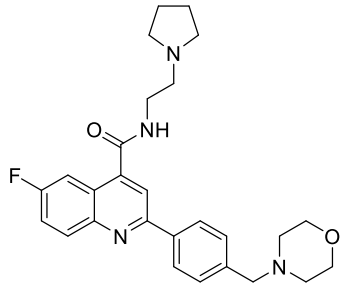
Product data sheet

MedKoo Cat#: 526858 Name: DDD107498 CAS#: 1469439-69-7 Chemical Formula: $C_{27}H_{31}FN_4O_2$ Exact Mass: 462.2431 Molecular Weight: 462.5694	
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:
DDD107498, also known as DDD 498, is a multiple-stage antimalarial agent that inhibits protein synthesis. DDD107498 demonstrates potential to address a variety of clinical needs, including single-dose treatment, transmission blocking and chemoprotection. DDD107498 was developed from a screening programme against blood-stage malaria parasites; its molecular target has been identified as translation elongation factor 2 (eEF2), which is responsible for the GTP-dependent translocation of the ribosome along messenger RNA, and is essential for protein synthesis. This discovery of eEF2 as a viable antimalarial drug target opens up new possibilities for drug discovery.

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	93.0	201.05
Water	93.0	201.05

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.16 mL	10.81 mL	21.62 mL
5 mM	0.43 mL	2.16 mL	4.32 mL
10 mM	0.22 mL	1.08 mL	2.16 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Baragaña B, Hallyburton I, Lee MC, Norcross NR, Grimaldi R, Otto TD, Proto WR, Blagborough AM, Meister S, Wirjanata G, Ruecker A, Upton LM, Abraham TS, Almeida MJ, Pradhan A, Porzelle A, Luksch T, Martínez MS, Luksch T, Bolscher JM, Woodland A, Norval S, Zuccotto F, Thomas J, Simeons F, Stojanovski L, Osuna-Cabello M, Brock PM, Churcher TS, Sala KA, Zakutansky SE, Jiménez-Díaz MB, Sanz LM, Riley J, Basak R, Campbell M, Avery VM, Sauerwein RW, Dechering KJ, Noviyanti R, Campo B, Frearson JA, Angulo-Barturen I, Ferrer-Bazaga S, Gamo FJ, Wyatt PG, Leroy D, Siegl P, Delves MJ, Kyle DE, Wittlin S, Marfurt J, Price RN, Sinden RE, Winzeler EA, Charman SA, Bebrevska L, Gray DW, Campbell S, Fairlamb AH, Willis PA, Rayner JC, Fidock DA, Read KD, Gilbert IH. A novel multiple-stage antimalarial agent that inhibits protein synthesis. Nature. 2015 Jun 18;522(7556):315-20. doi: 10.1038/nature14451. Erratum in: Nature. 2016 Sep 1;537(7618):122. PMID: 26085270; PMCID: PMC4700930.

In vivo study

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1. Baragaña B, Hallyburton I, Lee MC, Norcross NR, Grimaldi R, Otto TD, Proto WR, Blagborough AM, Meister S, Wirjanata G, Ruecker A, Upton LM, Abraham TS, Almeida MJ, Pradhan A, Porzelle A, Luksch T, Martínez MS, Luksch T, Bolscher JM, Woodland A, Norval S, Zuccotto F, Thomas J, Simeons F, Stojanovski L, Osuna-Cabello M, Brock PM, Churcher TS, Sala KA, Zakutansky SE, Jiménez-Díaz MB, Sanz LM, Riley J, Basak R, Campbell M, Avery VM, Sauerwein RW, Dechering KJ, Noviyanti R, Campo B, Frearson JA, Angulo-Barturen I, Ferrer-Bazaga S, Gamo FJ, Wyatt PG, Leroy D, Siegl P, Delves MJ, Kyle DE, Wittlin S, Marfurt J, Price RN, Sinden RE, Winzeler EA, Charman SA, Bebrevska L, Gray DW, Campbell S, Fairlamb AH, Willis PA, Rayner JC, Fidock DA, Read KD, Gilbert IH. A novel multiple-stage antimalarial agent that inhibits protein synthesis. Nature. 2015 Jun 18;522(7556):315-20. doi: 10.1038/nature14451. Erratum in: Nature. 2016 Sep 1;537(7618):122. PMID: 26085270; PMCID: PMC4700930.

7. Bioactivity

Biological target:

DDD107498 (M-5717, DDD-498) is a P. falciparum translation elongation factor 2 inhibitor.

In vitro activity

Furthermore, DDD107498 was more potent than artesunate in ex vivo assays against a range of clinical isolates of both P. falciparum (median EC50 = 0.81 [Range 0.29-3.29] nM, n=44) and P. vivax (median EC50 = 0.51 [Range 0.25-1.39] nM, n=28), collected from patients with malaria from Southern Papua, Indonesia, a region where high-grade multidrug-resistant malaria is endemic for both species (Extended Data Fig. 2b). In contrast the compound was not toxic to human cells (MRC5 and Hep-G2 cells) at much higher concentrations (> 20,000 fold selectivity, Extended Data Fig. 2c).

Reference: Nature. 2015 Jun 18; 522(7556): 315–320. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4700930/

In vivo activity

DDD107498 was very active in several mouse models of malaria, with comparable or greater efficacy than current antimalarials (Extended Data Table 1b). DDD107498 had an ED90 (90% reduction in parasitaemia) of 0.57 mg/kg after a single oral dose in mice infected with the rodent parasite P. berghei. Efficacy was also tested in NOD-scid IL-2R_null mice engrafted with human erythrocytes and infected with P. falciparum strain 3D70087/N9 (Fig. 2a)9. When dosed orally daily for 4 days, the ED90 on day 7 after infection was 0.95 mg/kg per day. Blood sampling from the infected SCID mice suggested a minimum parasiticidal concentration (MPC) for DDD107498 of 10-13 ng/mL for asexual blood stage infections.

Reference: Nature. 2015 Jun 18; 522(7556): 315–320. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4700930/

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.