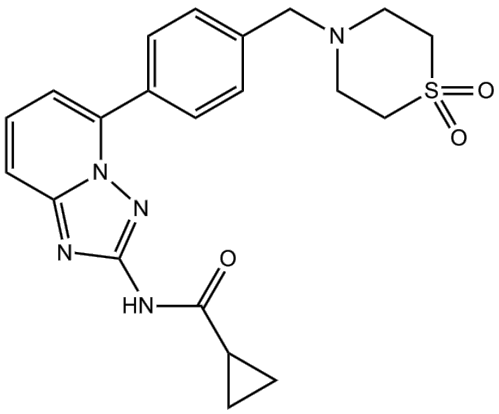
Product Data Sheet

Product Name: GLPG0634
Cat. No.: GC12579

Chemical Properties

Cas. No.	1206161-97-8		
Chemical Name	N-[5-[4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl]cyclopropanecarboxamide		
SMILES	C1CC1C(=O)NC2=NN3C(=N2)C=CC=C3C4=CC=C(C=C4)CN5CCS(=O)(=O)CC5		
Formula	C21H23N5O3S	M.Wt	425.5
Solubility	≥ 21.3mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Cell experiment [1]:

Cell lines	THP-1 cells (ATCC TIB-202)

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Preparation method	The solubility of this compound in DMSO is >21.3mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	1 μM
Applications	In THP-1 cells, GLPG0634 preferentially inhibited JAK signaling complexes containing JAK1 and also inhibited Th1 differentiation with similar potencies of 1 μM or lower.

Animal experiment [2]:

Animal models	Male Sprague Dawley rats (180–200 g) and CD1 mice (23–25 g)
Dosage form	orally dosed as a single esophageal gavage at 5 mg/kg (dosing volume of 5 ml/kg) and i.v. dosed as a bolus via the caudal vein at 1 mg/kg (dosing volume of 5 ml/kg)
Application	GLPG0634 dose-dependently reduced inflammation, cartilage, and bone degradation in the CIA model in rats and mice with significant effect of 3 mg/kg. Protection from bone damage was evidenced by a dose-dependent reduction, with significant effect from GLPG0634 (3 mg/kg), showed a marked reduction of the infiltration of inflammatory cells while protecting the articular cartilage and bone from 1 mg/kg onward.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Van Rompaey L, Galien R, van der Aar E M., et al. Preclinical characterization of GLPG0634, a selective inhibitor of JAK1, for the treatment of inflammatory diseases. The Journal of Immunology, 2013, 191(7): 3568-3577.

Background

GLPG0634 is a selective inhibitor of JAK1 with IC50 value of 10nM [1].

GLPG0634 is a small molecule inhibitor of JAK1. It shows potent inhibitory activity against both JAK1 and JAK2 with IC50 values of 10nM and 28nM, respectively. In cellular assays, GLPG0634 is most potent in inhibiting the JAK1/JAK3/γc signaling induced by IL-2– and IL-4 as well as the JAK1/TYK2 type II receptor signaling induced by IFN-αB2. However, it shows lower potent to inhibit JAK2 homodimer–mediated signaling induced by EPO or PRL. It demonstrates that GLPG0634 is specific to JAK1. In addition, GLPG0634 is found to inhibit the phosphorylation of STAT1 and STAT5 induced by cytokines. Moreover, GLPG0634 inhibits the differentiation of Th1 and Th2 cells with similar potencies. Th17 differentiation is also affected by GLPG0634 with a lower potency [1].

In the rat model of collagen-induced arthritis (CIA), oral administration of GLPG0634 shows a marked protection from bone damage at dose of 3 mg/kg. It reduces the infiltration of inflammatory cells significantly from 1 mg/kg onward [1].

References:
[1] Van Rompaey L, Galien R, van der Aar E M, et al. Preclinical characterization of GLPG0634, a selective inhibitor of JAK1, for the treatment of inflammatory diseases. The Journal of Immunology, 2013, 191(7): 3568-3577.

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