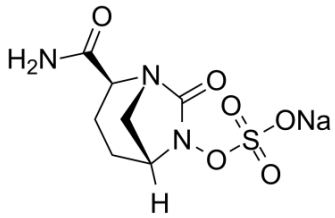
Avibactam sodium

Cat. No.:	HY-14879A
CAS No.:	1192491-61-4
Molecular Formula:	$C_7H_{10}N_3NaO_6S$
Molecular Weight:	287.23
Target:	Bacterial; Antibiotic
Pathway:	Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 50 mg/mL (**174.08 mM;** Need ultrasonic)
DMSO : ≥ 30 mg/mL (**104.45 mM**)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass → Concentration	1 mg	5 mg	10 mg
1 mM	3.4815 mL	17.4077 mL	34.8153 mL
5 mM	0.6963 mL	3.4815 mL	6.9631 mL
10 mM	0.3482 mL	1.7408 mL	3.4815 mL

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

BIOLOGICAL ACTIVITY

Description

Avibactam sodium (NXL-104) is a covalent and reversible non-β-lactam **β-lactamase** inhibitor which inhibits β-lactamase **TEM-1** and **CTX-M-15** with **IC_{50}**s of 8 nM and 5 nM, respectively.

IC_{50} & Target

IC50: 8 nM (TEM-1), 5 nM (CTX-M-15)[1]

In Vitro

Avibactam (NXL104) sodium is a molecule with little antibacterial activity, that inhibits class A and C β-lactamases. Avibactam inactivates most important β-lactamases except metallo types and Acinetobacter OXA carbapenemases[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Avibactam sodium (NXL-104) displays a slow return of activity with an off-rate of 0.045±0.022 min^{-1}, which converts to a residence time half-life ($t_{t1/2}$) of 16±8 min. The measured off-rate for Avibactam suggests that slow deacylation through hydrolysis or reversibility is occurring, and it is in contrast to previously reported extremely long $t_{1/2}$ values

	of >1 or >7 d for Avibactam inhibition of TEM-1[1]. Avibactam is a new promising β-lactamase inhibitor, to overcome resistance caused by β-lactamases. Mice are infected with ca.10^6 CFU of Pseudomonas aeruginosa intramuscularly into the thigh or intranasally to cause pneumonia and are given 8 different (single) subcutaneous doses of GR20263 and Avibactam in various combined concentrations, ranging from 1 to 128 mg/kg of body weight in 2-fold increases. The mean estimated half-life in plasma of GR20263 in the terminal phase is 0.28 h (SD, 0.02 h), and that of Avibactam is 0.24 h (SD, 0.04 h). Volumes of distribution are 0.80 liters/kg (SD, 0.14 liters/kg) and 1.18 liters/kg (SD, 0.34 liters/kg), respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	In a 200 μL reaction volume, 1 μM TEM-1 is incubated with and without 5 μM Avibactam for 5 min at 37°C and subjected to two ultrafiltration cartridge (UFC) steps to remove excess inhibitor (Ultrafree-0.5 with Biomax membrane, 5-kDa cutoff). Centrifugation at 10,600× g for 8 min is performed at 4°C. After each ultrafiltration step, 20 μL retentate are diluted with 180 μL assay buffer to restore the original enzyme concentration. After two UFC treatments, the amount of free Avibactam is quantified by liquid chromotography/MS/MS and found to be <5% of the original concentration. Loss of protein during UFC is assessed by measuring TEM-1 activity (on 4,000-fold dilution) in the acyl-enzyme sample compare with non-UFC-treated enzyme, and loss is found to be <5%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cells (~10^9 cfu) from overnight broth culture are spread on Mueller-Hinton agar supplemented with either (i) Ceftaroline plus Avibactam (1 or 4 mg/L) at 1-16× the MICs or (ii) Ceftaroline at 1 or 4 mg/L plus Avibactam at 1-8× the concentration needed to reduce the Ceftaroline MIC to 1 or 4 mg/L. Colonies are counted after overnight incubation and representatives are retained[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Avibactam is reconstituted in sterile water to a stock solution of 5,120 mg/L and further solution is prepared in Mueller-Hinton broth. Outbred female CD-1 mice, 7 to 8 weeks old and weighing 20 to 25 g, are used in the experiments. Eight dose combinations are used. For the thigh-infected animals, the combinations of GR20263 and Avibactam are 16/4, 8/1, 64/32, and 2/128 mg/kg. For the lung-infected mice, combinations of 32/16, 4/2, 128/8, and 1/64 mg/kg of the respective constituents are used. These combinations are chosen in order to detect possible pharmacokinetic interactions between the two compounds (GR20263 and Avibactam) and to cover a wide range of doses of each compound. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **J Clin Microbiol**. 2020 Jun 24;JCM.00932-20.
- **J Antimicrob Chemother**. 2020 Jun 26;dkaa217.
- **J Antimicrob Chemother**. 2017 Jul 1;72(7):1930-1936.
- **J Antimicrob Chemother**. 2017 Sep 1;72(9):2483-2488.
- **J Infect Dis**. 2019 Jul 2;220(3):484-493.

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REFERENCES

[1]. Ehmann DE, et al. Avibactam is a covalent, reversible, non-β-lactam β-lactamase inhibitor. Proc Natl Acad Sci U S A. 2012 Jul 17;109(29):11663-8.

[2]. Livermore DM, et al. Characterization of β-lactamase and porin mutants of Enterobacteriaceae selected with ceftaroline + avibactam (NXL104). J Antimicrob Chemother. 2012 Jun;67(6):1354-8.

[3]. Berkhout J, et al. Pharmacokinetics and penetration of GR20263 and avibactam into epithelial lining fluid in thigh- and lung-infected mice. Antimicrob Agents Chemother. 2015 Apr;59(4):2299-304.

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