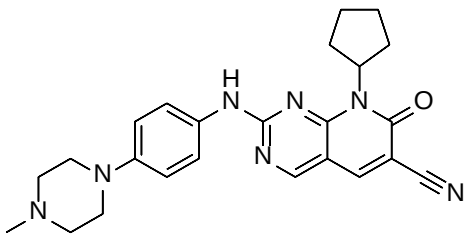
Product data sheet

MedKoo Cat#: 206460 Name: ON-123300 CAS: 1357470-29-1 Chemical Formula: $C_{24}H_{27}N_7O$ Exact Mass: 429.2277 Molecular Weight: 429.528	
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:
ON123300 is a potent multikinase inhibitor and may be potential useful for brain tumor chemotherapy. ON123300 strongly inhibits Ark5 and CDK4, as well as growth factor receptor tyrosine kinases such as β-type platelet-derived growth factor receptor (PDGFRβ). ON123300 inhibits U87 glioma cell proliferation with an IC(50) 3.4 ± 0.1 μmol/L. ON123300 exhibits potent activity against mantle cell lymphomas (MCLs) both in vitro and in vivo. ON123300 might be an effective agent in MCL, including ibrutinib-resistant forms of the disease.

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
DMF	16.0	37.25
DMF:PBS (pH 7.2) (1:2)	0.3	0.70
DMSO	18.56	43.20
Ethanol	0.25	0.58

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.33 mL	11.64 mL	23.28 mL
5 mM	0.47 mL	2.33 mL	4.66 mL
10 mM	0.23 mL	1.16 mL	2.33 mL
50 mM	0.05 mL	0.23 mL	0.47 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. Perumal D, Kuo PY, Leshchenko VV, Jiang Z, Divakar SK, Cho HJ, Chari A, Brody J, Reddy MV, Zhang W, Reddy EP, Jagannath S, Parekh S. Dual Targeting of CDK4 and ARK5 Using a Novel Kinase Inhibitor ON123300 Exerts Potent Anticancer Activity against Multiple Myeloma. Cancer Res. 2016 Mar 1;76(5):1225-36. doi: 10.1158/0008-5472.CAN-15-2934. Epub 2016 Feb 12. PMID: 26873845; PMCID: PMC5968814.
2. Zhang X, Lv H, Zhou Q, Elkholi R, Chipuk JE, Reddy MV, Reddy EP, Gallo JM. Preclinical pharmacological evaluation of a novel multiple kinase inhibitor, ON123300, in brain tumor models. Mol Cancer Ther. 2014 May;13(5):1105-16. doi: 10.1158/1535-7163.MCT-13-0847. Epub 2014 Feb 25. PMID: 24568969; PMCID: PMC4013241.

In vivo study

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1. Divakar SK, Ramana Reddy MV, Cosenza SC, Baker SJ, Perumal D, Antonelli AC, Brody J, Akula B, Parekh S, Reddy EP. Dual inhibition of CDK4/Rb and PI3K/AKT/mTOR pathways by ON123300 induces synthetic lethality in mantle cell lymphomas. Leukemia. 2016 Jan;30(1):86-93. doi: 10.1038/leu.2015.185. Epub 2015 Jul 15. PMID: 26174628; PMCID: PMC4703501.
2. Zhang X, Lv H, Zhou Q, Elkholi R, Chipuk JE, Reddy MV, Reddy EP, Gallo JM. Preclinical pharmacological evaluation of a novel multiple kinase inhibitor, ON123300, in brain tumor models. Mol Cancer Ther. 2014 May;13(5):1105-16. doi: 10.1158/1535-7163.MCT-13-0847. Epub 2014 Feb 25. PMID: 24568969; PMCID: PMC4013241.

7. Bioactivity

Biological target:

Narazaciclib (ON123300), a strong and brain-penetrant multi-kinase inhibitor, inhibits CDK4 (IC_{50}=3.9 nM), Ark5 (IC_{50}=5 nM), PDGFRβ (IC_{50}=26 nM), FGFR1 (IC_{50}=26 nM), RET (IC_{50}=9.2 nM), and FYN (IC_{50}=11 nM).

In vitro activity

Treatment of multiple myeloma cell lines and primary samples with ON123300 in vitro resulted in rapid induction of cell-cycle arrest followed by apoptosis. ON123300-mediated ARK5 inhibition or ARK5-specific siRNAs resulted in the inhibition of the mTOR/S6K pathway and upregulation of the AMPK kinase cascade. AMPK upregulation resulted in increased SIRT1 levels and destabilization of steady-state MYC protein.

Reference: Cancer Res. 2016 Mar 1;76(5):1225-36. https://pubmed.ncbi.nlm.nih.gov/26873845/

In vivo activity

As seen here and in figure 6A, treatment with ON123300 significantly inhibited ($p<0.05$) tumor growth over a 2-week period, suggesting that this compound is a potent inhibitor of MCL proliferation in vivo. In addition, daily treatment with ON123300 did not cause a significant reduction in the total body weights of ON123300-treated mice (Fig 6C). (The increase in the body weights of the untreated animals is likely attributable to the rapid growth of tumors).

Reference: Leukemia. 2016 Jan;30(1):86-93. https://pubmed.ncbi.nlm.nih.gov/26174628/

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.