Abemaciclib methanesulfonate

Cat. No.: HY-16297
CAS No.: 1231930-82-7
Molecular Formula: C₂₈H₃₆F₂N₈O₃S
Molecular Weight: 602.7
Target: CDK
Pathway: Cell Cycle/DNA Damage
Storage: 4°C, sealed storage, away from moisture
* In solvent: -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)

SOLVENT & SOLUBILITY

In Vitro
H₂O: 125 mg/mL (207.40 mM; Need ultrasonic)
DMSO: 10 mg/mL (16.59 mM; ultrasonic and warming and heat to 80°C)

<table>
<thead>
<tr>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.6592 mL</td>
<td>8.2960 mL</td>
<td>16.5920 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3318 mL</td>
<td>1.6592 mL</td>
<td>3.3184 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1659 mL</td>
<td>0.8296 mL</td>
<td>1.6592 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: PBS
   Solubility: 25 mg/mL (41.48 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 0.5% HEC
   Solubility: 12.5 mg/mL (20.74 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.15 mM); Clear solution
6. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2 mg/mL (3.32 mM); Suspended solution; Need ultrasonic
7. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (3.32 mM); Clear solution

BIOLOGICAL ACTIVITY
Abemaciclib methanesulfonate (LY2835219 methanesulfonate) is a selective CDK4/6 inhibitor with IC₅₀ values of 2 nM and 10 nM for CDK4 and CDK6, respectively.[1][2][3].

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>Cdk4/cyclin D1 2 nM (IC₅₀)</th>
<th>CDK6/cyclinD1 10 nM (IC₅₀)</th>
<th>CDK9/cyclinT1 57 nM (IC₅₀)</th>
<th>CDK5/p35 287 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cdk5/p25 355 nM (IC₅₀)</td>
<td>CDK2/cyclinE 504 nM (IC₅₀)</td>
<td>CDK1/cyclinB1 1627 nM (IC₅₀)</td>
<td>CDK7/Mat1/cyclinH1 3910 nM (IC₅₀)</td>
</tr>
<tr>
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<td>PIM1 50 nM (IC₅₀)</td>
<td>PIM2 3400 nM (IC₅₀)</td>
<td>HIPK2 31 nM (IC₅₀)</td>
<td>DYRK2 61 nM (IC₅₀)</td>
</tr>
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<td>CK2 117 nM (IC₅₀)</td>
<td>GSK3b 192 nM (IC₅₀)</td>
<td>JNK3 389 nM (IC₅₀)</td>
<td>FLT3 (D835Y) 403 nM (IC₅₀)</td>
</tr>
<tr>
<td></td>
<td>DRAK1 659 nM (IC₅₀)</td>
<td>FLT3 3960 nM (IC₅₀)</td>
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</tr>
</tbody>
</table>

**In Vitro**
Abemaciclib (LY2835219) reduces cell viability with the IC₅₀ values ranging from 0.5 μM to 0.7 μM, inhibits Akt and ERK signaling but not mTOR activation at head and neck squamous cell carcinoma (HNSCC) cells.[1]. Abemaciclib (LY2835219) shows inhibition on A375R1-4, M14R, and SH4R with EC₅₀ values ranging from 0.3 to 0.6 μM; Abemaciclib inhibits the proliferation of the parental A375 and resistant A375RV1 and A375RV2 cells with similar potencies with IC₅₀ values of 395, 260, and 463 nM, respectively.[2]. Abemaciclib (LY2835219) inhibits CDK4 and CDK6 with low nanomolar potency, inhibits Rb phosphorylation resulting in a G1 arrest and inhibition of proliferation, and its activity is specific for Rb-proficient cells.[3].

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

**In Vivo**
Abemaciclib (LY2835219) (45 mg/kg, p.o.) in combination with RAD001 causes a cooperative antitumor effect in HNSCC xenograft tumor.[1]. Abemaciclib (LY2835219) (45 or 90 mg/kg, p.o.) shows significant tumor growth inhibition in an A375 xenograft model.[2].

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

**PROTOCOL**

**Cell Assay**[1]
Cells are seeded in a 96-well plate, allowed to adhere overnight, and treated with DMSO control (0.1% v/v) or the indicated compounds for 72 h. Cell viability and proliferation are determined using a Cell Counting Kit according to the manufacturer’s instructions. The interaction between Abemaciclib (LY2835219) and mTOR inhibitor is determined using CompuSyn. Combination index (CI) values of 1 indicates and additive drug interaction, whereas a CI of < 1 is synergistic and a CI of > 1 is antagonistic.

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**Animal Administration**[1]
Six-week-old BALB/c female nude mice are injected subcutaneously with OSC-19 (1×10⁶) cells. When tumor sizes reach approximately 100 mm³, mice are randomized by tumor size and subjected to each treatment. At least 5 mice per treatment group are included. Each group of mice is dosed via daily oral gavage with vehicle, Abemaciclib (LY2835219) (45 mg/kg/d or 90 mg/kg/d), RAD001 (5 mg/kg/d), or a combination of both. The Abemaciclib (LY2835219) is dissolved in 1% HEC in 20 mM phosphate buffer (pH2.0). Tumor size and body weight are measured twice weekly. Tumor volumes are calculated using the following formula: V=(L × W²)/2 (L, Length; W, width). Mice are gavaged a final time on day 14 and sacrificed the following day. The tumors are removed for Western blot and immunohistochemistry.

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CUSTOMER VALIDATION

- Cell. 2023 Jun 8;186(12):2628-2643.e21.
- Nat Metab. 2020 Jan;2(1):41-49.

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REFERENCES


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