Maribavir

Cat. No.: HY-16305  
CAS No.: 176161-24-3  
Molecular Formula: C₁₅H₁₉Cl₂N₃O₄  
Molecular Weight: 376.24  
Target: CMV  
Pathway: Anti-infection  
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 : 200 mg/mL (531.58 mM; Need ultrasonic)  

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td></td>
</tr>
<tr>
<td>5 mg</td>
<td></td>
</tr>
<tr>
<td>10 mg</td>
<td></td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.6579 mL</td>
<td>13.2894 mL</td>
<td>26.5788 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5316 mL</td>
<td>2.6579 mL</td>
<td>5.3158 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2658 mL</td>
<td>1.3289 mL</td>
<td>2.6579 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: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
   Solubility: ≥ 2.87 mg/mL (7.63 mM); Clear solution

2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.87 mg/mL (7.63 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution

4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution

5. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Maribavir is a potent inhibitor of histone phosphorylation catalyzed by wild-type pUL97 in vitro, with an IC₅₀ of 3 nM.  
Maribavir has potent antiviral activity against HCMV and Epstein-Barr virus (EBV).
Maribavir is a potent inhibitor of the autophosphorylation of the wild type and all the major Ganciclovir (GCV) resistant UL97 mutants analysed with a mean IC\textsubscript{50} of 35 nM. The M460I mutation results in hypersensitivity to Maribavir with an IC\textsubscript{50} of 4.8 nM. A Maribavir resistant mutant of UL97 (L397R) is functionally compromised as both a Ganciclovir kinase and a protein kinase (~ 10% of wild type levels). Enzyme kinetic experiments demonstrate that Maribavir is a competitive inhibitor of ATP with a K\textsubscript{i} of 10 nM\textsuperscript{[1]}. Maribavir (1263W94) inhibits viral replication in a dose-dependent manner, with IC\textsubscript{50} of 0.12±0.01 μM as measured by a multicycle DNA hybridization assay. The pUL97 protein kinase is strongly inhibited by Maribavir, with 50% inhibition occurring at 3 nM\textsuperscript{[2]}.

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

### PROTOCOL

**Kinase Assay\textsuperscript{[1]}**

Enzyme kinetic analysis is performed on the purified wild type and mutant UL97 protein species using increasing concentrations of ATP (2 μM to 20 μM). The amount of incorporated radiolabelled phosphate is plotted against the concentration of ATP in a Lineweaver Burke plot to determine the K\textsubscript{m} for ATP for each UL97 species. The effect of Maribavir upon the rate of radiolabelled phosphate incorporation by wild type or mutant UL97 is determined by protein kinase assays at a fixed concentration of Maribavir (0.5 μM) as above, or with increasing concentrations of Maribavir (0.01 μM to 5.0 μM) to determine the IC\textsubscript{50} of Maribavir for each UL97 species. In order to determine the nature of the inhibition mediated by Maribavir, plots of 1/v vs 1/ATP with increasing concentrations of Maribavir are constructed. Competitive inhibition is evident if the family of lines converge on the y-axis at 1/V\textsubscript{max}. The change in slope caused by the addition of Maribavir is used to calculate the K\textsubscript{i}\textsuperscript{[1]}.

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**Cell Assay\textsuperscript{[2]}**

For these studies MRC-5 cells are seeded in 24-well plates at ~5×10\textsuperscript{4} cells/well and grown for 3 days in MEM 8-1-1 to confluence (~1.1×10\textsuperscript{5} cells/well). The cells are infected with AD169 in MEM 2-1-1 at an MOI ranging from 1 to 3 and incubated at 37°C for 90 min to allow viral adsorption. The unadsorbed virus is removed and replaced with 1 mL of MEM 2-1-1. To test the effect of compounds on viral DNA synthesis or maturation, Maribavir, BDCRB, or GCV is added to the medium at the concentrations indicated for each experiment\textsuperscript{[2]}.

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### REFERENCES

