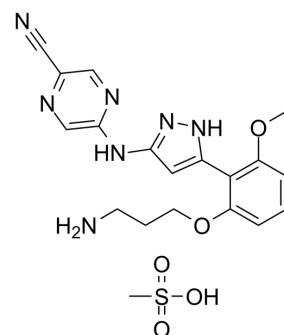


Prexasertib mesylate

Cat. No.:	HY-18174C
CAS No.:	1234015-55-4
Molecular Formula:	C ₁₉ H ₂₃ N ₇ O ₅ S
Molecular Weight:	461.49
Target:	Checkpoint Kinase (Chk); DNA/RNA Synthesis; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	<p>Prexasertib mesylate (LY2606368 mesylate) is a selective, ATP-competitive second-generation checkpoint kinase 1 (CHK1) inhibitor with a K_i of 0.9 nM and an IC₅₀ of <1 nM. Prexasertib mesylate inhibits CHK2 (IC₅₀=8 nM) and RSK1 (IC₅₀=9 nM). Prexasertib mesylate causes double-stranded DNA breakage and replication catastrophe resulting in apoptosis. Prexasertib mesylate shows potent anti-tumor activity^{[1][2]}.</p>														
IC₅₀ & Target	Chk1 0.9 nM (K _i)	Chk1 <1 nM (IC ₅₀)	Chk2 8 nM (IC ₅₀)												
In Vitro	<p>Prexasertib (LY2606368) mesylate inhibits MELK (IC₅₀=38 nM), SIK (IC₅₀=42 nM), BRSK2 (IC₅₀=48 nM), ARK5 (IC₅₀=64 nM). Prexasertib mesylate requires CDC25A and CDK2 to cause DNA damage^[1]. Prexasertib mesylate (33, 100 nM; for 7 hours) results in DNA damage during S-phase in HeLa cells^[1]. Prexasertib mesylate (8-250 nM; pre-treated for 15 minutes) inhibits CHK1 autophosphorylation (S296) and CHK2 autophosphorylation (S516) in HT-29 cells^[1]. Prexasertib mesylate (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 mesylate (33 nM; for 12 hours) causes chromosomal fragmentation in HeLa cells. Prexasertib mesylate (100 nM; 0.5 to 9 hours) induces replication stress and depletes the pool of available RPA2 for binding to DNA^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Cycle Analysis^[1]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>HeLa cells</td> </tr> <tr> <td>Concentration:</td> <td>33, 100 nM</td> </tr> <tr> <td>Incubation Time:</td> <td>7 hours</td> </tr> <tr> <td>Result:</td> <td>Had an IC₅₀ of 37 nM and resulted in the G2-M population received DNA damage during S-phase but continued to progress through the cell cycle into an early mitosis.</td> </tr> </table> <p>Western Blot Analysis^[1]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>HT-29 cells</td> </tr> <tr> <td>Concentration:</td> <td>8, 16, 31, 63, 125, 250 nM</td> </tr> </table>			Cell Line:	HeLa cells	Concentration:	33, 100 nM	Incubation Time:	7 hours	Result:	Had an IC ₅₀ of 37 nM and resulted in the G2-M population received DNA damage during S-phase but continued to progress through the cell cycle into an early mitosis.	Cell Line:	HT-29 cells	Concentration:	8, 16, 31, 63, 125, 250 nM
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Cell Line:	HT-29 cells														
Concentration:	8, 16, 31, 63, 125, 250 nM														

Incubation Time:	Pre-treated for 15 minutes
Result:	Inhibited CHK1 autophosphorylation (S296) and CHK2 autophosphorylation (S516) (IC50 of less than 31 nM) in HT-29 cells.

In Vivo

Prexasertib mesylate (1-10 mg/kg; SC; twice daily for 3 days, rest 4 days; for three cycles) causes growth inhibition in tumor xenografts^[1].
 Prexasertib mesylate (15 mg/kg; SC) causes CHK1 inhibition in the blood and the phosphorylation of both H2AX (S139) and RPA2 (S4/S8)^[1].
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female CD-1 nu-/nu- mice (26-28 g) with Calu-6 cells ^[1]
Dosage:	1, 3.3, or 10 mg/kg
Administration:	SC; twice daily for 3 days, rest 4 days; for three cycles
Result:	Caused statistically significant tumor growth inhibition (up to 72.3%).

CUSTOMER VALIDATION

- Nat Commun. 2019 Aug 2;10(1):3485.
- Thorax. 2021 Jul 5;thoraxjnl-2021-217377.
- Cell Biol Toxicol. 2021 Sep 14.
- Cancers (Basel). 2021 Aug 20;13(16):4200.
- Cancers. 2020 Aug 26;12(9):2426.

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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.

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

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