Navtemadlin

Cat. No.: HY-12296
CAS No.: 1352066-68-2
Molecular Formula: C_{28}H_{35}Cl_{2}NO_{5}S
Molecular Weight: 568.55
Target: MDM-2/p53; E1/E2/E3 Enzyme
Pathway: Apoptosis; Metabolic Enzyme/Protease
Storage: Powder, -20°C, 3 years; 4°C, 2 years

* The compound is unstable in solutions, freshly prepared is recommended.

### SOLVENT & SOLUBILITY

#### In Vitro

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>1.7589 mL</td>
<td>8.7943 mL</td>
<td>17.5886 mL</td>
</tr>
<tr>
<td>H_{2}O</td>
<td>≥ 0.1 mg/mL (0.18 mM)</td>
<td>≥ 0.1 mg/mL (0.18 mM)</td>
<td>≥ 0.1 mg/mL (0.18 mM)</td>
</tr>
</tbody>
</table>

* "≥" means soluble, but saturation unknown.

#### Preparing Stock Solutions

- **1 mM**: 1.7589 mL
- **5 mM**: 0.3518 mL
- **10 mM**: 0.1759 mL

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

#### In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   - Solubility: 10 mg/mL (17.59 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   - Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   - Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   - Solubility: ≥ 2.5 mg/mL (4.40 mM); Clear solution
5. Add each solvent one by one: PBS
   - Solubility: 1.5 mg/mL (2.64 mM); Clear solution; Need ultrasonic

### BIOLOGICAL ACTIVITY

**Description**

Navtemadlin (AMG 232) is a potent, selective and orally available inhibitor of p53-MDM2 interaction, with an IC_{50} of 0.6 nM. Navtemadlin binds to MDM2 with a K_{d} of 0.045 nM^{[1][2]}. 

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[BIOLOGICAL ACTIVITY](#)
IC₅₀ & Target

<table>
<thead>
<tr>
<th>IC₅₀</th>
<th>Target</th>
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</thead>
<tbody>
<tr>
<td>IC₅₀: 0.6 nM (p53-MDM2 interaction)¹</td>
<td></td>
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<tr>
<td>Kᵣ: 0.045 nM (MDM2)²</td>
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</tr>
</tbody>
</table>

**In Vitro**

Navtemadlin (AMG 232) (10 μM) induces p53 signaling and inhibits tumor cell proliferation in three p53 wild-type tumor cell lines¹.

Navtemadlin potently inhibits proliferation of non-MDM2-amplified HCT116 colorectal cells (IC₅₀=10 nM)³.

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

**Cell Viability Assay¹**

| Concentration: | 0-10 μM. |
| Incubation Time: | 72 hours. |
| Result: | Induced p53 signaling and inhibits tumor cell proliferation in three p53 wild-type tumor cell lines (SJSA-1, HCT116, and ACHN). Caused robust p21 mRNA induction between 9.76 and 34.9 fold with IC₅₀ values ranging from 12.8 to 46.8 nM. |

**In Vivo**

Navtemadlin (AMG 232) (10, 25, 75 mg/kg, once daily, p.o.) activates p53 pathway activity in vivo¹.

Navtemadlin (10, 25, 75 mg/kg, once daily, p.o.) potently inhibits growth of tumor xenografts in mice¹.

Navtemadlin (10, 25, 75 mg/kg, once daily, p.o.) blocks DNA synthesis and induces apoptosis in vivo¹.

Navtemadlin causes a dose-dependent tumor growth inhibition with an ED₅₀ of 16 mg/kg².

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

**Animal Model:**

Female athymic nude mice (n=10/group) based cancer models¹.

**Dosage:**

10, 25, 75 mg/kg.

**Administration:**

Once daily by oral gavage.

**Result:**

Resulted in significant tumor growth inhibition across all models. SJSA-1, an MDM2 amplified osteosarcoma model, was the most sensitive to AMG 232 treatment with an ED₅₀ of 9.1 mg/kg. In the highest dose group of 75 mg/kg, 10/10 tumors completely regressed and were undetectable after 10 days of treatment.

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**CUSTOMER VALIDATION**

- Evid-Based Compl Alt. 09 Jul 2021.

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**REFERENCES**


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