Nedisertib

Cat. No.: HY-101570
CAS No.: 1637542-33-6
Molecular Formula: C₂₄H₂₁ClFN₅O₃
Molecular Weight: 481.91
Target: DNA-PK
Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Storage: -20°C, protect from light, stored under nitrogen
* In solvent: -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)

SOLVENT & SOLUBILITY

In Vitro
DMSO : 100 mg/mL (207.51 mM; Need ultrasonic)
H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.0751 mL</td>
<td>10.3754 mL</td>
<td>20.7508 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4150 mL</td>
<td>2.0751 mL</td>
<td>4.1502 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2075 mL</td>
<td>1.0375 mL</td>
<td>2.0751 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 (5.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Nedisertib (M3814) is a potent, orally available and selective inhibitor of DNA-PK, with an IC₅₀ of <3 nM. Anti-tumor activity.

IC₅₀ & Target
DNA-PK
<3 nM (IC₅₀)

In Vitro
Nedisertib (Compound 136) is a potent and selective inhibitor of DNA-PK, with an IC₅₀ of <3 nM for DNA-PK and <0.5 μM for cellular pDNA-PK.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo
In combination with IR, Nedisertib shows efficacy in all of the 6 mouse models of human cancer. In all models, a dose of 2 Gy administered daily for 1 week in combination with Nedisertib induces statically significant tumor growth inhibition compare
The efficacy of Nedisertib in combination with IR is evaluated in 6 human xenograft models (HCT116, FaDu, NCI-H460, A549, Capan-1, BxPC3) in mice representing 4 different cancer types (colon, head and neck, lung, and pancreas). Tumor cells are injected s.c. into nude mice, and treatment starts when palpable tumors are established (~100 to 200 mm³). Nedisertib is given orally at different doses (25 to 300 mg/kg) 10 min prior to IR. IR is applied using a radiation therapy device for small rodents calibrated to deliver 2 Gy. Autophosphorylation of DNA-PK (serine²⁰⁵⁶) in FaDu tumor lysates is measured by immunoassay to assess pharmacological inhibition by Nedisertib[1].

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

REFERENCES

