Pavinetant

Cat. No.: HY-14432
CAS No.: 941690-55-7
Molecular Formula: C₂₆H₂₅N₃O₃S
Molecular Weight: 459.56
Target: Neurokinin Receptor
Pathway: GPCR/G Protein; Neuronal Signaling
Storage:
- Powder: -20°C for 3 years, 4°C for 2 years
- In solvent: 4°C for 2 years, -80°C for 6 months, -20°C for 1 month

SOLVENT & SOLUBILITY

In Vitro
DMSO: ≥ 50 mg/mL (108.80 mM)
H₂O: < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.1760</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4352</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2176</td>
</tr>
<tr>
<td></td>
<td>1 mg</td>
<td>2.1760</td>
</tr>
<tr>
<td></td>
<td>5 mg</td>
<td>10.8800</td>
</tr>
<tr>
<td></td>
<td>10 mg</td>
<td>21.7599</td>
</tr>
</tbody>
</table>

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 3 mg/mL (6.53 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 3 mg/mL (6.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Pavinetant (MLE-4901) is a neurokinin-3 receptor (NK3R) antagonist.

IC₅₀ & Target
NK3R[1]

In Vitro
Pavinetant (AZD2624) is a potent and selective NK3 receptor antagonist which is developed for the treatment of schizophrenia. Pavinetant exhibits an inhibitory effect on microsomal CYP3A4/5 activities with apparent IC₅₀ values of 7.1 and 19.8 μM for midazolam and testosterone assays, respectively. No time-dependent inactivation of CYP3A4/5.
activity by Pavinetant is observed. Pavinetant demonstrates weak to no inhibition of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6\(^1\).

**PROTOCOL**

**Kinase Assay**\(^1\)

The potential of Pavinetant (AZD2624) to cause time-dependent inhibition of CYP3A activities is evaluated by pre-incubating 10 μM of Pavinetant at 37°C for 0, 3, 10, 20, and 30 min in 0.1 M pH 7.4 phosphate buffer incubation mixture (0.2 mL) containing 2 mg/mL HLM and 1 mM NADPH. Verapamil, tested at 10 μM, is also incubated separately as a positive control. An aliquot of 20 μL is removed from pre-incubation tube at each time point and added to a secondary 5-min incubation (180 μL) containing 15 μM of midazolam and 1 mM of NADPH. The formation of 1′-hydroxymidazolam is used as the marker activity for CYP3A enzymes and analyzed using LC-MS. CYP3A enzyme activities after pre-incubation with Pavinetant are compared to activities following incubation with vehicle solvent (1% methanol) and without pre-incubation\(^1\). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**