Alisertib

Cat. No.: HY-10971

CAS No.: 1028486-01-2

Molecular Formula: $C_{27}H_{20}ClFN_4O_4$

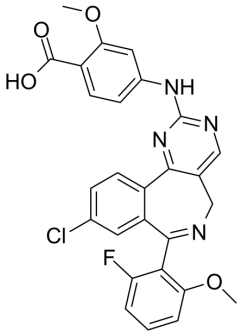
Molecular Weight: 518.92

Target: Aurora Kinase; Autophagy; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (48.18 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9271 mL	9.6354 mL	19.2708 mL
	5 mM	0.3854 mL	1.9271 mL	3.8542 mL
	10 mM	0.1927 mL	0.9635 mL	1.9271 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: 2.08 mg/mL (4.01 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.01 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Alisertib (MLN 8237) is an orally active and selective Aurora A kinase inhibitor (IC_{50}=1.2 nM), which binds to Aurora A kinase resulting in mitotic spindle abnormalities, mitotic accumulation. Alisertib (MLN 8237) induces apoptosis and autophagy through targeting the AKT/mTOR/AMPK/p38 pathway in leukemic cells. Antitumor activity[1][2][3].

IC_{50} & Target

Aurora A	Aurora B
1.2 nM (IC_{50})	396.5 nM (IC_{50})

In Vitro	Alisertib (MLN 8237) leads the MM cells to mitotic spindle abnormalities, mitotic accumulation, as well as inhibition of cell proliferation through apoptosis and senescence. Alisertib up-regulates p53 and tumor suppressor genes p21 and p27[1]. The decreased activity of Alisertib (MLN 8237) for the T217D/W277E Aurora A/TPX2 complex may reflect the increased affinity for ATP induced by cofactor binding to Aurora A[2]. Alisertib (MLN 8237) inhibits cell proliferation with IC_{50}s ranging from 15 to 469 nM in different tumer cell lines[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Alisertib (MLN 8237) (30 mg/kg, p.o.) significantly reduces tumor burden and increases overall survival in xenograft-murine model of human-MM[1]. Alisertib (3-30 mg/kg; p.o.; once daily for 3 weeks) causes tumor growth inhibition in solid tumor xenograft models[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nude mice bearing HCT-116 colon tumor xenograft[4]
Dosage:	3, 10, or 30 mg/kg
Administration:	P.o.; once daily for 3 weeks
Result:	Resulted in a dose-dependent TGI (tumor growth inhibition) of 43.3%, 84.2%, and 94.7% for the 3, 10, and 30 mg/kg groups,respectively.

CUSTOMER VALIDATION

- Cell. 2017 Jan 12;168(1-2):264-279.e15.
- J Hepatol. 2021 Aug;75(2):363-376.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2019 Jul 1;25(13):4179-4193.
- Theranostics. 2018 Feb 12;8(6):1740-1751.

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REFERENCES

[1]. Güllü G, et al. A novel Aurora-A kinase inhibitor MLN8237 induces cytotoxicity and cell-cycle arrest in multiple myeloma Blood June 24, 2010 vol. 115 no. 25 5202-5213.

[2]. Sloane DA, et al. Drug-Resistant Aurora A Mutants for Cellular Target Validation of the Small Molecule Kinase Inhibitors MLN8054 and MLN8237 ACS Chem. Biol., 2010, 5 (6), pp 563-576.

[3]. Bavetsias V, et al. Aurora Kinase Inhibitors: Current Status and Outlook. Front Oncol. 2015 Dec 21;5:278.

[4]. Manfredi MG, et al. Characterization of Alisertib (MLN8237), an investigational small-molecule inhibitor of aurora A kinase using novel in vivo pharmacodynamic assays.Clin Cancer Res. 2011 Dec 15;17(24):7614-7624.

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

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