Vesatolimod

Cat. No.: HY-15601
CAS No.: 1228585-88-3
Molecular Formula: C₂₂H₃₀N₆O₂
Molecular Weight: 410.51
Target: Toll-like Receptor (TLR)
Pathway: Immunology/Inflammation
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 : 4.8 mg/mL (11.69 mM; Need ultrasonic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparing Stock Solutions</td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>Mass 1 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>2.4360 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4872 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2436 mL</td>
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</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description

Vesatolimod (GS-9620) is a potent, selective and orally active agonist of Toll-Like Receptor (TLR7) with an EC₅₀ of 291 nM.

IC₅₀ & Target

EC₅₀: 291 nM (TLR7), 9 μM (TLR8)[3]

In Vitro

Vesatolimod (GS-9620) rapidly internalizes into cells and preferentially localizes to and signals from endo-lysosomal compartments. To test this hypothesis, the kinetics of cellular uptake of the compound in Daudi cells using tritiated Vesatolimod (³H-GS-9620) is measured. The kinetics of ³H-GS-9620 accumulation is rapid, reaching concentration-dependent steady-state equilibrium in approximately thirty minutes. Measured intracellular concentration of ³H-Vesatolimod is 5-fold higher than the extracellular concentration of ³H-GS-9620 used to treat cells. Increases in intracellular ³H-Vesatolimod concentrations are roughly proportional with increasing concentrations of ³H-GS-9620[1].

In Vivo

Single oral doses of Vesatolimod (GS-9620) at 0.3 and 1 mg/kg in uninfected chimpanzees demonstrates a dose- and
exposure-related induction of serum IFN-α, select cytokines/chemokines, and interferon-stimulated genes (ISG) in the peripheral blood and liver. Following oral administration at 0.3 (n=3), and 1 mg/kg (n=3 and n=4), Vesatolimod (GS-9620) C_{max} is 3.6±3.5, 36.8±34.5, and 55.4±81.0 nM, respectively. Peak serum interferon responses occur at 8 h post-dose. The mean peak levels of induced serum IFN-α are 66 and 479 pg/mL at doses of 0.3 and 1 mg/kg, respectively. Vesatolimod (GS-9620) treatment induces ISG transcripts including ISG15, OAS-1, MX1, IP-10 (CXCL10), and I-TAC (CXCL11) in peripheral blood mononuclear cells (PBMC) at 0.3 mg/kg and in both PBMC and the liver at 1 mg/kg.[2].

**PROTOCOL**

**Cell Assay[1]**

Daudi cells are incubated for indicated times with varying concentrations [³H]Vesatolimod (GS-9620) (0.7μCi/mL). Cell associated radioactivity is extracted with ice cold 80% ethanol and measured using liquid scintillation counting. The total amount of Vesatolimod in cells is calculated from a calibration curve for Vesatolimod (GS-9620) mass versus radioactivity. Cell volume is measured[1].

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

**Animal Administration[2]**

Chimpanzees[2]

Chimpanzees are used. The trial design includes 4 weeks of pre-study evaluation (Day-28, -13 and just prior to first dose) and two cycles of oral Vesatolimod (GS-9620) treatment every other day three times per week for 4 weeks with one cycle at 1 mg/kg, and, after a one week rest, a second cycle at 2 mg/kg. Animals are also intensely monitored for 14 weeks after treatment to assess tolerability and durability of response.

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

**CUSTOMER VALIDATION**

- Vaccine. 2018 Feb 1;36(6):794-801.

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**REFERENCES**

