Milciclib

Cat. No.: HY-10424  
CAS No.: 802539-81-7  
Molecular Formula: C₂₅H₃₂N₈O  
Molecular Weight: 460.57  
Target: CDK; Autophagy  
Pathway: Cell Cycle/DNA Damage; Autophagy  
Storage: Powder  
-20°C  3 years  
   4°C  2 years  
   In solvent  
-80°C  6 months  
   -20°C  1 month

SOLVENT & SOLUBILITY

In Vitro  
DMSO : 20 mg/mL (43.42 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.1712 mL</td>
<td>10.8561 mL</td>
<td>21.7122 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4342 mL</td>
<td>2.1712 mL</td>
<td>4.3424 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2171 mL</td>
<td>1.0856 mL</td>
<td>2.1712 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 mg/mL (4.34 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2 mg/mL (4.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
Milciclib (PHA-848125) is a potent, dual inhibitor of CDK and Tropomyosin receptor kinase (TRK), with IC₅₀s of 45, 150, 160, 363, 398 nM and 53 nM for cyclin A/CDK2, cyclin H/CDK7, cyclin D1/CDK4, cyclin E/CDK2, cyclin B/CDK1 and TRKA, respectively.

IC₅₀ & Target  
cyclin A/CDK2 45 nM (IC₅₀)  
cyclin H/CDK7 150 nM (IC₅₀)  
cyclin D1/CDK4 160 nM (IC₅₀)  
cyclin B/CDK1 398 nM (IC₅₀)  
TRKA 53 nM (IC₅₀)
**In Vitro**

Milciclib (PHA-848125; 0.156 or 0.625 μM) up-regulates the expression of PDCD4, DDIT4, SESN2/sestrin 2 and DEPDC6/DEPTOR in GL-Mel cells\[1\]. Milciclib (PHA-848125) potently inhibits the kinase activity of CDK2/cyclin A complex and of TRKA in a biochemical assay, with IC\(_{50}\)s of 45 and 53 nM, respectively. Milciclib induces a clear accumulation of cells in G1 phase. Milciclib strongly inhibits NGF-induced phosphorylation of TRKA in a dose-dependent manner\[2\].

**In Vivo**

Milciclib (PHA-848125; 5, 10, and 15 mg/kg, p.o.) inhibits the growth of tumor in 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat mammary carcinoma model. Milciclib has significant antitumor activity in various human xenografts and carcinogen-induced tumors as well as in disseminated primary leukemia models, with plasma concentrations in rodents in the same range as those found active in inhibiting cancer cell proliferation\[2\]. Milciclib (PHA-848125; 40 mg/kg) induces a significant tumor growth inhibition in K-Ras\(^{G12D}\)LA2 mice, and this is accompanied by a reduction in the cell membrane turnover\[3\].

**PROTOCOL**

**Cell Assay**\[2\]

Cells are seeded into 96- or 384-well plates at densities ranging from 10,000 to 30,000/cm\(^2\) in appropriate medium plus 10% FCS. After 24 hours, cells are treated in duplicate with serial dilutions of Milciclib, and 72 hours later, viable cell number is assessed using the CellTiter-Glo Assay. IC\(_{50}\)s are calculated using a Sigmoidal fitting algorithm. Experiments are done independently at least twice.

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

**Animal Administration**\[2\]

Rats are randomized and introduced into the study when at least one mammary tumor attained a diameter of 0.5 cm. Groups of 10 animals are treated orally twice a day continuously for 10 days with vehicle (glucosate) or with 5, 10, and 15 mg/kg of Milciclib, whereas a further group receives two cycles of Milciclib at 20 mg/kg orally twice a day for 5 days with an intervening rest period of 1 week. Tumor volume is measured regularly by caliper for the duration of the experiment.

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

**CUSTOMER VALIDATION**

- Technical University of Munich. 24.01.2018.

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**REFERENCES**


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

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