24(38), 5888-5896.
Dong W, Xie W, Liu Y, et al. Receptor tyrosine kinase inhibitors block proliferation of TGEV mainly through p38 mitogen-activated protein kinase pathways[J]. Antiviral Research. 2020, 173: 104651.
Chiang C, Zhang M, Wang D, et al. Therapeutic potential of targeting MKK3-p38 axis with Capsaicin for Nasopharyngeal Carcinoma[J]. Theranostics. 2020, 10(17): 7906.