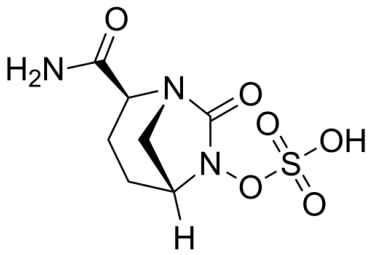
Data Sheet

Product Name:	Avibactam (free acid)
Cat. No.:	CS-0593
CAS No.:	1192500-31-4
Molecular Formula:	$C_7H_{11}N_3O_6S$
Molecular Weight:	265.24
Target:	Antibiotic; Bacterial
Pathway:	Anti-infection
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

Avibactam (NXL-104) free acid 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[1]. IC50 & Target: IC_{50}: 5 nM (CTX-M-15), 8 nM (TEM-1)[1] **In Vitro:** Avibactam is a molecule with little antibacterial activity, that inhibits class A and C β-lactamases, but not metallo types and Acinetobacter OXA carbapenemases[2].

Ceftazidime (HY-B0593)-Avibactam (0-256 mg/L) inhibits 16 bla_{KPC-2} positive and 1 of $bla_{OXA-232}$ positive Klebsiella pneumonia growth with MIC_{50} and MIC_{90} for both 8 mg/L[4]. **In Vivo:** Ceftazidime-Avibactam (0.375 mg/g; s.c.; q8h for 10 days) has a significant effect on the bacteria and led to a certain therapeutic efficacy in K. pneumoniae strain Y8 infected mouse model[3].

Avibactam (64 mg/kg; s.c.; once) shows mean estimated half-life in plasma in the terminal phase of 0.24 h in Pseudomonas aeruginosa infected neutropenic mice with lung infection[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Avibactam is prepared in sterile water[2].[2]Cells (~10^9 cfu) from overnight broth culture are spread on Mueller-Hinton agar supplemented with either (i) Ceftaroline plus Avibactam (NXL104) (1 or 4 mg/L) at 1-16× the MICs or (ii) Ceftaroline at 1 or 4 mg/L plus Avibactam (NXL104) 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]. **Animal Administration:** Avibactam is reconstituted in sterile water to a stock solution of 5120 mg/L and further solution is prepared in Mueller-Hinton broth (Mice)[3].;Ceftazidime-Avibactam is dissolved in PBS[4].[3]Mice[3]

Avibactam (NXL104) 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 Ceftazidime 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 (Ceftazidime and Avibactam (NXL104)) and to cover a wide range of doses of each compound.

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 ceftazidime and avibactam into epithelial lining fluid in thigh- and lung-infected mice. Antimicrob Agents Chemother. 2015 Apr;59(4):2299-304.

[4]. Zhang W, et al. In vitro and in vivo bactericidal activity of ceftazidime-avibactam against Carbapenemase-producing Klebsiella pneumoniae. Antimicrob Resist Infect Control. 2018 Nov 21;7:142.

CAIndexNames:

Sulfuric acid, mono[(1R,2S,5R)-2-(aminocarbonyl)-7-oxo-1,6-diazabicyclo[3.2.1]oct-6-yl] ester

SMILES:

O=S(ON1[C@]2([H])CC[C@@H](C(N)=O)[N@@](C2)C1=O)(O)=O

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA