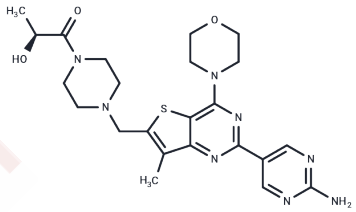
# Data Sheet (Cat.No.T1916)

TargetMol

## Apitolisib

### Chemical Properties



CAS No. : 1032754-93-0

Formula: C23H30N8O3S

Molecular Weight: 498.6

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

### Biological Description

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| Description | Apitolisib (RG 7422), an effective, class I PI3K inhibitor for PI3Kα(IC50=5 nM), PI3Kβ (IC50=27 nM), PI3Kδ(IC50=7 nM), PI3Kγ (IC50=14 nM), is used in trials study of solid cancers, breast cancer, prostate cancer, renal cell carcinoma, and endometrial carcinoma, among others. |
| Targets(IC50) | Apoptosis,mTOR,PI3K |
| In vitro | In PC3 (IC50=307 nM) and MCF7 cells (IC50=255 nM), GDC-0980 significantly inhibited cell proliferation. For class I PI3K and mTOR kinases, the selective inhibitory effect of GDC-0980 was significant for mTOR (Ki=17 nM), for PI3Kα (IC50=5 nM), β (IC50=27 nM), δ (IC50=7 nM), and γ (IC50=14 nM). |
| In vivo | In PC3 (IC50=307 nM) and MCF7 cells (IC50=255 nM), GDC-0980 significantly inhibited cell proliferation. For class I PI3K and mTOR kinases, the selective inhibitory effect of GDC-0980 was significant for mTOR (Ki=17 nM), for PI3Kα (IC50=5 nM), β (IC50=27 nM), δ (IC50=7 nM), and γ (IC50=14 nM). |
| Kinase Assay | Enzymatic activity: Enzymatic activity of the Class I PI3K isoforms is measured using a fluorescence polarization assay that monitors formation of the product 3,4,5-inositoltriphosphate molecule as it competes with fluorescently labeled PIP3 for binding to the GRP-1 pleckstrin homology domain protein. An increase in phosphatidyl inositide-3-phosphate product results in a decrease in fluorescence polarization signal as the labeled fluorophore is displaced from the GRP-1 protein binding site. Class I PI3K isoforms are expressed and purified as heterodimeric recombinant proteins. PI3K isoforms are assayed under initial rate conditions in the presence of 10 mM Tris (pH 7.5), 25 μM ATP, 9.75 μM PIP2, 5% glycerol, 4 mM MgCl2, 50 mM NaCl, 0.05% (v/v) Chaps, 1 mM dithiothreitol, 2% (v/v) DMSO at the following concentrations for each isoform: PI3Kα,β at 60 ng/mL; PI3Kγ at 8 ng/mL; PI3Kδ at 45 ng/mL. After assay for 30 minutes at 25°C, reactions are terminated with a final concentration of 9 mM EDTA, 4.5 nM TAMRA-PIP3, and 4.2 μg/mL GRP-1 detector protein before reading fluorescence polarization on an Envision plate reader. IC50s are calculated from the fit of the dose?response curves to a 4-parameter equation.Human recombinant mTOR(1360?2549) is expressed and purified from insect cells and assayed using a Lanthascreen fluorescence resonance energy transfer format in which phosphorylation of recombinant green fluorescent protein (GFP)-4-EBP1 is detected using a terbium-labeled antibody to phospho-threonine 37/46 of 4-EBP1. Reactions are initiated with ATP and conducted in the presence of 50 mM Hepes (pH 7.5), 0.25 nM mTOR, 400 nM GFP-4E-BP1, 8 μM ATP, 0.01% |

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| Kinase Assay | (v/v) Tween 20, 10 mM MnCl2, 1 mM EGTA, 1 mM dithiothreitol, and 1% (v/v) DMSO. Assays are conducted under initial rate conditions at room temperature for 30 minutes before terminating the reaction and detecting product in the presence of 2 nM Tb-anti-p4E-BP1 antibody and 10 mM EDTA.Dose?response curves are fit to an equation for competitive tight-binding inhibition and apparent Ki' s are calculated using the determined Km for ATP of 6.1 μM. |
| Cell Research | Antiproliferative cellular assays are conducted using PC3 and MCF7.1 human tumor cell lines. MCF7.1 is an in vivo selected line and originally derived from the parental human MCF7 breast cancer cell line. Cell lines are cultured in RPMI supplemented with 10% fetal bovine serum, 100 units/mL penicillin, and 100 μg/mL streptomycin, 10 mM HEPES, and 2 mM glutamine at 3°C under 5% CO2. MCF7.1 cells or PC3 cells are seeded in 384-well plates in media at 1000 cells/well or 3000 cells/well, respectively, and incubated overnight prior to the addition of GDC-0980 to a final DMSO concentration of 0.5% v/v. MCF7.1 cells and PC3 cells are incubated for 3 days and 4 days, respectively, prior to the addition of CellTiter-Glo reagen and reading of luminescence using an Analyst plate reader. For antiproliferative assays, a cytostatic agent such as aphidicolin and a cytotoxic agent such as staurosporine are included as controls. Dose?response curves are fit to a 4-parameter equation and relative IC50s are calculated using Assay Explorer software.(Only for Reference) |

## Solubility Information

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| Solubility | Ethanol: < 1 mg/mL (insoluble or slightly soluble),<br>DMSO: 13.9 mg/mL (27.88 mM),Sonication is recommended.<br>H2O: < 1 mg/mL (insoluble or slightly soluble),<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.01 mM),Sonication is recommended.<br>10% DMSO+90% Saline: 1.39 mg/mL (2.79 mM),Solution.<br>*Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.* |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|---|---|---|---|
| 1 mM | 2.0056 mL | 10.0281 mL | 20.0562 mL |
| 5 mM | 0.4011 mL | 2.0056 mL | 4.0112 mL |
| 10 mM | 0.2006 mL | 1.0028 mL | 2.0056 mL |
| 50 mM | 0.0401 mL | 0.2006 mL | 0.4011 mL |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Sutherlin DP, et al. J Med Chem, 2011, 54(21), 7579-7587.
Wallin JJ, et al. Mol Cancer Ther, 2011, 10(12), 2426-2436.
Makhov PB, et al. 2012. doi: 10.1158/1535-7163. MCT-11-0907.



Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481