Administration of Cefepime-taniborbactam

ICD-10-PCS Coordination & Maintenance Committee Meeting
March 2024

Venatorx PHARMACEUTICALS

Cefepime-taniborbactam Overview

Product Overview :

1. Cefepime-taniborbactam is an investigational beta-lactam antibiotic/beta-lactamase inhibitor combination under development for the treatment of cUTIs, including pyelonephritis, melioidosis, and HABP/VABP
2. Cefepime-taniborbactam has also demonstrated in vitro coverage against antibiotic resistant gram-negative bacteria, most notably ESBL-E, CRE, and MDR-PA, which can include CRPA
3. Cefepime-taniborbactam is under consideration for the FY 2025 NTAP

Naming Convention

Non-Proprietary Name:
Cefepime-taniborbactam

Proprietary Name:
To Be Determined

cUTI: Complicated Urinary Tract Infection; HABP: Hospital-Acquired Bacterial Pneumonia; VABP: Ventilator-Associated Bacterial Pneumonia; ESBL: Extended Spectrum Beta-Lactamase; ESBL-E: ESBL-Expressing *Enterobacterales*; MDR-PA: Multidrug-Resistant *Pseudomonas aeruginosa;* CRE: Carbapenem-Resistant *Enterobacterales;* CRPA: Carbapenem-Resistant *Pseudomonas aeruginosa;* NTAP: New Technology Add-on Payment

Venatorx PHARMACEUTICALS

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Cefepime-taniborbactam Components

Product Components:

Cefepime

A fourth-generation cephalosporin, is a widely used BL antibiotic with **more than two decades of proven safety and clinical utility** against susceptible gram-negative and gram-positive bacteria.

Taniborbactam

A BLI that, in combination with cefepime, may offer a potential treatment option for patients with serious bacterial infections caused by difficult-to-treat drug resistant gram-negative bacteria, most notably CRE and CRPA.

How Cefepime-taniborbactam Works:

Cefepime:	Taniborbactam:
• Inhibits bacterial cell wall synthesis by covalently binding PBP enzymes; causes defects in the bacterial cell wall leading to autolysis and bactericidal activity • Enables enhanced penetration of the gram-negative bacterial outer membrane	• Protects cefepime from hydrolysis by most beta-lactamases and other AMR mechanisms • Restores the activity of cefepime against many drug-resistant gram-negative pathogens • Taniborbactam on its own has no antibacterial activity

BL: Beta-Lactam Antibiotic; BLI Beta-Lactamase Inhibitor; cUTI: Complicated Urinary Tract Infection; HABP: Hospital-Acquired Bacterial Pneumonia; VABP: Ventilator-Associated Bacterial Pneumonia; ESBL: Extended Spectrum Beta-Lactamase; ESBL-E: ESBL-Expressing *Enterobacterales*; MDR-PA: Multidrug-Resistant *Pseudomonas aeruginosa;* PBP: Penicillin-Binding Protein; AMR: Anti-Microbial Resistance

Venatorx PHARMACEUTICALS

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Prevalence of Carbapenem Resistant Organisms

The CDC reported that rates of AMR have increased significantly in the U.S. among bacterial pathogens including those commonly causing cUTI, pyelonephritis, and bacteremia

- There are 2.8 million AMR infections annually, directly related to more than 5,000 deaths

Analysis of US UTI Patients from 2014 to 2019 found:

4.4%

of cases were CR

24.5%

of US UTI patients were bacteremic

1.7%

of bacteremic cases are due to CR pathogens

Source: Antibiotic Resistance Threats in the United States, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2019
CDC: Centers for Disease Control; AMR: Anti-Microbial Resistance; cUTI: Complicated Urinary Tract Infection; CR: Carbapenem Resistant

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Cefepime-taniborbactam Dosing Information

- The recommended dose of cefepime-taniborbactam is 2 g cefepime and 0.5 g taniborbactam administered together every 8 hours by intravenous infusion over 2 hours to adult patients with cUTI, including pyelonephritis, and with or without concurrent bacteremia caused by susceptible gram-negative pathogens
- Cefepime and taniborbactam are administered together intravenously to adult patients with cUTI, including pyelonephritis for 7 days (up to 14 days for patients with concurrent bacteremia)
- Monitor renal function in adult patients with changing renal function and adjust the dosage of cefepime-taniborbactam accordingly
- Dosage adjustments are needed for patients with renal impairment, with eGFR less than 50 mL/min/1.73 m^2 and patients with eGFR greater than or equal to 120 mL/min/1.73 m^2 (see Table 1)

cUTI: Complicated Urinary Tract Infection; eGFR: Estimated Glomerular Filtration Rate

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Cefepime-taniborbactam Preparation and Administration

Cefepime and taniborbactam are administered together intravenously, using aseptic technique for preparation and administration.

The product is supplied as sterile dry powder contained in 2 vials (one 2 g vial of cefepime and one 0.5 g vial of taniborbactam)

↓

Each vial must be individually constituted and diluted separately with sterile water and 0.9% sodium chloride using aseptic technique prior to IV infusion (see Table 2)

↓

Withdraw the volume from each vial required for dosing and add to an infusion bag, discard any cefepime or taniborbactam solutions if not diluted within 2 hours of preparation (see Table 3)

↓

Administration of an infusion solution prepared in **0.9% Sodium Chloride Injection** must be completed within 8 hours if stored at controlled room temperature 68°F to 77°F, or within 24 hours if stored in a refrigerator at 36°F to 46°F, and used within 8 hours of subsequent storage at room temperature

IV: Intravenous

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Cefepime-taniborbactam Dosing Adjustments

Dosage Adjustment in Patients with Renal Impairment and Patient with Augmented Renal Clearance:

Patients with renal impairment who have an eGFR less than 50 mL/min/1.73 m^2:

- The recommended dosages are available in Table 1

Patients with eGFR greater than or equal to 120 mL/min/1.73 m^2:

- Cefepime-taniborbactam 2.5 g administered every 6 hours by IV infusion over 2 hours is recommended

Table 1: Dosage Table of Cefepime-taniborbactam in Patients with Renal Impairment

eGFR* (mL/min/1.73 m^2)	Recommended Dosage Regimen for Cefepime 2g and Taniborbactam 0.5g**	Dosing Interval
30 to 49	2 g/0.5 g	q12h
20 to 29	1 g/0.025 g	q8h
15 to 19	1 g/0.025 g	q12h
5 to 14	Dose 1: 1 g/0.25 g Subsequent doses: 0.5 g/0.125 g	q24h
<5	Dose 1: 1 g/0.25 g Subsequent doses: 0.5 g/0.125 g	q48h

eGFR: Estimated Glomerular Filtration Rate

*As calculated using the Modified Diet in Renal Disease Formula

**All doses of cefepime-taniborbactam administered over 2 hours

**The total duration of treatment is 7 days or up to 14 days for patients with concurrent bacteremia

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Cefepime-taniborbactam Preparation and Dosing

Table 2: Preparation of Constituted Solutions:

Solution Component	Volume for Constitution	Approximate Volume of Constituted Solution	Approximate Concentration of Constituted Solution
Cefepime, 2 g (Vial 1)	10 mL	12.5 mL	160 mg/mL
Taniborbactam, 0.5 g (Vial 2)	10 mL	10.4 mL	48 mg/mL

Table 3: Preparation of Cefepime-taniborbactam Doses:

Preparation of Cefepime-taniborbactam Doses	Volume to Withdraw from each Constituted Vial for Further Dilution		Volume of Infusion Bag
	Cefepime (Vial 1)	Taniborbactam (Vial 2)	
2.5 g (2 g/0.5 g)	entire vial contents (approximately 12.5 mL)	entire vial contents (approximately 10.4 mL)	250 mL
1.25 g (1 g/0.25 g)	6.3 mL	5.2 mL	100 mL or 125 mL
0.625 g (0.5 g/0.125 g)	3.1 mL	2.6 mL	50 mL

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Safety Profile Summary in the Phase 3 Clinical Trial for cUTI, Including Acute Pyelonephritis

The most common AEs were headache, diarrhea, constipation, and nausea

Table 4: TEAEs Occurring at >2% of Patients in Either Treatment Group

Adverse Reaction	Cefepime-taniborbactam N=440 n (%)	Meropenem N=217 n (%)
Patients with At Least One TEAE	156 (3.5)	63 (29.0)
Headache	27 (6.1)	8 (3.7)
Diarrhea	18 (4.1)	5 (2.3)
Constipation	14 (3.2)	3 (1.4)
Hypertension	10 (2.3)	2 (0.9)
Nausea	9 (2.0)	2 (0.9)
Alanine aminotransferase increased	4 (0.9)	5 (2.3)
Patients with At Least One Serious TEAE	9 (2.0)	4 (1.8)
Patients with At Least One TEAE with Action of Drug Withdrawn	13 (3.0)	2 (0.9)
Patients with At Least One Fatal TEAE	1 (0.2)	0

TEAE: Treatment Emergent Adverse Events; AE: Adverse Event

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.

Administration and Documentation

The administration of cefepime-taniborbactam, it would be documented as described below:

Administration will predominantly be in the in-patient setting **at 85% of volume** and 15% in the out-patient setting

Medical record documentation of administration will be found in the Progress Notes and MAR

MAR: Medication Administration Record

©2022 Venatorx Pharmaceuticals, Inc. All Rights Reserved.