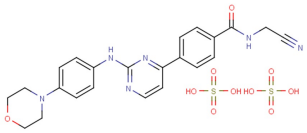
Data Sheet (Cat.No.T15038)

TargetMol
A DRUG SCREENING EXPERT

Momelotinib sulfate

Chemical Properties



CAS No.:	1056636-06-6
Formula:	C23H26N6O10S2
Molecular Weight:	610.62
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	Momelotinib sulfate is an ATP-competitive JAK1/JAK2 inhibitor (IC50: 11 nM/18 nM). It has 10-fold selectivity versus JAK3.
Targets(IC_{50})	JAK1: 11 nM JAK2: 18 nM JAK3: 155 nM
In vitro	Momelotinib sulfate inhibits growth of Ba/F3-JAK2V617F and Ba/F3-MPLW515L cells (IC50: 200 nM) or human erythroleukemia (HEL) cells (IC50: 1.5 μM). However, it has considerably less activity against BCR-ABL harboring K562 cells (IC50=58 μM) and FLT3 mutation harboring MV4-11 cells (IC50: 3 μM). Proliferation of parental Ba/F3 cells (Ba/F3-wt) stimulated with IL-3 is inhibited (IC50: 1.4 μM). This is same as the established role of IL-3-dependent signaling in the parental cell line [1].
In vivo	Momelotinib sulfate at twice the dose used in disease model (50 and 100 mg/kg) has little to no effect on peripheral blood counts over a period of 8 weeks. Median plasma peak concentrations are 7.1 μM with the lower dose and 32.1μM with the higher dose, with a half-life of approximately 2 hours. Trough levels at 12 hours are 10nM for the 25 mg/kg and 900nM for the 50 mg/kg dose. After oral dosing, Momelotinib sulfate shows high plasma concentrations (Cmax= 40.4 μM; Tmax=4 h), with quantitative absolute oral bioavailability and an apparent half life of 2.4 h. The high oral bioavailability, can likely be partly ascribed to the low blood clearance of Momelotinib sulfate (6.3 mL/min/kg) and therefore low susceptibility to hepatic first pass metabolism [3]. At day 34 after transplantation, the mean white blood cell counts and hematocrit values of the entire cohort exceeded the normal range for Balb/c mice by more than 1 SD. At this point, 6 mice are sacrificed and subjected to autopsy. In the remaining animals, treatment is initiated with 25 mg/kg Momelotinib sulfate, 50 mg/kg Momelotinib sulfate, or vehicle, administered twice daily by oral gavage (12 mice per treatment group). A rapid drop of the white cell counts is apparent in both dose cohorts as early as 6 days after initiation of treatment and a decline of the hematocrit is apparent after 20 days [2].

Solubility Information

Solubility	DMSO: 6.2 mg/mL (10.15 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.638 mL	8.188 mL	16.377 mL
5 mM	0.328 mL	1.638 mL	3.275 mL
10 mM	0.164 mL	0.819 mL	1.638 mL
50 mM	0.033 mL	0.164 mL	0.328 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Pardanani A, et al. CYT387, a selective JAK1/JAK2 inhibitor: in vitro assessment of kinase selectivity and preclinical studies using cell lines and primary cells from polycythemia vera patients. Leukemia, 2009, 23(8), 1441-1445.
2. Tyner JW, et al. CYT387, a novel JAK2 inhibitor, induces hematologic responses and normalizes inflammatory cytokines in murine myeloproliferative neoplasms. Blood, 2010, 115(25), 5232-5240.
3. Burns CJ, et al. Phenylaminopyrimidines as inhibitors of Janus kinases (JAKs). Bioorg Med Chem Lett. 2009 Oct 15;19(20):5887-92.

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