*FDA New Approval — April 3, 2024*

# ZEVTERA® (ceftobiprole medocaril sodium)

## Overview

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| **Manufacturer** | Basilea Pharmaceutica |
| **Approval Date** | April 3, 2024 |
| **Pathway** | NDA |
| **Type** | New Molecular Entity |
| **Formulation** | Powder for Injection |
| **Therapeutic Class** | Cephalosporin (Fifth Generation) |
| **Expected Market Launch** | Estimated availability is unavailable. |

## Approved Indications

ZEVTERA® is indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms in patients 18 years of age and older:

- Hospital-acquired pneumonia (HAP), excluding ventilator-associated pneumonia (VAP) caused by: Staphylococcus aureus including methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pneumoniae, Escherichia coli, and Klebsiella pneumoniae.
- Community-acquired pneumonia (CAP) caused by: Staphylococcus aureus (including MRSA), Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae, and Haemophilus influenzae.

## Mechanism of Action (MoA)

Ceftobiprole exerts in vitro bactericidal activity over a broad range of pathogens, including both Gram-positive and Gram-negative bacteria, due to its binding to important penicillin-binding proteins (PBPs) such as PBP2a, that confers β-lactam resistance in staphylococci.

Ceftobiprole is resistant to hydrolysis by the S. aureus PC1 Class A β-lactamase, and is relatively resistant to hydrolysis by many β-lactamases of Class C and Class A Gram-negative bacteria. Like the extended-spectrum cephalosporins, ceftobiprole is hydrolyzed by extended-spectrum βlactamases (ESBLs) and metallo-β-lactamases. The minimum concentration at which 90% of tested strains are inhibited (MIC90) against methicillin resistant staphylococci is ≤ 4 mcg/mL (MIC range: 0.12 to 8.0 mcg/mL), including MRSA from the major epidemic clones. Ceftobiprole has a similar spectrum of activity as cefepime and ceftazidime against P. aeruginosa and other Gram-negative organisms. Stable or high-level resistance selection in staphylococci and pneumococci and Haemophilus influenzae has been difficult to select in vitro.

## Dosing & Administration

Each vial contains 500 mg of ceftobiprole (as 666.6 mg of ceftobiprole medocaril sodium). After reconstitution, each mL of concentrate contains 50 mg of ceftobiprole (as 66.7 mg of ceftobiprole medocaril sodium).

The recommended dose of ZEVTERA® is 500 mg administered as a 2-hour intravenous infusion every 8 hours. The usual treatment duration is 4–14 days for CAP, and 7–14 days for HAP, depending on disease severity and the patient's clinical response.

## Place in Therapy

- Amid the shortage of amoxicillin oral powder for suspension, the Food and Drug Administration (FDA) has approved ZEVTERA® for children and adults with community-acquired bacterial pneumonia (CABP).
- ZEVTERA® is indicated for the treatment of adult patients with Staphylococcus aureus bloodstream infections (bacteremia) (SAB), including right-sided infective endocarditis, and adult patients with acute bacterial skin and skin structure infections (ABSSSI) and for adult and pediatric patients (3 months to less than 18 years old) with CABP.

## Clinical Trial Information

ZEVTERA®'s efficacy in treating Staphylococcus aureus bloodstream infections (bacteremia) SAB was evaluated in a randomized, controlled, double-blind, multinational, multicenter trial. In the trial, researchers randomly assigned 390 subjects to receive ZEVTERA® (192 subjects) or daptomycin plus optional aztreonam (198 subjects). Primary efficacy, defined as survival, symptom improvement, S. aureus bacteremia clearance, no new complications, and no other effective antibiotics, was evaluated 70 days post-treatment. ZEVTERA® achieved 69.8% overall success vs. 68.7% for the comparator.

ZEVTERA®'s efficacy in treating acute bacterial skin and skin structure infections (ABSSSI) was evaluated in a randomized, controlled, double-blind, multinational trial. In the trial, researchers randomly assigned 679 subjects to receive either ZEVTERA® (335 subjects) or vancomycin plus aztreonam (344 subjects). The primary measure of efficacy was early clinical response 48-72 hours after start of treatment. Early clinical response required a reduction of the primary skin lesion by at least 20%, survival for at least 72 hours and the absence of additional antibacterial treatment or unplanned surgery. Of the subjects who received ZEVTERA®, 91.3% achieved an early clinical response vs. 88.1% of subjects who received the comparator.

ZEVTERA®'s efficacy in treating adult patients with CABP was evaluated in a randomized, controlled, double-blind, multinational, multicenter trial. In the trial, researchers randomly assigned 638 adults hospitalized with CABP and requiring IV antibacterial treatment for at least 3 days to receive either ZEVTERA® (314 subjects) or ceftriaxone with optional linezolid (324 subjects). The primary measurement of efficacy were clinical cure rates at test-of-cure visit, which occurred 7-14 days after end-of-treatment. Of the subjects who received ZEVTERA®, 76.4% achieved clinical cure compared to 79.3% of subjects who received the comparator. An additional analysis considered an earlier time point of clinical success at Day 3, which was 71% in patients receiving ZEVTERA® and 71.1% in patients receiving the comparator.

## Expected Cost

Estimated cost has not been made public yet.

## Product Discontinuation

Not available