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Zuschläge

- Mindermengenzuschlag
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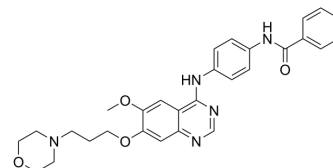
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ZM-447439

Cat. No.:	HY-10128
CAS No.:	331771-20-1
Molecular Formula:	C ₂₉ H ₃₁ N ₅ O ₄
Molecular Weight:	513.59
Target:	Aurora Kinase; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 25 mg/mL (48.68 mM; Need ultrasonic)				
	Preparing Stock Solutions	<div><div>Solvent</div><div>Concentration</div><div>Mass</div></div>	1 mg	5 mg	10 mg
		1 mM	1.9471 mL	9.7354 mL	19.4708 mL
		5 mM	0.3894 mL	1.9471 mL	3.8942 mL
		10 mM	0.1947 mL	0.9735 mL	1.9471 mL
Please refer to the solubility information to select the appropriate solvent.					
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	ZM-447439 is an aurora kinase inhibitor with IC ₅₀ s of 110 and 130 nM for aurora A and B, respectively.	
IC ₅₀ & Target	Aurora A 110 nM (IC ₅₀)	Aurora B 130 nM (IC ₅₀)
In Vitro	Cells treated with ZM-447439 progress through interphase, enter mitosis normally, and assemble bipolar spindles. However, chromosome alignment, segregation, and cytokinesis all fail. ZM-447439 inhibits cell division and inhibit mitotic phosphorylation of histone H3. ZM-447439 prevents chromosome alignment and segregation. ZM-447439 compromises spindle checkpoint function. ZM-447439 inhibits kinetochore localization of BubR1, Mad2, and Cenp-E ^[1] . Inhibition of Aurora kinase by ZM-447439 reduces histone H3 phosphorylation at Ser10 in Hep2 carcinoma cells. Multipolar spindles are	

induced in these ZM-treated G2/M-arrested cells with accumulation of 4N/8N DNA, similar to cells with genetically suppressed Aurora-B. ZM-447439 treatment induces cell apoptosis. ZM-447439 inhibition of Aurora kinase is potently in association with decrease of Akt phosphorylation at Ser473 and its substrates GSK3 α / β phosphorylation at Ser21 and Ser9^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

1 ng purified recombinant enzyme is added to a reaction cocktail containing buffer, 10 μ M peptide substrate, 10 μ M for Aurora A or 5 μ M ATP for Aurora B, and 0.2 μ Ci γ [³³P]ATP, and is then incubated at room temperature for 60 min. Reactions are stopped by addition of 20% phosphoric acid, and the products are captured on P30 nitrocellulose filters and assayed for incorporation of ³³P with a Betaplate counter. No enzyme and no compound control values are used to determine the concentration of ZM-447439, which gave 50% inhibition of enzyme activity^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay ^[1]

To determine cloning efficiency, MCF7 cells are plated in phenol red free DME plus 5% stripped serum, and are then treated with or without the anti-estrogen ICI 182780 at 1 μ M for 48 h. ZM-447439 is then added at the indicated concentrations for 72 h. The cells are harvested, washed, and ~400 cells plated in each well of a 6-well plate in complete media without ZM-447439. After 10 d, the colonies are fixed, stained with crystal violet, and counted. The cloning efficiency represents the number of colonies on ZM-447439-treated plates compared with DMSO-treated controls^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- EBioMedicine. 2021 Aug 5;70:103510.
- Elife. 2020 Dec 7;9:e61405.
- bioRxiv. 2021 Feb 5.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

- [1]. Ditchfield C, et al. Aurora B couples chromosome alignment with anaphase by targeting BubR1, Mad2, and Cenp-E to kinetochores. J Cell Biol. 2003 Apr 28;161(2):267-80.
- [2]. Long ZJ, et al. ZM 447439 inhibition of aurora kinase induces Hep2 cancer cell apoptosis in three-dimensional culture. Cell Cycle. 2008 May 15;7(10):1473-9.

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

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