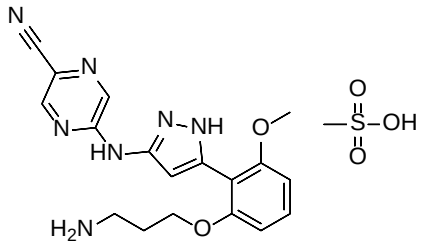
Product data sheet

MedKoo Cat#: 206787 Name: Prexasertib mesylate CAS#: 1234015-55-4 (mesylate) Chemical Formula: $C_{19}H_{23}N_7O_5S$ Molecular Weight: 461.50	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Prexasertib, also known as LY2606368, is a potent and selective Chk1/Chk2 inhibitor. Prexasertib increases the effectiveness of conventional therapy in B-/T- cell progenitor acute lymphoblastic leukemia. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Treatment of cells with LY2606368 results in the rapid appearance of TUNEL and pH2AX-positive double-stranded DNA breaks in the S-phase cell population.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	24.0	52.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.17 mL	10.83 mL	21.67 mL
5 mM	0.43 mL	2.17 mL	4.33 mL
10 mM	0.22 mL	1.08 mL	2.17 mL
50 mM	0.04 mL	0.22 mL	0.43 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Ghelli Luserna Di Rorà A, Iacobucci I, Imbrogno E, Papayannidis C, Derenzini E, Ferrari A, Guadagnuolo V, Robustelli V, Parisi S, Sartor C, Abbenante MC, Paolini S, Martinelli G. Prexasertib, a Chk1/Chk2 inhibitor, increases the effectiveness of conventional therapy in B-/T- cell progenitor acute lymphoblastic leukemia. Oncotarget. 2016 Aug 16;7(33):53377-53391. doi: 10.18632/oncotarget.10535. PMID: 27438145; PMCID: PMC5288194.
2. Brill E, Yokoyama T, Nair J, Yu M, Ahn YR, Lee JM. Prexasertib, a cell cycle checkpoint kinases 1 and 2 inhibitor, increases in vitro toxicity of PARP inhibition by preventing Rad51 foci formation in BRCA wild type high-grade serous ovarian cancer. Oncotarget. 2017 Oct 31;8(67):111026-111040. doi: 10.18632/oncotarget.22195. PMID: 29340034; PMCID: PMC5762302.

In vivo study

1. Zeng L, Nikolaev A, Xing C, Della Manna DL, Yang ES. CHK1/2 Inhibitor Prexasertib Suppresses NOTCH Signaling and Enhances Cytotoxicity of Cisplatin and Radiation in Head and Neck Squamous Cell Carcinoma. Mol Cancer Ther. 2020 Jun;19(6):1279-1288. doi: 10.1158/1535-7163.MCT-19-0946. Epub 2020 May 5. PMID: 32371584.
2. Sen T, Tong P, Stewart CA, Cristea S, Valliani A, Shames DS, Redwood AB, Fan YH, Li L, Glisson BS, Minna JD, Sage J, Gibbons DL, Piwnica-Worms H, Heymach JV, Wang J, Byers LA. CHK1 Inhibition in Small-Cell Lung Cancer Produces Single-Agent Activity in Biomarker-Defined Disease Subsets and Combination Activity with Cisplatin or Olaparib. Cancer Res. 2017 Jul 15;77(14):3870-3884. doi: 10.1158/0008-5472.CAN-16-3409. Epub 2017 May 10. PMID: 28490518; PMCID: PMC5563854.

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7. Bioactivity

Biological target: Prexasertib inhibits CHK1, CHK2, and RSK1 with IC50s of <1 nM, 8 nM, and 9 nM, respectively.

In vitro activity

The efficacy of the Checkpoint kinase 1/2 (Chk 1/2) inhibitor prexasertib mesylate in B-/T- cell progenitor acute lymphoblastic leukemia (ALL) was evaluated. Prexasertib reduced the cell viability in a dose and time dependent manner in all treated cell lines. The cytotoxic activity was confirmed by the increment of apoptotic cells (Annexin V/Propidium Iodide staining), by the increase of γH2A.X protein expression and by the activation of different apoptotic markers (Parp-1 and pro-Caspase3 cleavage). Furthermore, the inhibition of Chk1 changed the cell cycle profile. Prexasertib reduced the amount of cells in G1 and G2/M phase while increasing the number of cells in S phase.

Reference: Oncotarget. 2016 Aug 16;7(33):53377-53391. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5288194/

In vivo activity

The antitumor efficacy of LY2606368 was investigated in a syngeneic flank tumor model generated from subcutaneous injection of cells (TKO.mTmG) derived from a GEMM (genetically engineered mouse model) with conditional loss of Trp53, p130, and Rb1 in the neuroendocrine cells of the lung (23, 24). These mice developed tumors that closely resembled human SCLC (small cell lung cancer). Tumor-bearing mice (n = 9 per group) were treated with LY2606368 or vehicle. Within 1 week of the start of treatment with LY2606368, remarkable tumor regression was observed (Fig. 3A; Supplementary Fig. S3B). Of the 9 mice treated with LY2606368 (10 mg/kg, twice daily, days 1–3 of a 7-day cycle; i.e., 60 mg/kg per week), 6 had a complete response (100% reduction) and the other 3 had >75% reduction in tumor volume. The tumor–control ratio at day 12 was 0.02 ($P < 0.001$). Mice treated with a lower dose of LY2606368 (16 mg/kg, twice daily, day 1 of a 7-day cycle; i.e., 32 mg/kg per week) had stable disease for up to 30 days, with a tumor–control ratio of 0.16 ($P < 0.001$; Fig. 3A; Supplementary Fig. S3B). In contrast, all vehicle-treated mice (n = 9) experienced rapid tumor progression and were removed from the experiment because of excessive tumor volume within two weeks (Fig. 3A and B; Supplementary Fig. S3B).

Reference: Cancer Res. 2017 Jul 15;77(14):3870-3884. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5563854/