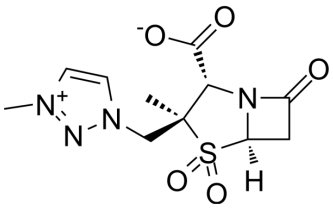
Enmetazobactam

Cat. No.:	HY-103095
CAS No.:	1001404-83-6
Molecular Formula:	$C_{11}H_{14}N_4O_5S$
Molecular Weight:	314
Target:	Bacterial; Beta-lactamase
Pathway:	Anti-infection
Storage:	-20°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 113.3 mg/mL (360.83 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1847 mL	15.9236 mL	31.8471 mL
	5 mM	0.6369 mL	3.1847 mL	6.3694 mL
	10 mM	0.3185 mL	1.5924 mL	3.1847 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.62 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Enmetazobactam (AAI101) is an extended-spectrum β-lactamase inhibitor, against many resistant Gram-negative pathogens [1][2].

In Vitro

Enmetazobactam shows potent activity against specific resistance phenotypes with MIC_{50} and MIC_{90} of 0.125 mg/L and 64 mg/L[1]. Cefepime-Enmetazobactam MICs decreases with increasing concentrations of Enmetazobactam (over the range from 1 to 16 mg/L) for most strains, demonstrating a concentration dependence of Enmetazobactam on restoration of the antibacterial activity of the cephalosporin[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In neutropenic animals, cefepime-Enmetazobactam treatment results in reductions in bacterial density of ≥0.5 log_{10} CFU for 12 of the 20 strains tested and reductions of ≥1 log_{10} CFU for 6 of these. Increases in bacterial density are for only four strains, three of which have cefepime-Enmetazobactam MICs of ≥64 mg/L, irrespective of the Enmetazobactam concentration[2].

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PROTOCOL

Animal Administration [2]

The 20 Enterobacteriaceae strains are used to infect groups of three mice each. At 2 h after inoculation, mice are treated with humanized regimens of cefepime or cefepime-AAI101. All doses are administered as 0.2-mL subcutaneous injections. To serve as control animals, an additional group of mice is administered normal saline at the same volume and frequency and by the same route. Thighs from all animals are harvested at 24 h after initiation of therapy. The harvesting procedure for all study mice began with euthanasia by CO_2 exposure, followed by cervical dislocation. After sacrifice, thighs are removed and homogenized individually in normal saline. For determinations of the numbers of CFU, serial dilutions of thigh homogenates are spread onto Trypticase soy agar with 5% sheep blood using a spiral plater. In addition to the aforementioned treatment and control groups, another group of three infected but untreated mice is harvested at the initiation of dosing and served as a 0-h control. Efficacy, expressed as the change in bacterial density, is determined by calculation of the change in the log_{10} number of CFU obtained in mice after 24 h of treatment from the densities observed in the 0-h control animals.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Int J Antimicrob Agents. 2023 Feb 1;106738.
- ACS Infect Dis. 2021 Mar 16.
- Antimicrob Agents Chemother. 2023 May 31;e0033923.
- Antimicrob Agents Chemother. 2021 Nov 22;AAC0167621.

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REFERENCES

[1]. Crandon JL, et al. In vivo activities of simulated human doses of cefepime and cefepime-AAI101 against multidrug-resistant Gram-negative Enterobacteriaceae. Antimicrob Agents Chemother. 2015 May;59(5):2688-94.

[2]. Crandon JL, et al. In Vitro Activity of Cefepime/AAI101 and Comparators against Cefepime Non-susceptible Enterobacteriaceae. Pathogens. 2015 Aug 18;4(3):620-5.

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