Vecabrutinib

Cat. No.: HY-109078
CAS No.: 1510829-06-7
Molecular Formula: C_{22}H_{24}ClF_{4}N_{7}O_{2}
Molecular Weight: 529.92
Target: Btk; Itk
Pathway: Protein Tyrosine Kinase/RTK
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: 125 mg/mL (235.88 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent 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>1.8871 mL</td>
<td>9.4354 mL</td>
<td>18.8708 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3774 mL</td>
<td>1.8871 mL</td>
<td>3.7742 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1887 mL</td>
<td>0.9435 mL</td>
<td>1.8871 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 (3.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.93 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Vecabrutinib is a potent, noncovalent BTK and ITK inhibitor, with $K_d$ of 0.3 nM and 2.2 nM, respectively; Vecabrutinib shows an $IC_{50}$ of 24 nM for ITK.

$IC_{50}$ & Target
$IC_{50}$: 24 nM (ITK)$^{[2]}$
$K_d$: 0.3 nM (BTK), 2.2 nM (ITK)$^{[1]}$
Vecabrutinib inhibits pBTK in human whole blood with an average IC₅₀ of 50 nM. Vecabrutinib inhibits WT and C481S BTK with similar IC₅₀s (pBTK IC₅₀s: WT BTK 2.9 nM, C481S BTK 4.4 nM)[1]. In a recombinant kinase assay, IC₅₀s of Vecabrutinib against WT BTK and C481S BTK are 4.6 nM and 1.1 nM. Vecabrutinib retains activity against the mutated BTK variant. Vecabrutinib is six times more potent than ibrutinib and greater than 640 times more potent than acalabrutinib against C481S BTK. Vecabrutinib demonstrates dose-dependent inhibition of BTK in primary patient CLL cells comparable to ibrutinib via immunoblot for BTK phosphorylation. Vecabrutinib decreases viability of primary CLL cells in the presence of HS5 stromal protection by 5.5%[2].

Vecabrutinib has good oral bioavailability in rat and dog (%F ≥ 40%) and a terminal half-life of 5 to 6 hours. Vecabrutinib is well tolerated with continuous drug levels and at exposures much greater than those achieved for ibrutinib[1].

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REFERENCES
