Filgotinib

Cat. No.: HY-18300
CAS No.: 1206161-97-8
Molecular Formula: C₂₁H₂₃N₅O₃S
Molecular Weight: 425.5
Target: JAK
Pathway: Epigenetics; JAK/STAT Signaling; 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)
H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.3502 mL</td>
<td>11.7509 mL</td>
<td>23.5018 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4700 mL</td>
<td>2.3502 mL</td>
<td>4.7004 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2350 mL</td>
<td>1.1751 mL</td>
<td>2.3502 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Filgotinib (GLPG0634) is a selective JAK1 inhibitor with IC₅₀ of 10 nM, 28 nM, 810 nM, and 116 nM for JAK1, JAK2, JAK3, and TYK2, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>JAK1</th>
<th>10 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JAK2</td>
<td>28 nM (IC₅₀)</td>
</tr>
<tr>
<td>Tyk2</td>
<td>116 nM (IC₅₀)</td>
</tr>
<tr>
<td>JAK3</td>
<td>810 nM (IC₅₀)</td>
</tr>
</tbody>
</table>
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].

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].

PROTOCOL
Animal Administration
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

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REFERENCES