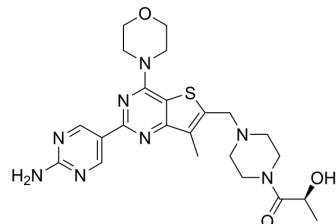


## Apitolisib

<b>Cat. No.:</b>	HY-13246		
<b>CAS No.:</b>	1032754-93-0		
<b>Molecular Formula:</b>	C <sub>23</sub> H <sub>30</sub> N <sub>8</sub> O <sub>3</sub> S		
<b>Molecular Weight:</b>	498.6		
<b>Target:</b>	PI3K; mTOR; Apoptosis		
<b>Pathway:</b>	PI3K/Akt/mTOR; Apoptosis		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 14.29 mg/mL (28.66 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
	<b>Preparing Stock Solutions</b>		10 mg	
	<b>1 mM</b>	2.0056 mL	10.0281 mL	20.0562 mL
	<b>5 mM</b>	0.4011 mL	2.0056 mL	4.0112 mL
	<b>10 mM</b>	0.2006 mL	1.0028 mL	2.0056 mL
Please refer to the solubility information to select the appropriate solvent.				
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 1.43 mg/mL (2.87 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 1.43 mg/mL (2.87 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 1.43 mg/mL (2.87 mM); Clear solution</li> </ol>			

### BIOLOGICAL ACTIVITY

<b>Description</b>	Apitolisib (GDC-0980; GNE 390; RG 7422) is a selective, potent, orally bioavailable Class I PI3 kinase and mTOR kinase (TORC1/2) inhibitor with IC <sub>50</sub> s of 5 nM/27 nM/7 nM/14 nM for PI3Kα/PI3Kβ/PI3Kδ/PI3Kγ, and with a K <sub>i</sub> of 17 nM for mTOR.			
<b>IC<sub>50</sub> &amp; Target</b>	PI3Kα 5 nM (IC <sub>50</sub> )	PI3Kδ 7 nM (IC <sub>50</sub> )	PI3Kγ 14 nM (IC <sub>50</sub> )	PI3Kβ 27 nM (IC <sub>50</sub> )
	mTOR 17 nM (K <sub>i</sub> )	TORC1	TORC2	

<b>In Vitro</b>	<p>Apitolisib (GDC-0980) is remarkably selective for several other members of the closely related PIKK family kinases: C2alpha IC<sub>50</sub>=1300 nM; C2beta IC<sub>50</sub>=7 94 nM; VPS34 IC<sub>50</sub>=2000 nM; PI4Kalpha &gt;10 μM; PI4Kbeta &gt;10 μM; DNA-PK Kiapp=623 nM, respectively<sup>[1]</sup>. A recent study shows that Apitolisib (GDC-0980) reduces cancer cell viability by inhibiting cell-cycle procession and inducing apoptosis with most potency in prostate (IC<sub>50</sub> &lt; 200 nM 50%, &lt;500 nM 100%), breast (IC<sub>50</sub> &lt;200 nM 37%, &lt;500 nM 78%) and NSCLC lines (IC<sub>50</sub> &lt;200 nM 29%, &lt;500 nM 88%) and less potency in pancreatic (IC<sub>50</sub> &lt;200 nM 13%, &lt;500 nM 67%) and melanoma cell lines (IC<sub>50</sub> &lt;200 nM 0%, &lt;500 nM 33%)<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>Apitolisib (GDC-0980) (1 mg/kg, p.o.) demonstrates significant efficacy in mouse xenografts and is currently in phase I clinical trials for cancer. Clearance and PPB are low, and Apitolisib (GDC-0980) shows dose-proportional exposure from 5 mg/kg dosed in PEG to 50 mg/kg dosed in suspension in MCT, a finding attributed partially to the compound's good solubility<sup>[1]</sup>. Apitolisib (GDC-0980) (5 mg/kg, p.o.) results in greater than 50% TGI in 15 of the 20 xenograft models. The difference in tumor response to Apitolisib (GDC-0980) treatment correlates with the duration of knockdown of pAkt/tAkt<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Kinase Assay</b> <sup>[2]</sup>	<p>Ten centimeter square dishes are seeded with 2 million cells in a volume of 10 mL followed by incubation at 37°C under 5% CO<sub>2</sub> overnight (appr 16 hours). Cells are treated with the indicated concentration of GDC-0941, Apitolisib (GDC-0980), or mTOR1/2 inhibitor for the time indicated. Following treatment, cells are washed with cold PBS and lysed in 1X Cell Extraction Buffer, 1 mM PMSF, and Phosphatase Inhibitor Cocktails 1 and 2 are all needed. Protein concentration is determined using the Pierce BCA Protein Assay Kit. For immunoblots, equal protein amounts are separated by electrophoresis through NuPage Bis-Tris 10% gradient gels; proteins are transferred onto polyvinylidene difluoride membranes using the Criterion system and protocol.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Cell Assay</b> <sup>[2]</sup>	<p>Three hundred and eighty-four-well plates are seeded with 2,000 cells/well in a volume of 54 μL per well followed by incubation at 37°C under 5% CO<sub>2</sub> overnight (appr 16 hours). Compounds are diluted in dimethyl sulfoxide to generate the desired stock concentrations then added in a volume of 6 μL per well. All treatments are tested in quadruplicate. After 4 days incubation, relative numbers of viable cells are estimated using CellTiter-Glo and total luminescence is measured on a Wallac Multilabel Reader. The concentration of drug resulting in 50% inhibition of cell viability (IC<sub>50</sub>) or 50% maximal effective concentration (EC<sub>50</sub>) is determined using Prism software. For cell lines that failed to achieve an IC<sub>50</sub> the highest concentration tested (20 μM) is listed.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[1]</sup>	<p>Human prostate cancer PC3 cells are resuspended in Hank's Balanced Salt Solution and 3×10<sup>6</sup> cells implanted subcutaneously into the right hind flank of athymic nu/nu (nude) mice. Tumors are monitored until they reach a mean tumor volume of 150-200 mm<sup>3</sup> prior to the initiation of dosing. MCF7.1 cells resuspended in a 1:1 mixture of Hank's Buffered Salt Solution and Matrigel Basement Membrane Matrix are 5×10<sup>6</sup> subcutaneously implanted into the right hind flank of athymic nu/nu (nude) mice. Prior to cell inoculation, 17β-estradiol (0.36 mg/pellet, 60-day release, no. SE-121) are implanted into the dorsal shoulder blade area of each nude mouse. After implantation of cells, tumors are monitored until they reach a mean tumor volume of 250-350 mm<sup>3</sup> prior to initiating dosing. Compound 2 is dissolved in 0.5% methylcellulose with 0.2% Tween-80 (MCT). Female nude (nu/nu) mice that are 6-8 weeks old and weighed 20-30 g are obtained from Charles River Laboratories. Tumor bearing mice are dosed daily for 14-21 days depending on the xenograft model with 100 μL of vehicle (MCT) or test agent orally.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## CUSTOMER VALIDATION

- Nature. 2018 Aug;560(7719):499-503.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.

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## REFERENCES

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[1]. Sutherlin DP, et al. Discovery of a potent, selective, and orally available class I phosphatidylinositol 3-kinase (PI3K)/mammalian target of rapamycin (mTOR) kinase inhibitor (GDC-0980) for the treatment of cancer. J Med Chem, 2011, 54(21), 7579-7587.

[2]. Wallin JJ, et al. GDC-0980 is a novel class I PI3K/mTOR kinase inhibitor with robust activity in cancer models driven by the PI3K pathway. Mol Cancer Ther, 2011, 10(12), 2426-2436.

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

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