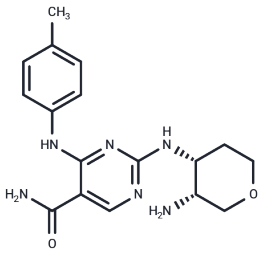
Data Sheet (Cat.No.T38626)

TargetMol

GSK143

Chemical Properties



CAS No. : 1240390-27-5

Formula: C17H22N6O2

Molecular Weight: 342.403

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	GSK143 is a potent orally active and highly selective inhibitor of spleen tyrosine kinase (SYK) with a pIC 50 of 7.5. Furthermore, GSK143 effectively inhibits phosphorylated Erk (pErk) with a pIC 50 value of 7.1. In addition, GSK143 exhibits promising anti-inflammatory properties by reducing inflammation and impeding the recruitment of immune cells in the intestinal muscularis of mice.
Targets(IC50)	ERK,Others,Syk
In vitro	GSK143 (compound 20) effectively inhibits several enzymes and receptors, displaying inhibitory activities against ZAP-70 (pIC 50 =4.7), LCK (pIC 50 =5.3), LYN (pIC 50 =5.4), JAK1/2/3 (pIC 50 =5.8/5.8/5.7), Aurora B (pIC 50 =4.8), hWB (pIC 50 =6.6), and hERG (pIC 50 =4.7)[1]. When tested on chronic lymphocytic leukemia (CLL) cells with concentrations ranging from 10-10000 nM over a period of every 24 hours for three days, GSK143 achieves an IC 50 of 323 nM, demonstrating its efficacy in reducing cell viability[2]. Furthermore, exposure to GSK143 (1 μM; 30 mins) interrupts early signaling pathways by hindering SYK phosphorylation and calcium flux[2], and its application (0.1-10 μM; for 30 min) diminishes cytokine expression in bone marrow-derived macrophages in a concentration-dependent manner[3].
In vivo	GSK143, administered orally at dosages ranging from 0.1 to 10 mg/kg 1.5 hours prior to intestinal manipulation, significantly reduces inflammation and prevents the recruitment of immune cells in the intestinal muscularis of mice, demonstrating its anti-inflammatory capabilities. When administered orally at dosages of 3, 10, 30, and 100 mg/kg 1 hour before an ovalbumin challenge, GSK143 diminishes the severity of the cutaneous reverse passive Arthus reaction in a dose-dependent manner, with reductions of approximately 50% and 70% observed at doses of 10 mg/kg and 30 mg/kg, respectively. Pharmacokinetic analysis in rats reveals that GSK143, at an intravenous dosage of 1 mg/kg and an oral dosage of 3 mg/kg, has a half-life (T 1/2) of 4.2 hours, low clearance (16 mL/min/kg), a bioavailability of 30%, and a steady-state volume of distribution (Vss) of 4.1 L/kg. The studies were conducted in wild-type C57NL/BL6 mice aged 10-12 weeks and male CD rats weighing 175-200 g.

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.9206 mL	14.6028 mL	29.2056 mL
5 mM	0.5841 mL	2.9206 mL	5.8411 mL
10 mM	0.2921 mL	1.4603 mL	2.9206 mL
50 mM	0.0584 mL	0.2921 mL	0.5841 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

John Liddle, et al. Discovery of GSK143, a Highly Potent, Selective and Orally Efficacious Spleen Tyrosine Kinase Inhibitor. Bioorg Med Chem Lett. 2011 Oct 15;21(20):6188-94.
Abraham M Varghese, et al. Highly Selective SYK Inhibitor, GSK143, Abrogates Survival Signals in Chronic Lymphocytic Leukaemia. Br J Haematol. 2018 Sep;182(6):927-930.
Sjoerd H W van Bree, et al. Inhibition of Spleen Tyrosine Kinase as Treatment of Postoperative Ileus. Gut. 2013 Nov; 62(11):1581-90.