Nedisertib

Cat. No.: HY-101570
CAS No.: 1637542-33-6
Molecular Formula: C$_{24}$H$_{21}$ClFN$_5$O$_3$
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**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>100 mg/mL</td>
<td>2.0751 mL, 10.3754 mL, 20.7508 mL</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>&lt; 0.1 mg/mL</td>
<td>(insoluble)</td>
</tr>
</tbody>
</table>

Preparation of Stock Solutions:

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Solvent</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>DMSO</td>
<td>2.0751 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>DMSO</td>
<td>0.4150 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>DMSO</td>
<td>0.2075 mL</td>
</tr>
</tbody>
</table>

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

**In Vivo**

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 IC$_{50}$ of <3 nM. Anti-tumor activity$^{[1][2][3]}$.

**IC$_{50}$ & Target**

DNA-PK
<3 nM (IC$_{50}$)

**In Vitro**

Nedisertib (Compound 136) is a potent and selective inhibitor of DNA-PK, with an IC$_{50}$ of <3 nM for DNA-PK and <0.5 μM for cellular pDNA-PK$^{[3]}$.

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...
to IR alone. Nedisertib, alone or in combination with IR, does not induce significant weight loss or visual signs of toxicity in the mice in any study\(^1\).

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**PROTOCOL**

**Animal Administration**\(^1\)

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 mm\(^3\)). 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 (serine\(^{2056}\)) in FaDu tumor lysates is measured by immunoassay to assess pharmacological inhibition by Nedisertib\(^1\).

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**REFERENCES**


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**Caution:** Product has not been fully validated for medical applications. For research use only.

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