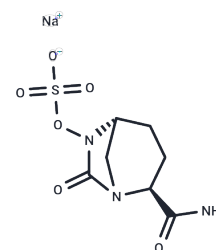


Avibactam sodium

Chemical Properties

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| CAS No. : | 1192491-61-4 |
| Formula: | C7H10N3NaO6S |
| Molecular Weight: | 287.22 |
| Storage: | Keep away from direct sunlight Powder: -20°C for 3 years In solvent: -80°C for 1 year <small>Actual storage temperature shall be subject to the COA.</small> |



Biological Description

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| Description | Avibactam sodium (NXL-104) is a non- β -lactam β -lactamase inhibitor that inhibits TEM-1, P99, and KPC-2 β -lactamases (IC ₅₀ =8/80/38 nM) covalently and reversibly. Avibactam sodium has antimicrobial activity and can be used to treat urinary tract infections. |
| Targets(IC50) | Antibacterial, Antibiotic |
| In vitro | <p>METHODS: Breast cancer cell lines were treated with (E/Z)-4-Hydroxytamoxifen for 4 h and cell growth was detected.</p> <p>RESULTS: (E/Z)-4-Hydroxytamoxifen was able to inhibit the growth of four breast cancer cell lines, MCF-7, MCF-7/Adr, MDA-MB-231 and MDA-MB-435, with IC₅₀s of 300 nM, 40,000 nM, 30,000 nM and 20,000 nM, respectively. [1]</p> <p>METHODS: HepG2 or MCF-7 cells were incubated with (E/Z)-4-Hydroxytamoxifen (5-50 μM) in labeled medium for 18 h. Kinetic parameters of human SULT-catalyzed sulfation were determined.</p> <p>RESULTS: (E/Z)-4-Hydroxytamoxifen can be metabolized by sulfation in HepG2 and MCF-7 cells. [2]</p> |
| In vivo | Avibactam sodium displays a slow return of activity with an off-rate of $0.045 \pm 0.022 \text{ min}^{-1}$, which converts to a residence time half-life (tt _{1/2}) of $16 \pm 8 \text{ min}$. Avibactam has slow deacylation through hydrolysis or reversibility, and this is in contrast to previously reported extremely long t _{1/2} values of >1 or >7 d for Avibactam inhibition of TEM-1[1]. 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 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 L/kg (SD, 0.14 L/kg) and 1.18 liters/kg (SD, 0.34 L/kg), respectively. |
| Kinase Assay | In a 200 μ L reaction volume, 1 μ M TEM-1 is incubated with and without 5 μ M 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 \times g for 8 min is performed at 4°C. After each ultrafiltration step, 20 μ L retentate is diluted with 180 μ L assay buffer to restore the original enzyme concentration. After two UFC treatments, the amount of free Avibactam is quantified by LC/MS/MS and found to be <5% of the original concentration. Loss of protein during UFC is assessed by |

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| Kinase Assay | measuring TEM-1 activity (on 4,000-fold dilution) in the acyl-enzyme sample compare with a non-UFC-treated enzyme, and loss is found to be <5%[1]. |
| Cell Research | Avibactam is prepared in sterile water[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]. |
| Animal Research | Avibactam is reconstituted in sterile water to a stock solution of 5,120 mg/L and the 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) and to cover a wide range of doses of each compound. |

Solubility Information

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| Solubility | Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 257 mg/mL (894.78 mM),Sonication is recommended. H2O: 52 mg/mL (181.05 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (17.41 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i> |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|-------|-----------|------------|------------|
| 1 mM | 3.4817 mL | 17.4083 mL | 34.8165 mL |
| 5 mM | 0.6963 mL | 3.4817 mL | 6.9633 mL |
| 10 mM | 0.3482 mL | 1.7408 mL | 3.4817 mL |
| 50 mM | 0.0696 mL | 0.3482 mL | 0.6963 mL |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Palombo M, et al. In Vitro Evaluation of Increasing Avibactam Concentrations on Ceftazidime Activity against Ceftazidime/Avibactam-Susceptible and Resistant KPC-Producing *Klebsiella pneumoniae* Clinical Isolates. *Antibiotics (Basel)*. 2023 Dec 7;12(12):1707.

Berkhout J, et al. Pharmacodynamics of Ceftazidime and Avibactam in Neutropenic Mice with Thigh or Lung Infection. *Antimicrob Agents Chemother*. 2015 Nov 2;60(1):368-75.

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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