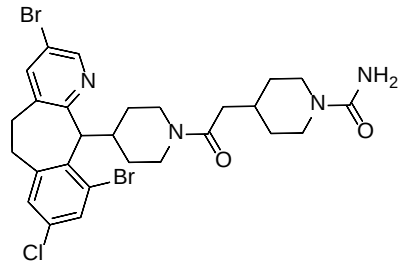
Product data sheet

MedKoo Cat#: 201760 Name: Lonafarnib CAS#: 193275-84-2 Chemical Formula: $C_{27}H_{31}Br_2ClN_4O_2$ Exact Mass: 636.0502 Molecular Weight: 638.82	
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:
Lonafarnib is a farnesyl transferase inhibitor. Structurely, it is also a synthetic tricyclic derivative of carboxamide with antineoplastic properties. Lonarfanib binds to and inhibits farnesyl transferase, an enzyme involved in the post-translational modification and activation of Ras proteins. Ras proteins participate in numerous signalling pathways (proliferation, cytoskeletal organization), and play an important role in oncogenesis. Mutated ras proteins have been found in a wide range of human cancers.

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	46.60	72.95
DMF	14.0	21.91
Ethanol	70.50	110.36
Ethanol:PBS (pH 7.2) (1:4)	0.20	0.31

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.57 mL	7.83 mL	15.65 mL
5 mM	0.31 mL	1.57 mL	3.13 mL
10 mM	0.16 mL	0.78 mL	1.57 mL
50 mM	0.03 mL	0.16 mL	0.31 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. Sun L, Xie S, Peng G, Wang J, Li Y, Qin J, Zhong D. Lonafarnib is a potential inhibitor for neovascularization. PLoS One. 2015 Apr 8;10(4):e0122830. doi: 10.1371/journal.pone.0122830. PMID: 25853815; PMCID: PMC4390146.

In vivo study

1. Hernandez I, Luna G, Rauch JN, Reis SA, Giroux M, Karch CM, Boctor D, Sibih YE, Storm NJ, Diaz A, Kaushik S, Zekanowski C, Kang AA, Hinman CR, Cerovac V, Guzman E, Zhou H, Haggarty SJ, Goate AM, Fisher SK, Cuervo AM, Kosik KS. A farnesyltransferase inhibitor activates lysosomes and reduces tau pathology in mice with tauopathy. Sci Transl Med. 2019 Mar 27;11(485):eaat3005. doi: 10.1126/scitranslmed.aat3005. PMID: 30918111; PMCID: PMC7961212.

7. Bioactivity
Biological target: Lonafarnib inhibits the activities of H-ras, K-ras and N-ras with IC50 values of 1.9 nM, 5.2 nM and 2.8 nM, respectively.

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In vitro activity

Lonafarnib, a specific inhibitor of farnesyl transferase, elicits inhibitory effect on vascular endothelial capillary assembly in vitro in a dose-dependent manner. Lonafarnib treatment led to a dose-dependent decrease in scratch wound closure in vitro, whereas it had little effect on endothelial cell proliferation. These data indicate that lonafarnib inhibits neovascularization via directly targeting endothelial cells and disturbing their motility. Moreover, pharmacological inhibition of farnesyl transferase by lonafarnib significantly impaired centrosome reorientation toward the leading edge of endothelial cells. Mechanistically, the catalytic β subunit of farnesyl transferase associated with a cytoskeletal protein important for the establishment and maintenance of cell polarity. Additionally, lonafarnib remarkably inhibited the expression of the cytoskeletal protein and interrupted its interaction with farnesyl transferase.

Reference: PLoS One. 2015 Apr 8;10(4):e0122830. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4390146/

In vivo activity

Tau inclusions are a shared feature of many neurodegenerative conditions and tau mutations lead to frontotemporal dementia. Approaches to treatment of these conditions have focused directly on the tau protein by targeting its post-translational modifications, its levels and its tendency to aggregate. A novel regulatory pathway for tau degradation was discovered that operates through the Rhes protein, a GTPase. Rhes is farnesylated and treatment with the farnesyl transferase inhibitor, lonafarnib, reduced Rhes, attenuated behavioral abnormalities, significantly reduced atrophy, tau inclusions, sumoylation and ubiquitination, as well as microgliosis in the rTg4510 tauopathy mouse. Direct reduction of Rhes levels reproduced the results observed with lonafarnib. The mechanism of lonafarnib action, as mediated by Rhes to reduce tau pathology, operates through its lysosomal degradation.

Reference: Sci Transl Med. 2019 Mar 27;11(485):eaat3005. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7961212/