BMS-986165

Cat. No.: HY-117287
CAS No.: 1609392-27-9
Molecular Formula: C₂₀H₁₉D₃N₈O₃
Molecular Weight: 425.46
Target: JAK; Interleukin Related
Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt; Immunology/Inflammation
Storage: Powder -20°C 3 years
In solvent -80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro DMSO : 62.5 mg/mL (146.90 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.3504 mL</td>
<td>11.7520 mL</td>
<td>23.5040 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4701 mL</td>
<td>2.3504 mL</td>
<td>4.7008 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2350 mL</td>
<td>1.1752 mL</td>
<td>2.3504 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: ≥ 2.08 mg/mL (4.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description BMS-986165 is a highly selective, orally bioavailable allosteric TYK2 inhibitor for the treatment of autoimmune diseases, which selectively binds to TYK2 pseudokinase (JH2) domain (IC₅₀=1.0 nM) and blocks receptor-mediated Tyk2 activation by stabilizing the regulatory JH2 domain. BMS-986165 inhibits IL-12/23 and type I IFN pathways[1][2].

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Tyk2 JH2</th>
<th>JAK1 JH2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2 nM (IC₅₀)</td>
<td>1 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

In Vitro BMS-986165 is differentiated from previous JAK inhibitors due its unique ability to selectively bind to the pseudokinase (JH2) domain of TYK2 and inhibit its function through an allosteric mechanism[1]. BMS-986165 maintains excellent potency in human and mouse whole blood (IC₅₀s=13 and 100 nM, respectively) and
shows no significant hERG inhibition in the flux assay (IC\textsubscript{50} > 80 \(\mu\)M\textsuperscript{[1]}).

REFERENCES
