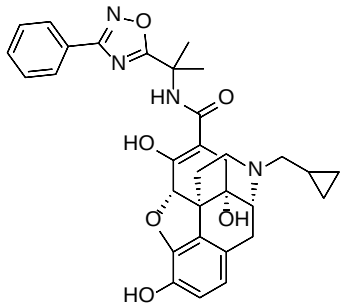
Product data sheet

MedKoo Cat#: 326729 Name: Naldemedine CAS: 916072-89-4 (free base) Chemical Formula: $C_{32}H_{34}N_4O_6$ Exact Mass: 570.2478 Molecular Weight: 570.646	
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:

Naldemedine, also known as S 297995, is a peripherally-selective μ-opioid receptor antagonist under development by Shionogi for the treatment of opioid-induced adverse effects including constipation, nausea, and vomiting. Clinical studies have thus far found it to possess statistically significant effectiveness for these indications and to be generally well-tolerated with predominantly mild to moderate gastrointestinal side effects. No effects indicative of central opioid withdrawal or impact on the analgesic or mydriatic effects of co-administered opioids have been observed.

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
TBD	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.75 mL	8.76 mL	17.52 mL
5 mM	0.35 mL	1.75 mL	3.50 mL
10 mM	0.18 mL	0.88 mL	1.75 mL
50 mM	0.04 mL	0.18 mL	0.35 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. Gondoh E, Hamada Y, Mori T, Iwazawa Y, Shinohara A, Narita M, Sato D, Tezuka H, Yamauchi T, Tsujimura M, Yoshida S, Tanaka K, Yamashita K, Akatori H, Higashiyama K, Arakawa K, Suda Y, Miyano K, Iseki M, Inada E, Kuzumaki N, Narita M. Possible mechanism for improving the endogenous immune system through the blockade of peripheral μ-opioid receptors by treatment with naldemedine. Br J Cancer. 2022 Nov;127(8):1565-1574. doi: 10.1038/s41416-022-01928-x. Epub 2022 Aug 9. PMID: 35945243; PMCID: PMC9553910.

2. Kanemasa T, Koike K, Arai T, Ono H, Horita N, Chiba H, Nakamura A, Morioka Y, Kihara T, Hasegawa M. Pharmacologic effects of naldemedine, a peripherally acting μ-opioid receptor antagonist, in in vitro and in vivo models of opioid-induced constipation. Neurogastroenterol Motil. 2019 May;31(5):e13563. doi: 10.1111/nmo.13563. Epub 2019 Feb 28. PMID: 30821019; PMCID: PMC6850587.

In vivo study

1. Yasufuku K, Koike K, Kobayashi M, Chiba H, Kitaura M, Takenouchi S, Hasegawa M, Morioka Y, Mishima H, Suzuki T, Fujita M. Involvement of the Peripheral μ-Opioid Receptor in Tramadol-Induced Constipation in Rodents. Biol Pharm Bull. 2021;44(11):1746-1751. doi: 10.1248/bpb.b21-00474. PMID: 34719650.

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2. Kanemasa T, Matsuzaki T, Koike K, Hasegawa M, Suzuki T. Preventive effects of naldemedine, peripherally acting μ-opioid receptor antagonist, on morphine-induced nausea and vomiting in ferrets. Life Sci. 2020 Sep 15;257:118048. doi: 10.1016/j.lfs.2020.118048. Epub 2020 Jul 2. PMID: 32622946.

7. Bioactivity

Biological target:

Naldemedine (S-297995) is an orally active μ-opioid receptor antagonist (PAMORA).

In vitro activity

The binding affinity and antagonist activity of naldemedine against recombinant human μ-, δ-, and κ-opioid receptors were assayed in vitro. Naldemedine showed potent binding affinity and antagonist activities for recombinant human μ-, δ-, and κ-opioid receptors.

Reference: Br J Cancer. 2022 Nov;127(8):1565-1574. https://pubmed.ncbi.nlm.nih.gov/30821019/

In vivo activity

Therefore, this study used naldemedine, a peripherally acting MOR (μ-opioid receptor) antagonist, and MOR-knockout mice to investigate the involvement of peripheral MOR in tramadol-induced constipation using a small intestinal transit model. A single dose of tramadol (3-100 mg/kg, per os (p.o.)) inhibited small intestinal transit dose-dependently in rats. Naldemedine (0.01-10 mg/kg, p.o.) blocked the inhibition of small intestinal transit induced by tramadol (30 mg/kg, p.o.) in rats. The transition rate increased dose-dependently over the range of naldemedine 0.01-0.3 mg/kg, and complete recovery was observed at 0.3-10 m/kg.

Reference: Biol Pharm Bull. 2021;44(11):1746-1751. https://pubmed.ncbi.nlm.nih.gov/34719650/

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.