CEP-40783

Cat. No.: HY-100946
CAS No.: 1437321-24-8
Molecular Formula: \( C_{31}H_{26}F_2N_4O_6 \)
Molecular Weight: 588.56
Target: TAM Receptor; c-Met/HGFR
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 : 7.6 mg/mL (12.91 mM; Need ultrasonic and warming)

<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>Solvent</td>
<td>1 mM</td>
<td>5 mM</td>
<td>10 mM</td>
</tr>
<tr>
<td></td>
<td>Mass</td>
<td>1.6991 mL</td>
<td>8.4953 mL</td>
<td>16.9906 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3398 mL</td>
<td>1.6991 mL</td>
<td>3.3981 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1699 mL</td>
<td>0.8495 mL</td>
<td>1.6991 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
CEP-40783 is a potent, selective and orally available inhibitor of AXL and c-Met with IC\(_{50}\) values of 7 nM and 12 nM, respectively.

IC\(_{50}\) & Target
IC\(_{50}\): 7 nM (AXL) and 12 nM (c-Met)[1]

In Vitro
In AXL-transfected 293GT cells, CEP-40783 is 27-fold more active compared to recombinant enzyme with an IC\(_{50}\) value of 0.26 nM. CEP-40783 also demonstrates superior activity against c-Met in GTL-16 cells (IC\(_{50}\)=6 nM). The increased inhibitory activity of CEP-40783 in cells could be attributed to its extended residence time on both AXL and c-Met, consistent with a Type II mechanism. CEP-40783 shows high kinome selectivity against 298 kinases with an S90 of 0.04 (fraction of kinases showing >90% inhibition at 1 µM)[1].

In Vivo
CEP-40783 shows dose- and time-dependent inhibition of AXL phosphorylation using NCI-H1299 NSCL xenografts with 80% target inhibition at 0.3 mg/kg 6 h post dose and complete target inhibition to >90% inhibition at 1 mg/kg between 6-24 h, while a 10 mg/kg po dose resulted in complete AXL inhibition up to 48 h post dosing[1]. In 3/5 (60%)
of the tumor models, CEP-40783 shows in vivo efficacy, including tumor regressions, significantly superior to that achieved with an optimal regimen of paclitaxel. In 4/4 (100%) of the erlotinib-insensitive tumor models, CEP-40783 demonstrates significant efficacy (66 to 118% TGI) compared to the control group at the 30 mg/kg dose. Additionally, CEP-40783 in combination with erlotinib demonstrate superior anti-tumor efficacy compared to CEP-40783 and erlotinib single agents in the one erlotinib-sensitive model evaluated. CEP-40783 as a single agent and in combination with erlotinib are well tolerated[2].

**PROTOCOL**

**Animal Administration**[2]

Mice: Mice bearing established Champions TumorGrafts are treated orally with 10 mg/kg and 30 mg/kg qd of CEP-40783 for 10 to 34 days and anti-tumor efficacy and tolerability are evaluated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**
