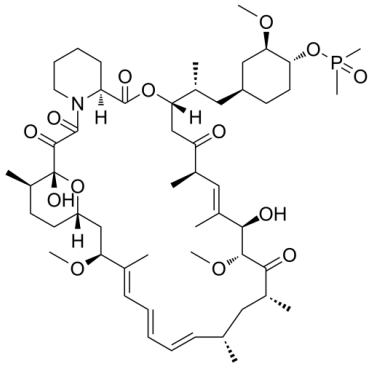
Data Sheet

Product Name:	Deforolimus
Cat. No.:	CS-0122
CAS No.:	572924-54-0
Molecular Formula:	C53H84NO14P
Molecular Weight:	990.21
Target:	Autophagy; mTOR
Pathway:	Autophagy; PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 44 mg/mL (44.44 mM)



BIOLOGICAL ACTIVITY:

Deforolimus (AP23573; MK-8669) is a potent and selective **mTOR** inhibitor; inhibits ribosomal protein S6 phosphorylation with an **IC_{50}** of 0.2 nM in HT-1080 cells. IC50 & Target: IC50: 0.5 nM (HT-1080 cells)[1] **In Vitro:** Treatment of HT-1080 fibrosarcoma cells with deforolimus results in a dose-dependent inhibition of phosphorylation of both S6 and 4E-BP1, with IC_{50}s of 0.2 and 5.6 nM, respectively, and EC_{50}s of 0.2 and 1.0 nM, respectively. In HT-1080 cells, the EC_{50} for inhibition of cell proliferation (0.5 nM) is similar to the EC_{50}s for inhibition of S6 and 4E-BP1 phosphorylation. Exposure to deforolimus reduces the proliferation of cell lines representing a variety of tumor types. Administration of deforolimus to tumor cells in vitro elicit dose-dependent inhibition of mTOR activity with concomitant effects on cell growth and division. Deforolimus exhibits a predominantly cytostatic mode of action, consistent with the findings for other mTOR inhibitors. Potent inhibitory effects on vascular endothelial growth factor secretion, endothelial cell growth, and glucose metabolism[1]. **In Vivo:** Deforolimus inhibits tumor growth in mice bearing PC-3 (prostate), HCT-116 (colon), MCF7 (breast), PANC-1 (pancreas), or A549 (lung) xenografts. Deforolimus inhibits tumor growth in a dose-dependent manner, with 0.3 mg/kg being the lowest dose that inhibits tumor growth significantly and 3 and 10 mg/kg doses achieving maximum inhibition[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Cells are treated with 10-fold serial dilutions of deforolimus (1,000 to 0.0001 nM) or vehicle (ethanol). Following 72 hours culture at 37°C, the plates are aspirated and stored at −80°C for proliferation analysis[1]. **Animal Administration:** [1]Mice: Animals selected with tumors in the proper size range are assigned to various treatment groups. Deforolimus, at dosages of 3 and 10 mg/kg, is administered i.p. on 2 different treatment schedules: (a) daily, 5 continuous days every other week and (b) once weekly. The control group is untreated[1].

References:

[1]. Rivera VM, et al. Deforolimus (AP23573; MK-8669), a potent mTOR inhibitor, has broad antitumor activity and can be optimally administered using intermittent dosing regimens. Mol Cancer Ther. 2011 Jun;10(6):1059-71.

[2]. Brandt M, et al. mTORC1 Inactivation Promotes Colitis-Induced Colorectal Cancer but Protects from APC Loss-Dependent Tumorigenesis. Cell Metab. 2018 Jan 9;27(1):118-135.e8.

CAIndexNames:

Rapamycin, 42-(dimethylphosphinate) (9CI)

SMILES:

O=C([C@@]1(O)[C@@H](CC[C@@H](C[C@@H](/C(C)=C/C=C/C=C/[C@H](C[C@@H](C)C([C@@H]([C@@H](/C(C)=C/[C@H]2C)O)OC)=O)C)OC)O1)C)C(N3CCCC[C@H]3C(O[C@@H](CC2=O)[C@@H](C[C@@H]4C[C@H]([C@H](OP(C)(C)=O)CC4)OC)C)=O)=O

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

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