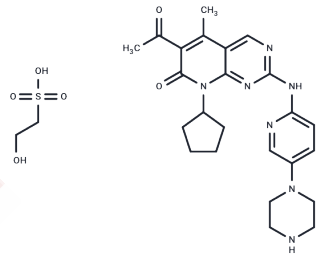
Data Sheet (Cat.No.T6240)

TargetMol

Palbociclib Isethionate

Chemical Properties



CAS No. : 827022-33-3

Formula: C24H29N7O2·C2H6O4S

Molecular Weight: 573.66

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	Palbociclib Isethionate (PD 0332991 isethionate) is a selective inhibitor of CDK4/6 (IC50s: 11/16 nM). It exhibits no inhibition against a panel of 36 additional protein kinases.
Targets(IC50)	CDK
In vitro	Palbociclib is a highly specific inhibitor of Cdk4 (IC50, 0.011 micromol/L) and Cdk6 (IC50, 0.016 micromol/L). It is a potent antiproliferative agent against retinoblastoma (Rb)-positive tumor cells in vitro, inducing an exclusive G1 arrest, with a concomitant reduction of phospho-Ser780/Ser795 on the Rb protein [1]. In all of the cell lines except KP-MRT-YM, Palbociclib inhibited cell proliferation >50% (IC50 values 0.01 to 0.6 μM), and induced G1-phase cell cycle arrest. The sensitivity of the MRT cell lines to Palbociclib was inversely correlated with p16 expression. KP-MRT-YM cells overexpress p16 and were resistant to the growth inhibitory effect of Palbociclib [2]. Cell lines representing luminal estrogen receptor-positive (ER+) subtype (including those that are HER2 amplified) were most sensitive to growth inhibition by Palbociclib while nonluminal/basal subtypes were most resistant [3].
In vivo	Oral administration of PD 0332991 to mice bearing the Colo-205 human colon carcinoma produces marked tumor regression. Therapeutic doses of PD 0332991 cause elimination of phospho-Rb and the proliferative marker Ki-67 in tumor tissue and down-regulation of genes under the transcriptional control of E2F [1].
Kinase Assay	CDK assays for IC50determinations and kinetic evaluation were performed in 96-well filter plates. All CDK-cyclin kinase complexes were expressed in insect cells through baculovirus infection and purified as described previously. The substrate for the assays was a fragment (amino acids 792–928) of pRb fused to GST. The total volume for each well was 0.1 ml containing a final concentration of 20 mM Tris-HCl, pH 7.4, 50 mMNaCl, 1 mM dithiothreitol, 10 mMMgCl2, 25 μM ATP (for CDK4-cyclin D1, CDK6-cyclin D2, and CDK6-cyclin D3) or 12 μM ATP (for CDK2-cyclin E, CDK2-cyclin A, and CDC2-cyclin B) containing 0.25 μCi of [γ-32P]ATP, 20 ng of enzyme, 1 μg of GST·RB-Cterm, and appropriate dilutions of inhibitor. All components except the [γ-32P]ATP were added to the wells, and the plate was placed on a plate mixer for 2 min. The reaction was then started by adding the [γ-32P]ATP, and the plate was incubated at 25?°C for 15 min. The reaction was terminated by addition of 0.1 ml of 20% trichloroacetic acid, and the plate was kept at 4?°C for at least 1 h to allow the substrate to precipitate. The wells were then washed five times with 0.2 ml of 10% trichloroacetic acid, and radioactive incorporation

Kinase Assay	was determined with a β plate counter. Kinase assays for PDGFr, FGFr, EGFr, SRC, and PKC kinases were performed as described previously [4].
Cell Research	Cells were seeded at 2 × 10^4 per well in a 96-well Cytostar T plate and incubated overnight to allow cells to attach. Varying concentrations of PD 0332991 were added to the wells and incubated for 24 hours at 37°C. [14C]thymidine (0.1 μCi) was added to each well and incorporation of the radiolabel was allowed to proceed for 72 hours. Incorporated radioactivity was determined with a β plate counter [1].
Animal Research	Mice (18-22 g) were randomized and then implanted s.c. with tumor fragments (~ 30 mg) into the region of the right axilla. Treatment was initiated when tumors reached 100 to 150 mg. PD 0332991 was given according to the schedule and dose indicated in the table and figure legends by gavage as a solution in sodium lactate buffer (50 mmol/L, pH 4.0) based on mean group body weight. In all experiments, there were 12 mice in the control group and 8 mice each in the treated groups. Additional details for each experiment are given in the table legends [1].

Solubility Information

Solubility	DMSO: 40 mg/mL (69.73 mM),Sonication is recommended. H2O: 57.4 mg/mL (100.06 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7432 mL	8.716 mL	17.4319 mL
5 mM	0.3486 mL	1.7432 mL	3.4864 mL
10 mM	0.1743 mL	0.8716 mL	1.7432 mL
50 mM	0.0349 mL	0.1743 mL	0.3486 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

Fry DW, et al. Specific inhibition of cyclin-dependent kinase 4/6 by PD 0332991 and associated antitumor activity in human tumor xenografts. Mol Cancer Ther. 2004 Nov;3(11):1427-38.
Katsumi Y, et al. Sensitivity of malignant rhabdoid tumor cell lines to PD 0332991 is inversely correlated with p16 expression. Biochem Biophys Res Commun, 2011, 413(1), 62-68.
Finn RS, et al. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. Breast Cancer Res. 2009;11(5):R77.
Fry DW, et al. Cell cycle and biochemical effects of PD 0183812. A potent inhibitor of the cyclin D-dependent kinases CDK4 and CDK6. J Biol Chem. 2001 May 18;276(20):16617-23.

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