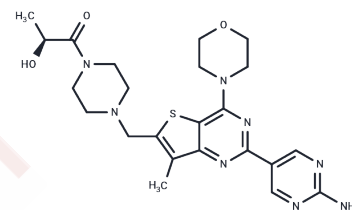


Apitolisib

Chemical Properties

CAS No. :	1032754-93-0
Formula:	C ₂₃ H ₃₀ N ₈ O ₃ S
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

Description	Apitolisib (RG 7422), an effective, class I PI3K inhibitor for PI3K α (IC ₅₀ =5 nM), PI3K β (IC ₅₀ =27 nM), PI3K δ (IC ₅₀ =7 nM), PI3K γ (IC ₅₀ =14 nM), is used in trials study of solid cancers, breast cancer, prostate cancer, renal cell carcinoma, and endometrial carcinoma, among others.
Targets(IC ₅₀)	Apoptosis, mTOR, PI3K
In vitro	In PC3 (IC ₅₀ =307 nM) and MCF7 cells (IC ₅₀ =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 (K _i =17 nM), for PI3K α (IC ₅₀ =5 nM), β (IC ₅₀ =27 nM), δ (IC ₅₀ =7 nM), and γ (IC ₅₀ =14 nM).
In vivo	In PC3 (IC ₅₀ =307 nM) and MCF7 cells (IC ₅₀ =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 (K _i =17 nM), for PI3K α (IC ₅₀ =5 nM), β (IC ₅₀ =27 nM), δ (IC ₅₀ =7 nM), and γ (IC ₅₀ =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 PIP ₃ 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 μ M ATP, 9.75 μ M PIP ₂ , 5% glycerol, 4 mM MgCl ₂ , 50 mM NaCl, 0.05% (v/v) Chaps, 1 mM dithiothreitol, 2% (v/v) DMSO at the following concentrations for each isoform: PI3K α , β at 60 ng/mL; PI3K γ at 8 ng/mL; PI3K δ 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-PIP ₃ , and 4.2 μ g/mL GRP-1 detector protein before reading fluorescence polarization on an Envision plate reader. IC ₅₀ s are calculated from the fit of the dose-response curves to a 4-parameter equation. Human recombinant mTOR(13602549) 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 phosphothreonine 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 μ M ATP, 0.01%

Kinase Assay	(v/v) Tween 20, 10 mM MnCl ₂ , 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 K _i 's are calculated using the determined K _m 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% CO ₂ . 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 reagent 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 IC ₅₀ s are calculated using Assay Explorer software. (Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 13.9 mg/mL (27.88 mM), Sonication is recommended. H ₂ O: < 1 mg/mL (insoluble or slightly soluble), (< 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. <i>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.</i>

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

Sutherland 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.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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