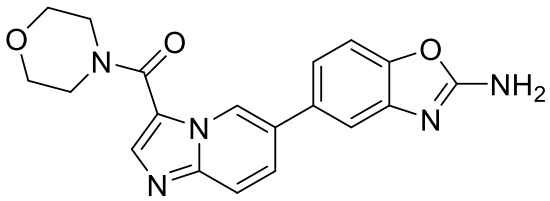
Product data sheet

MedKoo Cat#: 205743 Name: MLN-1117 CAS#: 1268454-23-4 Chemical Formula: $C_{19}H_{17}N_5O_3$ Exact Mass: 363.1331 Molecular Weight: 363.377	
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:

Serabelisib (also known as MLN1117, INK1117, and TAK-117) is an orally bioavailable inhibitor of the class I phosphoinositide 3-kinase (PI3K) alpha isoform with potential antineoplastic activity. PI3K alpha inhibitor INK1117 selectively inhibits PI3K alpha kinase, including mutations of PIK3CA, in the PI3K/Akt/mTOR pathway, which may result in tumor cell apoptosis and growth inhibition in PI3K alpha-expressing tumor cells. By specifically targeting class I PI3K alpha, this agent may be more efficacious and less toxic than pan-PI3K inhibitors.

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	4.0	11.01

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.75 mL	13.76 mL	27.52 mL
5 mM	0.55 mL	2.75 mL	5.50 mL
10 mM	0.28 mL	1.38 mL	2.75 mL
50 mM	0.06 mL	0.28 mL	0.55 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. So L, Yea SS, Oak JS, Lu M, Manmadhan A, Ke QH, Janes MR, Kessler LV, Kucharski JM, Li LS, Martin MB, Ren P, Jessen KA, Liu Y, Rommel C, Fruman DA. Selective inhibition of phosphoinositide 3-kinase p110α preserves lymphocyte function. J Biol Chem. 2013 Feb 22;288(8):5718-31. doi: 10.1074/jbc.M112.379446. Epub 2012 Dec 28. PMID: 23275335; PMCID: PMC3581375.
2. Yea SS, So L, Mallya S, Lee J, Rajasekaran K, Malarkannan S, Fruman DA. Effects of novel isoform-selective phosphoinositide 3-kinase inhibitors on natural killer cell function. PLoS One. 2014 Jun 10;9(6):e99486. doi: 10.1371/journal.pone.0099486. PMID: 24915189; PMCID: PMC4051752.

In vivo study

1. So L, Yea SS, Oak JS, Lu M, Manmadhan A, Ke QH, Janes MR, Kessler LV, Kucharski JM, Li LS, Martin MB, Ren P, Jessen KA, Liu Y, Rommel C, Fruman DA. Selective inhibition of phosphoinositide 3-kinase p110α preserves lymphocyte function. J Biol Chem. 2013 Feb 22;288(8):5718-31. doi: 10.1074/jbc.M112.379446. Epub 2012 Dec 28. PMID: 23275335; PMCID: PMC3581375.
2. Yea SS, So L, Mallya S, Lee J, Rajasekaran K, Malarkannan S, Fruman DA. Effects of novel isoform-selective phosphoinositide 3-kinase inhibitors on natural killer cell function. PLoS One. 2014 Jun 10;9(6):e99486. doi: 10.1371/journal.pone.0099486. PMID: 24915189; PMCID: PMC4051752.

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7. Bioactivity

Biological target:

Serabelisib (MLN1117) is a selective p110α inhibitor with an IC50 of 15 nM.

In vitro activity

The effects of inhibitors on the proliferation of purified, CFSE-labeled B cells were compared. Statistical analysis of normalized data showed that the effects of GDC-0941 and IC87114 were highly significant, yet there was no significant effect of 1 μm A66, MLN1117, or TGX-221. At a higher concentration (2 μm), A66 or MLN1117 did significantly suppress B cell proliferation driven by anti-IgM alone but not by anti-IgM plus IL-4 (Fig. 4, A and B). Notably, CFSE histograms for three independent experiments did show a consistent, dose-dependent reduction in the extent of B cell division by each of the isoform-selective PI3K inhibitors (data not shown). Similar results were obtained using human peripheral blood B cells stimulated with anti-human IgD and IL-4 (Fig. 4C). Next the effects of PI3K inhibitors were tested on survival of purified B cells cultured in the presence of the cytokines BAFF or IL-4. At higher concentrations (1 μm) both A66 and MLN1117 caused only a minor decrease in survival.

Reference: J Biol Chem. 2013 Feb 22; 288(8): 5718–5731. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3581375/

In vivo activity

To compare the effects of PI3K inhibitors on B cell and T cell-mediated immune responses in vivo, antibody production was measured in mice vaccinated with hapten-carrier conjugates. To model T cell-independent antibody responses driven by BCR cross-linking, TNP-Ficoll was used as the immunogen. GDC-0941 treatment abrogated TNP-specific IgG3 production (Fig. 9A). This indicates that the T cell-independent IgG3 response is completely PI3K dependent. Treatment with MLN1117 at 30 and 60 mg/kg caused little reduction of TNP-specific IgG3 (Fig. 9A). Notably, reduction of TNP-specific IgG3 was observed at higher doses of MLN1117 (120 mg/kg), consistent with the partial reduction in cell division in B cells treated with MLN1117 before anti-IgM stimulation in vitro. However, 120 mg/kg is above the effective dose of MLN1117 for tumor growth inhibition (30–60 mg/kg).

Reference: J Biol Chem. 2013 Feb 22; 288(8): 5718–5731. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3581375/

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.