PF-4136309

Cat. No.: HY-13245
CAS No.: 1341224-83-6
Molecular Formula: C₂₉H₃₁F₃N₆O₃
Molecular Weight: 568.59
Target: CCR
Pathway: GPCR/G Protein; Immunology/Inflammation
Storage: Powder -20°C 3 years
In solvent -80°C 6 months

SOLVENT & SOLUBILITY

In Vitro
DMSO: ≥ 34 mg/mL (59.80 mM)
* "≥" means soluble, but saturation unknown.

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>1.7587 mL</td>
<td>8.7937 mL</td>
<td>17.5874 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3517 mL</td>
<td>1.7587 mL</td>
<td>3.5175 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1759 mL</td>
<td>0.8794 mL</td>
<td>1.7587 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 (3.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
PF-4136309 is a potent, selective, and orally bioavailable CCR2 antagonist, with IC₅₀s of 5.2 nM, 17 nM and 13 nM for human, mouse and rat CCR2.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Human CCR2</th>
<th>Mouse CCR2</th>
<th>Rat CCR2</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2 nM (IC₅₀)</td>
<td>13 nM (IC₅₀)</td>
<td>17 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

In Vitro
PF-4136309 is potent in human chemotaxis activity (IC₅₀=3.9 nM) and in the whole blood assay (IC₅₀=19 nM), with IC₅₀ of 16 and 2.8 nM in mouse and rat chemotaxis assays. PF-4136309 is potent in inhibiting CCR2 mediated signaling.
events such as intracellular calcium mobilization and ERK (extracellular signal-regulated kinase) phosphorylation with IC\textsubscript{50} values of 3.3 and 0.5 nM, respectively. In hERG patch clamp assay, PF-4136309 inhibits hERG potassium current with an IC\textsubscript{50} of 20 μM. PF-4136309 is not a cytochrome P450 (CYP) inhibitor, with IC\textsubscript{50} values of >30 μM against five major CYP isoforms CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Moreover, PF-4136309 is not a CYP inducer at concentrations up to 30 μM\textsuperscript{[1]}.

<table>
<thead>
<tr>
<th>In Vivo</th>
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</thead>
<tbody>
<tr>
<td>PF-4136309 (2 mg/kg) exhibits a moderate half-life in both species after iv administration (2.5 and 2.4 h). When administered orally, PF-4136309 (10 mg/kg) is absorbed rapidly, with peak concentration time (T\textsubscript{max}) at 1.2 h for rats and 0.25 h for dogs. A similar half-life is observed in both species between iv dosing and po dosing. PF-4136309 is well absorbed, with an oral bioavailability of 78% in both species\textsuperscript{[1]}.</td>
</tr>
</tbody>
</table>

REFERENCES