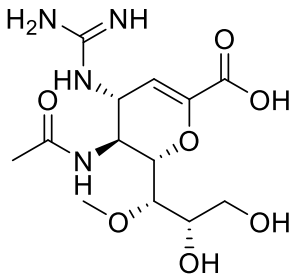
Product data sheet

MedKoo Cat#: 598292 Name: Laninamivir free base CAS#: 203120-17-6 (free base) Chemical Formula: $C_{13}H_{22}N_4O_7$ Exact Mass: 346.1488 Molecular Weight: 346.34	
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:
Laninamivir, also known as CS-8958, is a neuraminidase inhibitor that is a drug used for the treatment and prophylaxis of Influenzavirus A and Influenzavirus B. It is a long-acting neuraminidase inhibitor administered by nasal inhalation. Laninamivir was approved for influenza treatment in Japan in 2010 and for prophylaxis in 2013

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
H2O	5.0	14.44

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.89 mL	14.44 mL	28.87 mL
5 mM	0.58 mL	2.89 mL	5.77 mL
10 mM	0.29 mL	1.44 mL	2.89 mL
50 mM	0.06 mL	0.29 mL	0.58 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. Jeong JH, Choi WS, Antigua KJC, Choi YK, Govorkova EA, Webby RJ, Baek YH, Song MS. In Vitro Profiling of Laninamivir-Resistant Substitutions in N3 to N9 Avian Influenza Virus Neuraminidase Subtypes and Their Association with In Vivo Susceptibility. J Virol. 2020 Dec 9;95(1):e01679-20. doi: 10.1128/JVI.01679-20. Erratum in: J Virol. 2021 Feb 24;95(6): PMID: 33055248; PMCID: PMC7737746.
2. Ann J, Abed Y, Beaulieu E, Bouhy X, Joly MH, Dubé K, Carbonneau J, Hamelin ME, Mallett C, Boivin G. Impact of a large deletion in the neuraminidase protein identified in a laninamivir-selected influenza A/Brisbane/10/2007 (H3N2) variant on viral fitness in vitro and in ferrets. Influenza Other Respir Viruses. 2016 Mar;10(2):122-6. doi: 10.1111/irv.12356. Epub 2016 Jan 29. PMID: 26526406; PMCID: PMC4746560.

In vivo study

1. Koyama K, Takahashi M, Oitate M, Nakai N, Takakusa H, Miura S, Okazaki O. CS-8958, a prodrug of the novel neuraminidase inhibitor R-125489, demonstrates a favorable long-retention profile in the mouse respiratory tract. Antimicrob Agents Chemother. 2009 Nov;53(11):4845-51. doi: 10.1128/AAC.00731-09. Epub 2009 Aug 17. PMID: 19687241; PMCID: PMC2772300.
2. Kubo S, Tomozawa T, Kakuta M, Tokumitsu A, Yamashita M. Laninamivir prodrug CS-8958, a long-acting neuraminidase inhibitor, shows superior anti-influenza virus activity after a single administration. Antimicrob Agents Chemother. 2010 Mar;54(3):1256-64. doi: 10.1128/AAC.01311-09. Epub 2010 Jan 4. PMID: 20047917; PMCID: PMC2825999.

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7. Bioactivity

Biological target:

Laninamivir (R 125489) is a potent influenza neuraminidase (NA) inhibitor with IC50s of 0.90 nM, 1.83 nM and 3.12 nM for avian H12N5 NA (N5), pH1N1 N1 NA (p09N1) and A/RI/5+/1957 H2N2 N2 (p57N2), respectively.

In vitro activity

In this study, the viral fitness of an NAI-resistant influenza A/Brisbane/10/2007-like (H3N2) strain containing a large NA deletion and a P194L HA substitution that emerged under in vitro laninamivir pressure was evaluated. This variant corresponds to the 9th passage in which the growth medium contained 2 μM of laninamivir.9 In addition to the P194L mutation, the HA protein of this variant contained an S138A substitution, which is unlikely to be linked to the NAI pressure as it was also detected in the virus that was subjected to 9 passages without drug.9 When blast analyses using GenBank database sequences were performed, the 194L HA genotype was detected in numerous American, Asian, and Australian A(H3N2) viruses that have circulated since 2007 whereas no large NA deletion equivalent to that of LRVp9 could be detected. Residue 194 of influenza A(H3N2) HA is located at the globular head of the molecule and is part of the RBS. Therefore, changes at this position could naturally occur during influenza evolution contrasting to the internal region of NA protein which contains the highly conserved active site whose deletion seems to be strictly linked to the NAI pressure.

Reference: Influenza Other Respir Viruses. 2016 Mar; 10(2): 122–126. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4746560/

In vivo activity

In this study, the tissue distribution profiles after a single intranasal administration of CS-8958 (0.5 μmol/kg of body weight) to mice were investigated, focusing especially on the retention of CS-8958 in the respiratory tract by comparing it with R-125489 and a marketed drug, zanamivir. After administration of [14C]CS-8958, radioactivity was retained in the respiratory tract over long periods. At 24 h postdose, the radioactivity concentrations after administration of [14C]CS-8958 were approximately 10-fold higher in both the trachea and the lung than those of [14C]R-125489 and [14C]zanamivir. The [14C]CS-8958-derived radioactivity present in these two tissues consisted both of unchanged CS-8958 and of R-125489 at 1 h postdose, while only R-125489, and no other metabolites, was detected at 24 h postdose. After administration of unlabeled CS-8958, CS-8958 was rapidly eliminated from the lungs, whereas the lung R-125489 concentration reached a maximum at 3 h postdose and gradually declined, with an elimination half-life of 41.4 h. The conversion of CS-8958 to R-125489 was observed in mouse trachea and lung S9 fractions and was inhibited by esterase inhibitors, such as diisopropylfluorophosphate and bis-p-nitrophenylphosphate. These results demonstrated that CS-8958 administered intranasally to mice was efficiently converted to R-125489 by a hydrolase(s) such as carboxylesterase, and then R-125489 was slowly eliminated from the respiratory tract. These data support the finding that CS-8958 has potential as a long-acting neuraminidase inhibitor, leading to significant efficacy as an anti-influenza drug by a single treatment.

Reference: Antimicrob Agents Chemother. 2009 Nov; 53(11): 4845–4851. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2772300/