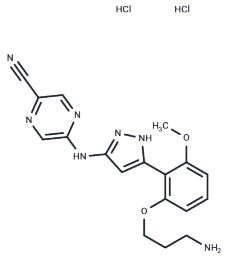
# Data Sheet (Cat.No.T4327)

TargetMol

## Prexasertib dihydrochloride

### Chemical Properties



CAS No. : 1234015-54-3

Formula: C18H21Cl2N7O2

Molecular Weight: 438.31

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 | Prexasertib dihydrochloride (LY2606368) is an ATP-competitive CHK1 inhibitor (Ki: 0.9 nmol/L). in the cell-free assay, its IC50 values are 8 nM and 9 nM for CHK2 and RSK, respectively. |
| Targets(IC50) | Apoptosis,Chk,S6 Kinase |
| In vitro | LY2606368 induces DNA damage and increases in pH2A.X. In cells, LY2606368 causes the rapid appearance of TUNEL and pH2AX-positive double-stranded DNA breaks in the S-phase cell population. In a functional assay, LY2606368 effectively abrogates the G2-M checkpoint activated by doxorubicin in p53-deficient HeLa cells (EC50: 9 nM). LY2606368 was broadly antiproliferative in the most sensitive cell lines (IC50s50 nM) with a minority of cell lines showing considerable resistance (IC50s >1,000 nM). LY2606368 requires CDK2 and CDC25A to cause DNA damage. |
| In vivo | In cancer xenografts, LY2606368 inhibits tumor growth by monotherapy and combined with other agents. In an orthotopic SKOV3 ovarian cancer model, LY2606368 inhibits the growth of primary tumors and markedly reduces the incidence of metastases and ascites accumulation. In an SW1990 orthotopic pancreatic cancer model, LY2606368 also causes a 92% inhibition of primary tumor growth and the elimination of metastases to the lymph node, spleen, and intestine. |
| Kinase Assay | The interaction of COTI-2 with 227 kinases is tested using the AMBIT BIOSCIENCES KINOMESCAN assay. In brief, streptavidin-coated magnetic beads are treated with biotinylated small molecule ligands for 30 min at 25°C to generate affinity resins for kinase assays. The liganded beads are blocked with excess biotin and washed with blocking buffer (1% BSA, 0.05% Tween 20, 1 mM DTT) to remove unbound ligand and to reduce non-specific binding. Binding reactions are assembled by combining phage lysates, liganded affinity beads, and COTI-2 in 1× binding buffer (20% SeaBlock, 0.17× PBS, 0.05% Tween 20, 6 mM DTT). All reactions are carried out in polystyrene 96-well plates that have been pre-treated with blocking buffer in a final volume of 0.1 mL. |
| Cell Research | HeLa cells were plated onto T25 flasks and allowed to recover for 24 hours.LY2606368 was then added to give final concentrations of 33 or 100 nmol/L.In some experiments,20 μMol/L Z-VAD-FMK was included during the drug treatment.Cells were treated for 12 hours,and during the last 2 hours,colchicine was added to 1 μg/mL.Fixation of nuclei for metaphase spreads was done following the method of Bayani and Squire.Chromosome spreads were done.A 12-μL volume of cell suspension in 3:1 methanol/acetic acid fixative was dropped from a height of 3 cm onto dry glass slides or coverslips.The slides |

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| Cell Research | were then heated for 45 seconds on a 43°C metal block,before being removed to allow drying to complete at room temperature.Coverslips were mounted on slides with Vectashield Hard Set mounting medium with DAPI.Slides were examined with a Leica DMR fluorescence microscope and images were captured using a SPOT RT3 Slider camera. |
| Animal Research | LY2606368 is formulated in a vehicle consisting of 20% Captisol.Female CD-1 nu-/nu-mice (26-28 g) are used for this study. Tumor growth is initiated by subcutaneous injection of 1×106 Calu-6 cells in a 1:1 mixture of serum-free growth medium and Matrigel in the rear flank of each subject animal. When tumor volumes reach approximately 150 mm3 in size, the animals are randomized by tumor size and body weight and placed into their respective treatment groups. The vehicle consisting of 20% Captisol pH4 or LY2606368 is administered by subcutaneous injection in a volume of 200 µL. Four, eight, 12, 24, and 48 hours after drug administration, blood for plasma drug exposure is extracted via cardiac puncture and assayed on a Sciex API 4000 LC/MS-MS system. The xenograft tissue is promptly removed and prepared. Lysates were analyzed by immunoblot analysis for protein phosphorylation levels. |

## Solubility Information

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| Solubility | DMSO: 25 mg/mL (57.04 mM),Sonication is recommended.<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|---|---|---|---|
| 1 mM | 2.2815 mL | 11.4075 mL | 22.8149 mL |
| 5 mM | 0.4563 mL | 2.2815 mL | 4.563 mL |
| 10 mM | 0.2281 mL | 1.1407 mL | 2.2815 mL |
| 50 mM | 0.0456 mL | 0.2281 mL | 0.4563 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

Hong D,etal.Phase I Study of LY2606368, a Checkpoint Kinase 1 Inhibitor, in Patients With Advanced Cancer.J Clin Oncol. 2016 May 20;34(15):1764-71.
King C,etal.LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms.Mol Cancer Ther. 2015 Sep;14(9):22004-13.
McNeely S,etal.CHEK again: revisiting the development of CHK1 inhibitors for cancer therapy.Pharmacol Ther. 2014 Apr;142(1):1-10.
Yin Y, et al. Chk1 inhibition potentiates the therapeutic efficacy of PARP inhibitor BMN673 in gastric cancer. Am J Cancer Res. 2017 Mar 1;7(3):473-483.

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