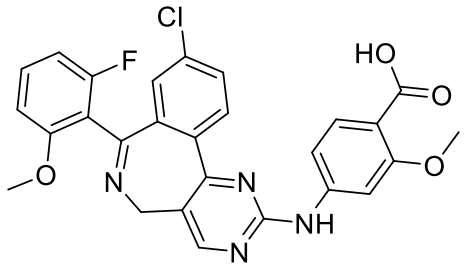
Product data sheet

MedKoo Cat#: 201931 Name: Alisertib CAS#: 1028486-01-2 Chemical Formula: $C_{27}H_{20}ClFN_4O_4$ Exact Mass: 518.11571 Molecular Weight: 518.9	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Alisertib, also known as MLN8237, is a second-generation, orally bioavailable, highly selective small molecule inhibitor of the serine/threonine protein kinase Aurora A kinase with potential antineoplastic activity. Aurora kinase inhibitor MLN8237 binds to and inhibits Aurora A kinase, which may result in disruption of the assembly of the mitotic spindle apparatus, disruption of chromosome segregation, and inhibition of cell proliferation.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	25	48.18

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.93 mL	9.64 mL	19.27 mL
5 mM	0.39 mL	1.93 mL	3.85 mL
10 mM	0.19 mL	0.96 mL	1.93 mL
50 mM	0.04 mL	0.19 mL	0.39 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Görgün G, Calabrese E, Hideshima T, Ecsedy J, Perrone G, Mani M, Ikeda H, Bianchi G, Hu Y, Cirstea D, Santo L, Tai YT, Nahar S, Zheng M, Bandi M, Carrasco RD, Raje N, Munshi N, Richardson P, Anderson KC. A novel Aurora-A kinase inhibitor MLN8237 induces cytotoxicity and cell-cycle arrest in multiple myeloma. Blood. 2010 Jun 24;115(25):5202-13. doi: 10.1182/blood-2009-12-259523. Epub 2010 Apr 9. PMID: 20382844; PMCID: PMC2892955.

2. Manfredi MG, Ecsedy JA, Chakravarty A, Silverman L, Zhang M, Hoar KM, Stroud SG, Chen W, Shinde V, Huck JJ, Wysong DR, Janowick DA, Hyer ML, Leroy PJ, Gershman RE, Silva MD, Germanos MS, Bolen JB, Claiborne CF, Sells TB. 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):7614-24. doi: 10.1158/1078-0432.CCR-11-1536. Epub 2011 Oct 20. PMID: 22016509.

In vivo study

1. Görgün G, Calabrese E, Hideshima T, Ecsedy J, Perrone G, Mani M, Ikeda H, Bianchi G, Hu Y, Cirstea D, Santo L, Tai YT, Nahar S, Zheng M, Bandi M, Carrasco RD, Raje N, Munshi N, Richardson P, Anderson KC. A novel Aurora-A kinase inhibitor MLN8237 induces cytotoxicity and cell-cycle arrest in multiple myeloma. Blood. 2010 Jun 24;115(25):5202-13. doi: 10.1182/blood-2009-12-259523. Epub 2010 Apr 9. PMID: 20382844; PMCID: PMC2892955.

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2. Manfredi MG, Ecsedy JA, Chakravarty A, Silverman L, Zhang M, Hoar KM, Stroud SG, Chen W, Shinde V, Huck JJ, Wysong DR, Janowick DA, Hyer ML, Leroy PJ, Gershman RE, Silva MD, Germanos MS, Bolen JB, Claiborne CF, Sells TB. 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):7614-24. doi: 10.1158/1078-0432.CCR-11-1536. Epub 2011 Oct 20. PMID: 22016509.

7. Bioactivity

Biological target:

Alisertib (MLN8237) is a selective Aurora A inhibitor with IC50 of 1.2 nM in a cell-free assay.

In vitro activity

To determine the inhibitory effect of MLN8237 on the mitotic cell population, cell division in MM cell lines was first synchronized by treatment with nocodazole, and then phosphorylation of Aurora-A kinase at threonine 288 (pThr288) was measured by Western blotting. Decreased phosphorylation of Aurora-A kinase was shown in MLN8237-treated MM1.S and OPM1 MM cells (Figure 1B), compared with the DMSO and nocodazole-treated cells. To further analyze inhibition of Aurora-A kinase phosphorylation by MLN8237 in unsynchronized MM cell lines, immunofluorescein staining was performed in MM1.S and OPM1 cells. Costaining with α-tubulin, pAurora-A kinase (Thr288), and 4,6-diamidino-2-phenylindole (nucleus) showed that DMSO-treated MM1.S (Figure 1C) and OPM1 (Figure 1D) cells were proliferating with phosphorylated Aurora-A kinase (Thr288), whereas all MLN8237-treated cells accumulated at the nondividing prometaphase and metaphase stages, with no detectable phosphorylation of Aurora-A kinase. In addition, analysis of DMSO-treated cells by fluorescein microscopy demonstrated ongoing mitosis, within the 15% MM1.S cells and 28.5% OPM-1 cells mitotic cell population expressing pAurora-A kinase (Thr288). Importantly, after 24 hours of MLN8237 treatment, there was an accumulation of prometaphase and metaphase cells, with no detectable expression of pAurora-A kinase (Thr288), in both MM cell lines. In addition, Figure 1E shows that MLN8237 does not inhibit histone H3 phosphorylation at ser10 in these cells, indicating mitosis and active Aurora-B kinase in the MLN8237-treated cells.

Reference: Blood. 2010 Jun 24;115(25):5202-13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2892955/

In vivo activity

To determine the in vivo antitumor activity of alisertib, mice bearing solid and hematologic human tumor xenografts were administered increasing doses of alisertib. Figure 3A shows average tumor volumes in nude mice bearing subcutaneous HCT-116 tumors after 3 weeks of oral alisertib at 3, 10, or 30 mg/kg once daily. Alisertib treatment resulted in a dose-dependent TGI of 43.3%, 84.2%, and 94.7% for the 3, 10, and 30 mg/kg groups, respectively. The greatest antitumor response in this model was tumor stasis. All doses were well tolerated with the maximum body weight loss of 7.4% in the 30 mg/kg group. As shown in Figure 3B, alisertib treatment in the non-Hodgkin's lymphoma model OCI-LY19 also resulted in tumor regression. Rituximab was used as a control for this model and resulted in moderate antitumor activity when dosed at 10 mg/kg once per week. Alisertib dosed at either 20 mg/kg twice daily or 30 mg/kg once daily resulted in a reduction in luminescent signal below baseline and a TGI of 106% for both groups. Moreover, tumors in the 20 mg/kg dose group did not grow back after more than 60 days of monitoring. Finally, alisertib showed broad antitumor activity across a diverse set of xenograft models, with TGI of greater than 76% at 30 mg/kg in all models tested (Table 3).

Reference: Clin Cancer Res. 2011 Dec 15;17(24):7614-24.
http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22016509

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.