ZM-447439

Cat. No.: HY-10128
CAS No.: 331771-20-1
Molecular Formula: C₂₉H₃₁N₅O₄
Molecular Weight: 513.59
Target: Aurora Kinase
Pathway: Cell Cycle/DNA Damage; Epigenetics
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

<table>
<thead>
<tr>
<th>In Vitro</th>
<th>DMSO : ≥ 100 mg/mL (194.71 mM)</th>
</tr>
</thead>
</table>

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Solvent</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td>1 mM</td>
<td>1.9471 mL</td>
</tr>
<tr>
<td>1 mg</td>
<td>5 mM</td>
<td>9.7354 mL</td>
</tr>
<tr>
<td>1 mg</td>
<td>10 mM</td>
<td>19.4708 mL</td>
</tr>
<tr>
<td>5 mg</td>
<td>1 mM</td>
<td>0.3894 mL</td>
</tr>
<tr>
<td>5 mg</td>
<td>5 mM</td>
<td>1.9471 mL</td>
</tr>
<tr>
<td>5 mg</td>
<td>10 mM</td>
<td>3.8942 mL</td>
</tr>
<tr>
<td>10 mg</td>
<td>1 mM</td>
<td>0.1947 mL</td>
</tr>
<tr>
<td>10 mg</td>
<td>5 mM</td>
<td>0.9735 mL</td>
</tr>
<tr>
<td>10 mg</td>
<td>10 mM</td>
<td>1.9471 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 (4.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
ZM-447439 is an aurora kinase inhibitor with IC₅₀s of 110 and 130 nM for aurora A and B, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Aurora A</th>
<th>Aurora B</th>
</tr>
</thead>
<tbody>
<tr>
<td>110 nM (IC₅₀)</td>
<td>130 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

In Vitro
Cells treated with ZM-447439 progress through interphase, enter mitosis normally, and assemble bipolar spindles. However, chromosome alignment, segregation, and cytokinesis all fail. ZM-447439 inhibits cell division and inhibit mitotic phosphorylation of histone H3. ZM-447439 prevents chromosome alignment and segregation. ZM-447439
compromises spindle checkpoint function. ZM-447439 inhibits kinetochore localization of BubR1, Mad2, and Cenp-E. Inhibition of Aurora kinase by ZM-447439 reduces histone H3 phosphorylation at Ser10 in Hep2 carcinoma cells. Multipolar spindles are induced in these ZM-treated G2/M-arrested cells with accumulation of 4N/8N DNA, similar to cells with genetically suppressed Aurora-B. ZM-447439 treatment induces cell apoptosis. ZM-447439 inhibition of Aurora kinase is potently in association with decrease of Akt phosphorylation at Ser473 and its substrates GSK3α/β phosphorylation at Ser21 and Ser9.

**PROTOCOL**

**Kinase Assay**

1 ng purified recombinant enzyme is added to a reaction cocktail containing buffer, 10 μM peptide substrate, 10 μM for Aurora A or 5 μM ATP for Aurora B, and 0.2 μCi γ[33P]ATP, and is then incubated at room temperature for 60 min. Reactions are stopped by addition of 20% phosphoric acid, and the products are captured on P30 nitrocellulose filters and assayed for incorporation of 33P with a Betaplate counter. No enzyme and no compound control values are used to determine the concentration of ZM-447439, which gave 50% inhibition of enzyme activity. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Cell Assay**

To determine cloning efficiency, MCF7 cells are plated in phenol red free DME plus 5% stripped serum, and are then treated with or without the anti-estrogen ICI 182780 at 1 μM for 48 h. ZM-447439 is then added at the indicated concentrations for 72 h. The cells are harvested, washed, and -400 cells plated in each well of a 6-well plate in complete media without ZM-447439. After 10 d, the colonies are fixed, stained with crystal violet, and counted. The cloning efficiency represents the number of colonies on ZM-447439-treated plates compared with DMSO-treated controls. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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**REFERENCES**


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