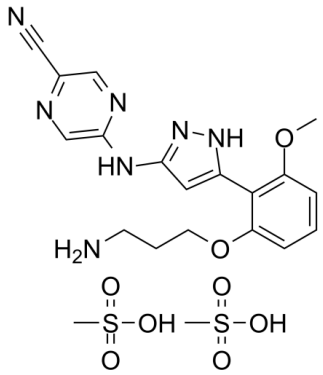
Data Sheet

Product Name:	Prexasertib (dimesylate)
Cat. No.:	CS-0130202
CAS No.:	1234015-58-7
Molecular Formula:	$C_{20}H_{27}N_7O_8S_2$
Molecular Weight:	557.60
Target:	Apoptosis; Checkpoint Kinase (Chk)
Pathway:	Apoptosis; Cell Cycle/DNA Damage
Solubility:	DMSO : 100 mg/mL (179.34 mM; Need ultrasonic); H2O : 50 mg/mL (89.67 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Prexasertib dimesylate (LY2606368 dimesylate) is a selective, ATP-competitive second-generation **checkpoint kinase 1 (CHK1)** inhibitor with a **K_i** of 0.9 nM and an **IC_{50}** of <1 nM. Prexasertib dimesylate inhibits CHK2 (IC_{50}=8 nM) and RSK1 (IC_{50}=9 nM). Prexasertib dimesylate causes double-stranded DNA breakage and replication catastrophe resulting in **apoptosis**. Prexasertib dimesylate shows potent anti-tumor activity[1][2]. **In Vitro:** Prexasertib dimesylate (LY2606368 dimesylate) inhibits MELK (IC_{50}=38 nM), SIK (IC_{50}=42 nM), BRSK2 (IC_{50}=48 nM), ARK5 (IC_{50}=64 nM). Prexasertib dimesylate requires CDC25A and CDK2 to cause DNA damage[1].

Prexasertib dimesylate (33, 100 nM; for 7 hours) results in DNA damage during S-phase in HeLa cells[1].

Prexasertib dimesylate (8-250 nM; pre-treated for 15 minutes) inhibits CHK1 autophosphorylation (S296) and CHK2 autophosphorylation (S516) in HT-29 cells[1].

Prexasertib dimesylate (4 nM; 24 hours) results in a large shift in cell-cycle populations from G1 and G2-M to S-phase with an accompanied induction of H2AX phosphorylation in U-2 OS cells[1].

Prexasertib dimesylate (33 nM; for 12 hours) causes chromosomal fragmentation in HeLa cells. Prexasertib dimesylate (100 nM; 0.5 to 9 hours) induces replication stress and depletes the pool of available RPA2 for binding to DNA[1].

In Vivo: Prexasertib dimesylate (LY2606368 dimesylate; 1-10 mg/kg; SC; twice daily for 3 days, rest 4 days; for three cycles) causes growth inhibition in tumor xenografts[1].

Prexasertib dimesylate (15 mg/kg; SC) causes CHK1 inhibition in the blood and the phosphorylation of both H2AX (S139) and RPA2 (S4/S8)[1].

References:

[1]. King C, et al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-1

[2]. 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.

CAIndexNames:

2-Pyrazinecarbonitrile, 5-[[5-[2-(3-aminopropoxy)-6-methoxyphenyl]-1H-pyrazol-3-yl]amino]-, methanesulfonate (1:2)

SMILES:

N#CC1=NC=C(NC2=NNC(C3=C(OC)C=CC=C3OCCCN)=C2)N=C1.CS(=O)(O)=O.CS(=O)(O)=O

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

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