Varlitinib

Cat. No.: HY-10530
CAS No.: 845272-21-1
Molecular Formula: C_{22}H_{19}ClN_{6}O_{2}S
Molecular Weight: 466.94
Target: EGFR
Pathway: JAK/STAT Signaling; 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 : 50 mg/mL (107.08 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>2.1416 mL</td>
<td>10.7080 mL</td>
<td>21.4160 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4283 mL</td>
<td>2.1416 mL</td>
<td>4.2832 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2142 mL</td>
<td>1.0708 mL</td>
<td>2.1416 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: ≥ 2.5 mg/mL (5.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Varlitinib (ARRY-334543; ASLAN001) is a potent, reversible, small molecule pan-EGFR inhibitor with IC_{50}s of 7, 2, 4 nM for HER1, HER2 and HER4, respectively.

IC_{50} & Target

<table>
<thead>
<tr>
<th>IC_{50} &amp; Target</th>
<th>HER1</th>
<th>HER2</th>
<th>HER4</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC_{50}</td>
<td>7 nM (IC_{50})</td>
<td>2 nM (IC_{50})</td>
<td>4 nM (IC_{50})</td>
</tr>
</tbody>
</table>

In Vitro
In cell-based assays using tumor cells that over-express EGFR (A431) or ErbB-2 (BT474), Varlitinib (ARRY-334543) potently inhibits substrate phosphorylation. Varlitinib is shown to be highly selective for EGFR/ErbB-2, and does not show any significant activity when screened against a panel of 104 kinases^{[2]}. 
Varlitinib treatment potently inhibits tumor growth with complete tumor regression observed at dosing of 100 mg/kg twice a day. After five days of Varlitinib treatment, phosphorylation of HER1-3, RAS/RAF/MEK/MAPK, p70S6K, S6 ribosomal, 4EBP1, Cdk-2, Cdc-2 and retinoblastoma are strongly inhibited. Varlitinib treatment results in a significant reduction in survivin and a concomittant increase in Caspase 3 cleavage products. In murine xenograft models, Varlitinib (ARRY-334543) demonstrates significant dose-related (25, 50, 100 mg/kg) tumor growth inhibition in A431-derived tumors when administered orally, twice a day, for 21 days.

**PROTOCOL**

**Animal Administration**

Mice: The effects of Varlitinib is tested in patient-derived HCC xenograft in SCID mice (HCC29-0909A) with co-expression of HER1, HER2 and HER3 receptors. Mice are treated with Varlitinib when the tumors reach the size of approximately 100-150 mm$^3$. Tumor size measurements are performed twice a week and tumor volumes are calculated. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**


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