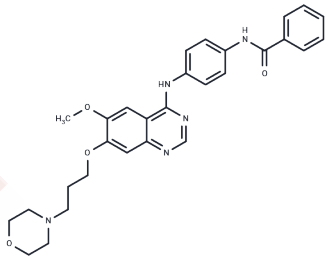
Data Sheet (Cat.No.T6077)

TargetMol

ZM-447439

Chemical Properties



CAS No. : 331771-20-1

Formula: C29H31N5O4

Molecular Weight: 513.59

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

Description	ZM 447439 is a selective and ATP-competitive inhibitor for Aurora A and Aurora B with IC50 of 110 nM and 130 nM, respectively. It is more than 8-fold selective for Aurora A/B than MEK1, Src, Lck and has little effect against CDK1/2/4, Plk1, Chk1, etc.
Targets(IC50)	Apoptosis,MEK,Aurora Kinase,Src
In vitro	In vitro, ZM-447439 selectively inhibits recombinant human Aurora A and B with IC50 values of 110 and 130 nM, respectively, while other protein kinases of diverse structural types including the mitotic kinases CDK1 and PLK1 are inhibited with IC50 values >10 μM. [1] Aurora kinase inhibitor, ZM-447439 time- and dose-dependently inhibits the growth of all three cell lines with IC50 values of 3 μM (BON), 0.9 μM (QGP-1) and 3 μM (MIP-101) after 72 hours of continuous exposure. In addition, ZM-447439 potently induces cell apoptosis by promoting DNA fragmentation and caspase 3 and 7 activation, and arrests GEP-NET cells in the G0 /G1and G2/M phase of the cell cycle. [2] In mouse embryo, inhibition of Aurora kinase activity by ZM-447439 results in abnormalities during mitosis by regulating the phosphorylation of histone H3 serine 10 (H3S10Ph) from G2 to metaphase with different perturbations in each embryonic cycle. [3] A recent study shows that ZM-447439 exhibits growth inhibitory and proapoptotic effect on cervical cancer SiHa cells, and enhances the chemosensitivity to cisplatin. [4]
Kinase Assay	In vitro kinase assays : Recombinant Aurora A and B are expressed as NH2-terminal His6-tagged fusion proteins using a baculovirus expression system. Aurora A is purified by affinity chromatography using Ni-NTA agarose, and Aurora B is purified by ion exchange chromatography using CM Sepharose Fast Flow. 1 ng purified recombinant enzyme is added to a reaction cocktail containing 25 mM Tris-HCl, pH 7.5, 12.5 mM KCl, 2.5 mM NaF, 0.6 mM DTT, 6.25 mM MnCl2, 10 μM peptide substrate, 10 μM for Aurora A or 5 μM ATP for Aurora B, and 0.2 μCi γ-[33P]ATP (specific activity ≥2,500 Ci/mmol), and is then incubated at RT for 60 minutes. 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 BetaplateTM counter. No enzyme and no compound control values are used to determine the concentration of ZM447439, which gave 50% inhibition of enzyme activity. Further details are available on request from Nicholas Keen.
Cell Research	Cell number is evaluated by crystal violet staining. In brief, cells in 96-well plates are fixed with 1% glutaraldehyde. Then cells are stained with 0.1% crystal violet. The unbound dye is removed by washing with water. Bound crystal violet is solubilized with

Cell Research	0.2% Triton X-100. Light extinction which increases linearly with the cell number is analyzed at 570 nm using an ELISA reader.(Only for Reference)

Solubility Information

Solubility	DMSO: 16.7 mg/mL (32.52 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: 1.67 mg/mL (3.25 mM),Suspension. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (1.95 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0389 mL	0.1947 mL	0.3894 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

Ditchfield C, et al. J Cell Biol. 2003, 161(2), 267-280.
Georgieva I, et al. Neuroendocrinology. 2010, 91(2), 121-130.
Teperek-Tkacz M, et al. Cell Cycle. 2010, 9(23), 4674-4687.
Zhang L, et al. J Obstet Gynaecol Res. 2011, 37(6), 591-600.