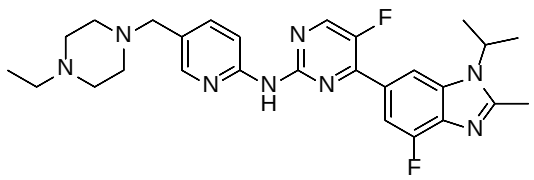
Product data sheet

MedKoo Cat#: 205911 Name: Abemaciclib free base CAS#: 1231929-97-7 (free base) Chemical Formula: $C_{27}H_{32}F_2N_8$ Exact Mass: 506.2718 Molecular Weight: 506.59	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Abemaciclib, also known as LY2835219, is orally available cyclin-dependent kinase (CDK) inhibitor that targets the CDK4 (cyclin D1) and CDK6 (cyclin D3) cell cycle pathway, with potential antineoplastic activity. LY2835219 inhibits CDK4 and CDK6 with low nanomolar potency. LY2835219 specifically inhibits CDK4 and 6, thereby inhibiting retinoblastoma (Rb) protein phosphorylation in early G1. Inhibition of Rb phosphorylation prevents CDK-mediated G1-S phase transition, thereby arresting the cell cycle in the G1 phase, suppressing DNA synthesis and inhibiting cancer cell growth.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	2.67	5.27
Ethanol	9.0	17.77
DMF	1.0	1.97
PBS (pH 7.2)	1.0	1.97

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.97 mL	9.87 mL	19.74 mL
5 mM	0.39 mL	1.97 mL	3.95 mL
10 mM	0.20 mL	0.99 mL	1.97 mL
50 mM	0.04 mL	0.20 mL	0.39 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Kadi AA, Darwish HW, Abuelizz HA, Alsubi TA, Attwa MW. Identification of reactive intermediate formation and bioactivation pathways in Abemaciclib metabolism by LC-MS/MS: in vitro metabolic investigation. R Soc Open Sci. 2019 Jan 23;6(1):181714. doi: 10.1098/rsos.181714. PMID: 30800400; PMCID: PMC6366225.

In vivo study

1. O'Brien N, Conklin D, Beckmann R, Luo T, Chau K, Thomas J, Mc Nulty A, Marchal C, Kalous O, von Euw E, Hurvitz S, Mockbee C, Slamon DJ. Preclinical Activity of Abemaciclib Alone or in Combination with Antimitotic and Targeted Therapies in Breast Cancer. Mol Cancer Ther. 2018 May;17(5):897-907. doi: 10.1158/1535-7163.MCT-17-0290. Epub 2018 Feb 26. PMID: 29483214.

7. Bioactivity

Product data sheet

Biological target: Abemaciclib (LY2835219) is a CDK4/6 inhibitor with IC50 values of 2 nM and 10 nM for CDK4 and CDK6, respectively.

In vitro activity

Abemaciclib's main mechanism of action has been demonstrated to be the inhibition of cell cycle progression leading to senescence in Rb-positive cells. Additionally, abemaciclib has been reported in other cancer types to cause apoptosis. An increase in cleaved caspase 3 levels—an early marker of apoptosis— was detected in Mia PaCa2 cells treated with abemaciclib compared to no treatment on days 1–3 of treatment, compared to staurosporine-treated cells which served as the positive control (Figure 2B). To confirm these findings, live cell staining for caspase 3/7 activity was performed and a significant increase in fluorescent caspase 3/7 cleavage activity (Figure 2C) over days 1 and 2 in Mia PaCa2 cells ($p<0.001$, $p<0.025$ respectively) was detected. Similar results were obtained in Panc-1 and HS 766T cells (Figure 2C). As a validating marker for early and late apoptosis, annexin V staining was performed after 3 days of abemaciclib treatment. An increase in apoptotic and dead cells was detected when compared to no treatment in all cell lines.

Reference: Mol Cancer Res. 2019 Oct;17(10):2029-2041. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6794000/#R22

In vivo activity

In an in vivo study using Mia PaCa2 cells in a subcutaneous xenograft mouse model, a significant decrease in tumor growth in the abemaciclib treated arm versus control ($p<0.0001$) was observed (Figure 5A, Supplemental 4A). Harvested tumors from the xenograft study were sectioned and stained for pRb, Rb, and Ki67. The abemaciclib-treated tumors demonstrated a decrease in pRb and total Rb expression compared to vehicle (Figure 5C, Supplemental 4C). Pathologist scoring and quantification of IHC staining shows that in the abemaciclib-treated tumors, there was 46.3% cells with positive pRb staining, compared to no treatment which had 74.5% cells with positive pRb. Additionally, compared to no treatment which had 78.8% cells with positive Ki67 staining, the abemaciclib-treated tumors had 59.5% cells with positive Ki67 staining (Figure 5D). Overall, when normalized to no treatment, abemaciclib-treated tumors had approximately 38% reduction in pRb staining and 25% reduction in pRb/ total Rb staining along with Ki67 stianing (Figure 5D). These results demonstrate that abemaciclib treatment induces apoptosis, decreases pRb and tumor growth, and induces senescence in this in vivo xenograft model.

Reference: Mol Cancer Res. 2019 Oct;17(10):2029-2041. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6794000/#R22