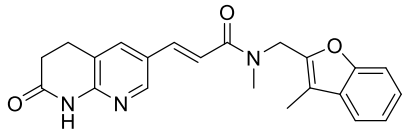
Product data sheet

MedKoo Cat#: 526918 Name: AFN-1252 CAS#: 620175-39-5 Chemical Formula: $C_{22}H_{21}N_3O_3$ Exact Mass: 375.1583 Molecular Weight: 375.428	
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:

AFN-1252, also known as AFN-12520000; API-1252; Debio-1452, is an enoyl-(acyl-carrier protein) reductase fabl inhibitor potentially for the treatment of acute bacterial skin. AFN-1252 exhibits typical MIC(90) values of ≤0 • 015 μ g/ml against diverse clinical isolates of S. aureus, oral absorption, long elimination half-live and efficacy in animal models. AFN-1252 demonstrates a Staphylococcus-specific spectrum of activity.

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	5.8	15.45

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.66 mL	13.32 mL	26.64 mL
5 mM	0.53 mL	2.66 mL	5.33 mL
10 mM	0.27 mL	1.33 mL	2.66 mL
50 mM	0.05 mL	0.27 mL	0.53 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. Yao J, Ericson ME, Frank MW, Rock CO. Enoyl-Acyl Carrier Protein Reductase I (FabI) Is Essential for the Intracellular Growth of Listeria monocytogenes. Infect Immun. 2016 Nov 18;84(12):3597-3607. doi: 10.1128/IAI.00647-16. PMID: 27736774; PMCID: PMC5116736.
2. Flamm RK, Rhomberg PR, Kaplan N, Jones RN, Farrell DJ. Activity of Debio1452, a FabI inhibitor with potent activity against Staphylococcus aureus and coagulase-negative Staphylococcus spp., including multidrug-resistant strains. Antimicrob Agents Chemother. 2015 May;59(5):2583-7. doi: 10.1128/AAC.05119-14. Epub 2015 Feb 17. PMID: 25691627; PMCID: PMC4394798.

In vivo study

1. Parsons JB, Kukula M, Jackson P, Pulse M, Simecka JW, Valtierra D, Weiss WJ, Kaplan N, Rock CO. Perturbation of Staphylococcus aureus gene expression by the enoyl-acyl carrier protein reductase inhibitor AFN-1252. Antimicrob Agents Chemother. 2013 May;57(5):2182-90. doi: 10.1128/AAC.02307-12. Epub 2013 Mar 4. PMID: 23459481; PMCID: PMC3632907.
2. Banevicius MA, Kaplan N, Hafkin B, Nicolau DP. Pharmacokinetics, pharmacodynamics and efficacy of novel FabI inhibitor AFN-1252 against MSSA and MRSA in the murine thigh infection model. J Chemother. 2013 Feb;25(1):26-31. doi: 10.1179/1973947812Y.0000000061. PMID: 23433441; PMCID: PMC3558988.

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7. Bioactivity

Biological target:

AFN-1252 (Debio 1452) is a potent inhibitor of enoyl-acyl carrier protein reductase (FabI).

In vitro activity

The effect of increasing concentrations of AFN-1252 on the growth rate of L. monocytogenes in planktonic culture was measured to determine the contribution of LmFabI versus LmFabK1 to fatty acid synthesis and growth. AFN-1252 caused the cessation of cell growth after 1 to 2 cellular doublings in bacterial genes encoding a single, essential FabI. In contrast, increasing concentrations of AFN-1252 slowed but did not stop the growth of L. monocytogenes (Fig. 3A). Pathway labeling experiments showed that AFN-1252 selectively inhibited lipid synthesis, with minimal perturbation to protein, DNA, and RNA synthesis (Fig. 3B). Therefore, the reduction of growth rate by AFN-1252 was attributed to on-target inhibition of LmFabI and fatty acid synthesis.

Reference: Infect Immun. 2016 Dec; 84(12): 3597–3607. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5116736/

In vivo activity

The first experiments involved administering a single oral dose of AFN-1252 (100 mg/kg) 2 h after infecting the granuloma pouches and examining the effect of AFN-1252 on pouch-associated CFU within 48 h of dosing (Fig. 3A). Little change in the bacterial load was detected within the first 12 h of AFN-1252 treatment, but between 24 and 48 h, there was a 3.0-log10 reduction in the mean CFU/ml of pouch fluid collected from AFN-1252-treated mice compared to untreated mice (Fig. 3A). Wood46 counts in untreated pouch fluid increased to 7.5 log10 CFU/ml at 24 h, while bacterial counts in AFN-1252-treated pouches dropped to 4.4 log10 CFU/ml in 24 h. When 100 mg/kg of AFN-1252 was orally administered once a day for 3 days (+2, +26, and +50 h), AFN-1252 reduced 72-hour S. aureus CFU counts in the pouches of treated animals by 5 orders of magnitude compared to untreated controls, which was near the detection limit for this model (Fig. 3B). These data illustrate that orally administered AFN-1252 can reach therapeutic levels in the mouse granuloma pouch and effectively resolve the S. aureus infection associated with the pouch fluid.

Reference: Antimicrob Agents Chemother. 2013 May; 57(5): 2182–2190. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3632907/