Ilginatinib

Cat. No.: HY-19631A  
CAS No.: 1239358-86-1  
Molecular Formula: C₂₁H₂₀FN₇  
Molecular Weight: 389.43  
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: 100 mg/mL (256.79 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.5679 mL</td>
<td>12.8393 mL</td>
<td>25.6786 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5136 mL</td>
<td>2.5679 mL</td>
<td>5.1357 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2568 mL</td>
<td>1.2839 mL</td>
<td>2.5679 mL</td>
<td></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 (6.42 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
Ilginatinib (NS-018) is a highly active and orally bioavailable JAK2 inhibitor, with an IC₅₀ of 0.72 nM, 46-, 54-, and 31-fold selectivity for JAK2 over JAK1 (IC₅₀, 33 nM), JAK3 (IC₅₀, 39 nM), and Tyk2 (IC₅₀, 22 nM).

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>JAK2</th>
<th>Tyk2</th>
<th>JAK1</th>
<th>JAK3</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC₅₀</td>
<td>0.72 nM (IC₅₀)</td>
<td>22 nM (IC₅₀)</td>
<td>33 nM (IC₅₀)</td>
<td>39 nM (IC₅₀)</td>
</tr>
</tbody>
</table>
**In Vitro**

Ilginatinib (NS-018) is a highly active JAK2 inhibitor, with an IC$_{50}$ of 0.72 nM, 46-, 54-, and 31-fold selectivity for JAK2 over JAK1 (IC$_{50}$, 33 nM), JAK3 (IC$_{50}$, 39 nM), and Tyk2 (IC$_{50}$, 22 nM). Ilginatinib (NS-018) also inhibits Src-family kinases, especially SRC and FYN, and weakly inhibits ABL and FLT3 with 45- and 90-fold selectivity for JAK2, respectively. NS-018 shows potent inhibitory activity against cell lines JAK2V617F or MPLW515L mutations or the TEL-JAK2 fusion gene (expressing a constitutively activated JAK2) with IC$_{50}$ of 11-120 nM, but has only minimal cytotoxicity against most other hematopoietic cell lines that have no constitutively activated JAK2[1]. Ilginatinib (NS-018) (0.5 μM) preferentially suppresses colony-forming unit-granulocyte/macrophage (CFU-GM) formation from myelodysplastic syndrome (MDS)-derived bone marrow mononuclear cells (BMMNCs). Ilginatinib (NS-018) (1 μM) suppresses the phosphorylation of STAT3 (the downstream kinase of JAK2) in CFU-GM-forming cells from MDS patients[2].

**In Vivo**

Ilginatinib (NS-018) (12.5, 25, 50, 100 mg/kg, p.o.) potently prolongs the survival of mice and reduces splenomegaly in a mouse Ba/F3-JAK2V617F disease model[1]. Ilginatinib (NS-018) (25, 50 mg/kg, p.o.) significantly reduces leukocytosis, hepatosplenomegaly and extramedullary hematopoiesis, improves nutritional status, and prolongs survival in JAK2V617F transgenic mice.

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**PROTOCOL**

**Cell Assay [2]**

Bone marrow mononuclear cells (BMMNCs) from healthy volunteers and myelodysplastic syndrome (MDS) patients are incubated in MethoCult GF H4434 methylcellulose medium containing various hematopoietic cytokines at 1.0 × 10$^5$ cells/mL with or without Ilginatinib (NS-018) at 37°C in a humidified atmosphere of 5% CO$_2$. Commercially available purified normal human CD34-positive (CD34$^+$) BM cells are used as a control. Burst-forming unit-erythroid (BFU-E) and colonyforming unit-granulocyte/macrophage (CFU-GM) colonies are counted under an inverted microscope on day 14 of culture[2].

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

**Animal Administration [1]**

Female BALB/c nude mice are placed in blanket cages in an environment maintained at 21-25°C and 45-65% relative humidity, with artificial illumination for 12 h and a ventilation frequency of at least 15 times/h. They are allowed free access to food pellets and tap water. Ba/F3-JAK2V617F cells (10$^6$ per mouse) are inoculated intravenously into 7-week-old mice. Administration of vehicle (0.5% methylcellulose) or Ilginatinib (NS-018) twice daily by oral gavage begins the day after cell inoculation. Survival is monitored daily, and moribund mice are humanely killed and their time of death is recorded for purposes of survival analysis. In a parallel study, all mice are humanely killed after 8 days of administration, and their spleens are removed and weighed[1].

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

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**REFERENCES**


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Caution: Product has not been fully validated for medical applications. For research use only.

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