LY-411575

Cat. No.: HY-50752
CAS No.: 209984-57-6
Molecular Formula: C₂₆H₂₃F₂N₃O₄
Molecular Weight: 479.48
Target: γ-secretase; Notch
Pathway: Neuronal 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

<table>
<thead>
<tr>
<th>In Vitro</th>
<th>DMSO : 33.33 mg/mL (69.51 mM; Need ultrasonic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparing Stock Solutions</td>
<td>Solvent Concentration</td>
</tr>
<tr>
<td>1 mM</td>
<td>2.0856 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4171 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2086 mL</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>In Vivo</th>
<th>1. Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubility: ≥ 2.5 mg/mL (5.21 mM); Clear solution</td>
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</tr>
<tr>
<td>2. Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil</td>
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</tr>
<tr>
<td>Solubility: ≥ 2.5 mg/mL (5.21 mM); Clear solution</td>
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BIOLOGICAL ACTIVITY

Description
LY-411575 is a potent γ-secretase inhibitor with IC₅₀ of 0.078 nM/0.082 nM (membrane/cell-based), and also inhibits Notch S3 cleavage with IC₅₀ of 0.39 nM.

IC₅₀ & Target
IC₅₀: 0.078 nM (γ-secretase in membrane), 0.082 nM (γ-secretase cell-based), 0.39 nM (Notch S3 cleavage cell-based) [1]

In Vitro
LY-411575 blocks Notch activation, and results in apoptosis in primary and immortalized KS cells. LY-411,575 (500 μ M) induces G2/M growth arrest SLK cells [2]. LY411575 treatment significantly decreases the amounts of intracellular HCV RNA with IC₅₀ of 0.56 ± 0.20 μM and extracellular HCV particles. LY411575 (0-40 nM) alone or in combination...
with daclatasvir (0-40 pM) decreases supernatant infectious titers in a dose-dependent manner, and is synergistic regarding production of infectious virus. LY411575 (10 µM) treatment impairs ROS production in HCVcc-infected cells [4]. LY411575 significantly attenuates EMT by inhibiting the Notch signaling activation in vitro[5].

<table>
<thead>
<tr>
<th>In Vivo</th>
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<tbody>
<tr>
<td>LY-411,575 (10 mg/kg) decreases brain and plasma Aβ40 and -42 robustly when chronically administered to TgCRND8 mice[1]. LY411,575 reduces cortical Aβ40 in young transgenic CRND8 mice (ED₅₀ appr 0.6 mg/kg) and produces significant thymus atrophy and intestinal goblet cell hyperplasia at higher doses (&gt;3 mg/kg). The extent of intestinal goblet cell hyperplasia induced by LY411,575 (10 mg/kg) is similar in young and aged mice[3]. LY411575 inhibits mouse proliferative vitreoretinopathy (PVR) formation in vivo[5].</td>
</tr>
</tbody>
</table>

**PROTOCOL**

**Animal Administration** [3]

Mice from the aged cohort (16-26 months old) are either retired breeders or experimentally naive mice. Before dosing begin and for the duration of the study, mice are singly housed with a plastic igloo and nesting material. Mice are sacrificed 2 to 4 h after their final dosing. For oral dosing, LY411,575 and LY-D are formulated as 10 mg/mL solutions and diluted 1:10 with 0.4% methylcellulose. In the case of subcutaneous dosing, the 10 mg/mL stock solution is diluted 1:10 with 20% hydroxypropyl-β-cyclodextrin. If necessary, serial dilutions are made from the 1 mg/mL solution using the appropriate 1:10 vehicle. The dosing volume is 10 mL/kg. After oral administration of 10 mg/kg LY411,575, inhibition of plasma Aβ is still significant 24, but not 48, h after dosing, so in an effort to maintain continuous γ-secretase inhibition, LY411,575 and LY-D are dosed once per day in all studies.

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

**CUSTOMER VALIDATION**

- BMC Biol. 2015 Sep 2;13(1):70.

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**REFERENCES**


