Filgotinib

Cat. No.: HY-18300

CAS No.: 1206161-97-8

Molecular Formula: $C_{21}H_{23}N_5O_3S$

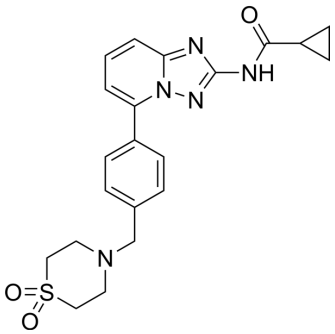
Molecular Weight: 425.5

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (58.75 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3502 mL	11.7509 mL	23.5018 mL
5 mM	0.4700 mL	2.3502 mL	4.7004 mL
10 mM	0.2350 mL	1.1751 mL	2.3502 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Filgotinib (GLPG0634) is a selective and orally active JAK1 inhibitor with IC_{50} of 10 nM, 28 nM, 810 nM, and 116 nM for JAK1, JAK2, JAK3, and TYK2, respectively.

IC_{50} & Target	JAK1	JAK2	Tyk2	JAK3
	10 nM (IC_{50})	28 nM (IC_{50})	116 nM (IC_{50})	810 nM (IC_{50})

In Vitro

Filgotinib (GLPG0634) dose-dependently inhibits the differentiation of Th2 cells mediated by IL-4, a cytokine that signals through JAK1 and JAK3. Filgotinib also inhibits Th1 differentiation with similar potencies of 1 μM or lower[1]. Filgotinib (GLPG0634)?does not inhibit JAK2 homodimer-mediated signaling induced by EPO or PRL (IC_{50} > 10 μM)[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Filgotinib (GLPG0634; 3, 10, 30 mg/kg, p.o.) dose-dependently prevents disease progression in the therapeutic rat CIA model. Filgotinib (50 mg/kg, o.p.) protects bone and cartilage from degradation, effectively reduces infiltration of T cells ($CD3^+$ cells) and macrophages ($F4/80^+$ cells) in the paw, and decreases the serum levels of all cytokines and chemokines measured, including IL-6, IP-10, XCL1, and MCP-1[1]. Filgotinib (GLPG0634; 0.1 and 0.3 mg/kg) shows efficacy in the rat CIA model[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]

Filgotinib is 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). In the rat study, each group consists of three rats and blood samples are collected via the jugular vein. In the mouse study, each group consists of 21 mice (n=3/time point) and blood samples are collected by intracardiac puncture under isoflurane anesthesia. Lithium heparin is used as anticoagulant and blood is taken at 0.05, 0.25, 0.5, 1, 3, 5, and 8 h (i.v. route) and 0.25, 0.5, 1, 3, 5, 8, and 24 h (by mouth).

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2022 Sep;609(7928):785-792.
- Science. 2017 Dec 1;358(6367):eaan4368.
- Nat Cancer. 2022 Sep;3(9):1071-1087.
- Leukemia. 2019 Aug;33(8):1964-1977.
- Mol Syst Biol. 2023 Dec 18.

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REFERENCES

[1]. Van Rompaey L, et al. Preclinical characterization of GLPG0634, a selective inhibitor of JAK1, for the treatment of inflammatory diseases. J Immunol. 2013, 191(7), 3568-3577.

[2]. Menet CJ, et al. Triazolopyridines as Selective JAK1 Inhibitors: From Hit Identification to GLPG0634. J Med Chem. 2014 Nov 17.

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