Product Data Sheet

Product Name: Avibactam
Cat. No.: GC14602

Chemical Properties

Cas. No.	1192500-31-4		
Chemical Name	(2R,5S)-7-oxo-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carbimidic acid		
SMILES	N=C(O)[C@@]1([H])CC[C@@](N2OS(O)(=O)=O)([H])CN1C2=O		
Formula	$C_7H_{11}N_3O_6S$	M.Wt	265.24
Solubility	DMSO : 125 mg/mL (471.27 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Avibactam		

Protocol

Cell experiment: Cells (~109 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].

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Animal experiment:

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.

Background

Avibactam free acid (NXL-104 free acid) is a covalent, reversible non-β-lactam β-lactamase inhibitor, inhibits β-lactamase TEM-1 and CTX-M-15 with IC50 of 8 nM and 5 nM, respectively.

Avibactam (NXL104) is a molecule with little antibacterial activity, that inhibits class A and C β-lactamases. Avibactam (NXL104) inactivates most important β-lactamases except metallo types and Acinetobacter OXA carbapenemases[2].

Avibactam (NXL104) sodium 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 (tt1/2) of 16±8 min. The measured off-rate for Avibactam (NXL104) suggests that slow deacylation through hydrolysis or reversibility is occurring, and it is in contrast to previously reported extremely long t1/2 values of >1 or >7 d for Avibactam (NXL104) 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.106 CFU of Pseudomonas aeruginosa

intramuscularly into the thigh or intranasally to cause pneumonia and are given 8 different (single) subcutaneous doses of Ceftazidime and Avibactam (NXL104) 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 Ceftazidime 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].

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.

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