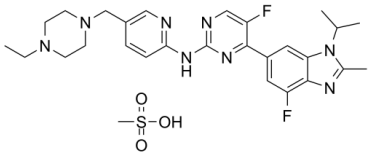
Data Sheet

Product Name:	Abemaciclib (methanesulfonate)
Cat. No.:	CS-1229
CAS No.:	1231930-82-7
Molecular Formula:	C28H36F2N8O3S
Molecular Weight:	602.70
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Solubility:	H2O : 125 mg/mL (207.40 mM; Need ultrasonic); DMSO : ≥ 25 mg/mL (41.48 mM)



BIOLOGICAL ACTIVITY:

Abemaciclib methanesulfonate (LY2835219 methanesulfonate) is a selective **CDK4/6** inhibitor with **IC_{50}**s of 2 nM and 10 nM for CDK4 and CDK6, respectively. IC50 & Target: IC50: 2 nM (CDK4), 10 nM (CDK6)[3] **In Vitro:** Abemaciclib (LY2835219) reduces cell viability with the IC_{50} 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 EC_{50} 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 IC_{50} 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: LY2835219 is dissolved in DMSO to a 10 mM concentration.[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. **Animal Administration:** LY2835219 is dissolved in 1% HEC in 20 mM phosphate buffer.[1]Six-week-old BALB/c female nude mice are injected subcutaneously with OSC-19 (1×10^6) cells. When tumor sizes reach approximately 100 mm^3, 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: $V=(L \times W^2)/2$ (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.

References:

[1]. Ku BM, et al. The CDK4/6 inhibitor LY2835219 has potent activity in combination with mTOR inhibitor in head and neck squamous cell carcinoma. Oncotarget. 2016 Mar 22;7(12):14803-13.

[2]. Yadav V, et al. The CDK4/6 inhibitor LY2835219 overcomes PLX4032 resistance resulting from MAPK reactivation and cyclin D1 upregulation. Mol Cancer Ther. 2014 Oct;13(10):2253-63.

[3]. Gelbert LM, et al. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with NSC 613327. Invest New Drugs. 2014 Oct;32(5):825-37.

[4]. Wu T, et al. Effect of abemaciclib (LY2835219) on enhancement of chemotherapeutic agents in ABCB1 and ABCG2 overexpressing cells in vitro and in vivo. Biochem Pharmacol. 2017 Jan 15;124:29-42.

CAIndexNames:

2-Pyrimidinamine, N-[5-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl]-5-fluoro-4-[4-fluoro-2-methyl-1-(1-methylethyl)-1H-benzimidazol-6-yl]-, methanesulfonate (1:1)

SMILES:

CC(N1C2=CC(C3=NC(NC4=NC=C(CN5CCN(CC)CC5)C=C4)=NC=C3F)=CC(F)=C2N=C1C)C.CS(=O)(O)=O

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