Eravacycline dihydrochloride

Cat. No.: HY-16980A

CAS No.: 1334714-66-7

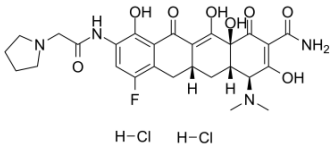
Molecular Formula: $C_{27}H_{33}Cl_2FN_4O_8$

Molecular Weight: 631.48

Target: Bacterial

Pathway: Anti-infection

Storage: 4°C, stored under nitrogen, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 150 mg/mL (237.54 mM; Need ultrasonic)
H_2O : 50 mg/mL (79.18 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5836 mL	7.9179 mL	15.8358 mL
	5 mM	0.3167 mL	1.5836 mL	3.1672 mL
	10 mM	0.1584 mL	0.7918 mL	1.5836 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: ≥ 7.5 mg/mL (11.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 7.5 mg/mL (11.88 mM); Clear solution
3. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (79.18 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Eravacycline dihydrochloride (TP-434 dihydrochloride) is a potent and broad-spectrum antibacterial agent.

In Vitro

Eravacycline is potent antibiotic against A. baumannii, including isolates that are resistant to sulbactam, SM 7338, and BAY 41-6551. Eravacycline shows greater activity than BAY 41-6551, and colistin. The eravacycline $MIC_{50/90}$ values are 0.5/1 mg/L [1]. Eravacycline shows inhibitory effects on six E. coli with MICs ranging from 0.125 to 0.25 mg/L[2]. Eravacycline dihydrochloride is a synthetic antibiotic, with inhibits bacterial protein synthesis through binding to the 30S ribosomal subunit. Eravacycline displays broad spectrum activity against gram-negative bacteria in the panel except P. aeruginosa, as well as excellent activity against major gram-positive pathogens, including methicillin-resistant S. aureus. Eravacycline also

	displays potent ribosomal inhibition[3]. Eravacycline shows potent broad-spectrum activity against 90% of the isolates (MIC_{90}) in each panel at concentrations ranging from ≤0.008 to 2 μg/mL for all species panels except those of Pseudomonas aeruginosa and Burkholderia cenocepacia ((MIC_{90}) values of 32 μg/mL for both organisms). Eravacycline is active against multidrug-resistant bacteria, including those expressing extended-spectrum β-lactamases and mechanisms conferring resistance to other classes of antibiotics, including carbapenem resistance[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Mice are treated with two-fold increasing doses (range 3.125 to 50 mg/kg) of eravacycline every 12 hours. The mean fAUC/MIC magnitude associated with net stasis and 1-log kill endpoint are 27.97 ± 8.29 and 32.60 ± 10.85, respectively[2]. Eravacycline is active in multiple murine models of infection against clinically important Gram-positive and Gram-negative pathogens. Eravacycline is efficacious in mouse septicemia models, demonstrating 50% protective dose values of ≤1 mg/kg of body weight once a day (q.d.) against Staphylococcus aureus. The PD_{50} values against Escherichia coli isolates are 1.2 to 4.4 mg/kg q.d[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3][5]	Rats: Pharmacokinetic (PK) parameters are determined in Sprague−Dawley rats. Animals are fasted overnight (minimum of 12 h) and given a single oral (10 mg/kg) or IV dose (1 mg/kg) of eravacycline followed by a sampling scheme for 24 h. Plasma and dosing solution concentrations are determined by TurboIonspray LC/MSMS analysis using appropriate standard curves. PK parameters are calculated by noncompartmental analysis[3]. Mice: Eravacycline is formulated in sterile 0.9% saline. BALB/c mice are inoculated with 0.2 mL of prepared bacterial inoculum via intravenous injection to seed the kidney. Animals are administered antibiotics (eravacycline) at 10 ml/kg i.v. via the tail vein 12 and 24 h postinfection. Then the bacterial burden is determined[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Clin Microbiol. 2020 Jan 28;58(2):e01603-19.
- J Clin Microbiol. 2020 Jan 28;58(2):e01603-19.
- J Antimicrob Chemother. 2020 Dec 1;dkaa499.
- Antimicrob Agents Chemother. 2021 Apr 5;AAC.00203-21.
- Antimicrob Agents Chemother. 2019 May 24;63(6). pii: e00470-19.

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REFERENCES

[1]. Seifert H, et al. In-vitro activity of the novel fluorocycline eravacycline against carbapenem non-susceptible Acinetobacter baumannii. Int J Antimicrob Agents. 2017 Jul 10.

[2]. Zhao M, et al. In Vivo Pharmacodynamic Target Assessment of Eravacycline against Escherichia coli in a Murine Thigh Infection Model. Antimicrob Agents Chemother. 2017 Jun 27;61(7).

[3]. Xiao XY, et al. Fluorocyclines: a potent, broad spectrum antibacterial agent. J Med Chem. 2012 Jan 26;55(2):597-605.

[4]. Sutcliffe JA, et al. Antibacterial activity of eravacycline (TP-434), a novel fluorocycline, against hospital and community pathogens. Antimicrob Agents Chemother. 2013

Nov;57(11):5548-58.

[5]. Grossman TH, et al. Eravacycline (TP-434) is efficacious in animal models of infection. Antimicrob Agents Chemother. 2015 May;59(5):2567-71.

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