Palbociclib isethionate

Cat. No.: HY-A0065
CAS No.: 827022-33-3
Molecular Formula: C₂₆H₃₅N₇O₆S
Molecular Weight: 573.66
Target: CDK
Pathway: Cell Cycle/DNA Damage
Storage: Powder -20°C 3 years
4°C 2 years
In solvent -80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

<table>
<thead>
<tr>
<th>Solvent</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O: 50 mg/mL</td>
<td>1.7432 mL</td>
<td>8.7160 mL</td>
<td>17.4319 mL</td>
</tr>
<tr>
<td>DMSO: 10 mg/mL</td>
<td>0.3486 mL</td>
<td>1.7432 mL</td>
<td>3.4864 mL</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

Molar mass: 573.66 g/mol

Solvent Concentration

- 1 mM
- 5 mM
- 10 mM

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1 mg/mL (1.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Palbociclib isethionate is a highly selective inhibitor of CDK4/6 with IC₅₀s of 11 nM/16 nM, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>Cdk4/cyclin D3 9 nM (IC₅₀)</th>
<th>Cdk4/cyclin D1 11 nM (IC₅₀)</th>
<th>Cdk6/cyclin D2 16 nM (IC₅₀)</th>
<th>DYRK1A 2000 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAPK</td>
<td>8000 nM (IC₅₀)</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

In Vitro
Palbociclib exhibits absolute selectivity for CDK4/6 with little or no activity against other CDKs. Palbociclib is effective at reducing Rb phosphorylation at Ser⁷⁸⁰ and Ser⁷⁹⁵ in MDA-MB-435 breast carcinoma cells with IC₅₀ of 66 nM and
63 nM, respectively. Palbociclib is a potent inhibitor of cell growth and suppresses DNA replication by preventing cells from entering S phase. Palbociclib inhibits thymidine incorporation into the DNA of Rb-positive human breast (such as MDA-MB-435, MCF-7), colon (H1299), and lung carcinomas (CRLF-CEM and K562), with IC50 values ranging from 0.04-0.17 μM. Palbociclib significantly increases the percentage of MDA-MB-453 in G1 period[1]. Palbociclib inhibits phosphorylation of Rb in cycling CD138+ primary bone marrow myeloma cells, nontransformed primary B cells, MM1.S and CAG HMCLs cells line with IC50 of <0.1 μM, 0.05 μM, and 60-70 nM, respectively. Palbociclib treatment also induces G1 arrest of CD138+ primary bone marrow myeloma and nontransformed primary B cells. Palbociclib induces G1 arrest in MM1.S with IC50 of appr 0.05 μM[2]. Palbociclib preferentially inhibits proliferation of luminal estrogen receptor-positive (including HER2-positive) human breast cancer cell lines. Palbociclib increases gene expression of pRb and cyclin D1 and decreases gene expression of CDKN2A (p16) in most sensitive lines. Palbociclib enhances sensitivity to tamoxifen in cell lines with conditioned resistance to ER blockade[3].

### In Vivo

Palbociclib(150 mg/kg. p.o.) produces rapid Colo-205 colon carcinoma xenografts regressions and a corresponding tumor growth delay. Palbociclib (150 mg/kg, p.o.) induces complete tumor stasis and cell kill in MDA-MB-435 breast carcinoma. Palbociclib (150 mg/kg) also induces significant tumor regression in mice bearing the SF-295 glioblastoma xenografts, and in ZR-75-1 breast and PC-3 prostate tumor models (complete suppression of tumor growth). Palbociclib (150 mg/kg) suppresses Rb Ser780 phosphorylation in MDA-MB-435 breast carcinoma over the full 24-hour period. Palbociclib (150 mg/kg) down-regulates expression of four E2F-regulated genes CDC2, CCNE2, TK1, and TOP2A in Colo-205 carcinoma xenografts[1]. Palbociclib also rapidly inhibits myeloma tumor growth[2].

### PROTOCOL

#### Cell Assay [3]

Cells are seeded in duplicate at 5,000 to 10,000 cells per well in 24-well plates. The day after plating, different concentrations of Palbociclib are added. Control wells without drug are also seeded. At the end of incubation, cells are trypsinized and placed in Isotone solution and counted immediately using a Coulter Z2 particle counter. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration [1]

Mice (18-22 g) are randomized and then implanted s.c. with tumor fragments (appr 30 mg) into the region of the right axilla. Treatment is initiated when tumors reach 100 to 150 mg. Palbociclib is given according to the schedule and dose indicated in the table and figure legends by gavage as a solution in sodium lactate buffer (50 mM, pH 4.0) based on mean group body weight. In all experiments, there are 12 mice in the control group and 8 mice each in the treated groups. Additional details for each experiment are given in the table legends. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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### REFERENCES
