Zevtera (ceftobiprole medocaril sodium) – New drug approval

- On April 3, 2024, the FDA announced the approval of Basilea Pharmaceutica's Zevtera (ceftobiprole medocaril sodium), for the treatment of:
    - Adult patients with *Staphylococcus aureus* bloodstream infection (bacteremia) (SAB), including those with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates;
    - Adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following gram-positive and gram-negative microorganisms: *Staphylococcus aureus* (methicillin-susceptible and methicillin-resistant isolates), *Streptococcus pyogenes*, and *Klebsiella pneumoniae;*
    - Adult and pediatric patients (3 months to less than 18 years old) with community-acquired bacterial pneumonia (CABP) caused by susceptible isolates of the following gram-positive and gram-negative microorganisms: *Staphylococcus aureus* (methicillin-susceptible isolates), *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Escherichia coli*, and *Klebsiella pneumoniae.*

- Zevtera is a cephalosporin antibacterial.

- The efficacy of Zevtera for SAB was established in a randomized, controlled, double-blind, study in 390 patients. Patients were randomized to receive Zevtera or daptomycin plus optional aztreonam (the comparator). The primary endpoint was the overall success (defined as survival, symptom improvement, *Staphylococcus aureus* bacteremia bloodstream clearance, no new *Staphylococcus aureus* bacteremia complications and no use of other potentially effective antibiotics) at the post-treatment evaluation visit, which occurred 70 days after being randomly assigned an antibiotic.
    - A total of 69.8% of patients who received Zevtera achieved overall success compared to 68.7% of patients who received the comparator.

- The efficacy of Zevtera for ABSSSI was established in a randomized, controlled, double-blind study in 679 patients. Patients were randomized to receive Zevtera or vancomycin plus aztreonam (the comparator). The primary endpoint was early clinical response 48 to 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 patients who received Zevtera, 91.3% achieved an early clinical response within the necessary timeframe compared to 88.1% of patients who received the comparator.

- The efficacy of Zevtera for CABP was established in a randomized, controlled, double-blind study in 638 adult patients hospitalized with CABP and requiring intravenous (IV) antibacterial treatment for at least 3 days. Patients were randomized to receive Zevtera or ceftriaxone with optional linezolid (the comparator). The primary endpoint was clinical cure rate at test-of-cure visit, which occurred 7 to 14 days after end-of-treatment.
    - Of the patients who received Zevtera, 76.4% achieved clinical cure compared to 79.3% of patients who received the comparator.
    - An additional analysis considered an earlier timepoint of clinical success at day 3, which was 71% in patients receiving Zevtera and 71.1% in patients receiving the comparator.

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- Given the similar course of CABP in adults and pediatric patients, the approval of Zevtera in pediatric patients three months to less than 18 years with CABP was supported by evidence from the CABP trial of Zevtera in adults and a trial in 138 pediatric subjects three months to less than 18 years of age with pneumonia.

- Warnings and precautions for Zevtera include increased mortality with unapproved use in ventilator-associated bacterial pneumonia patients; hypersensitivity reactions; seizures and other central nervous system reactions; *Clostridioides difficile*-associated diarrhea; and development of drug-resistant bacteria.

- The most common adverse reactions (≥ 4%) with Zevtera use for SAB were anemia, nausea, hypokalemia, vomiting, increased hepatic enzyme and bilirubin, diarrhea, increased blood creatinine, hypertension, leukopenia, and pyrexia.

- The most common adverse reactions (≥ 2%) with Zevtera use for ABSSSI were nausea, diarrhea, headache, injection site reaction, increased hepatic enzyme, rash, vomiting, and dysgeusia.

- The most common adverse reactions (≥ 2%) with Zevtera use in adults with CABP were nausea, increased hepatic enzyme, vomiting, diarrhea, headache, rash, insomnia, abdominal pain, phlebitis, hypertension, and dizziness. The most common adverse reactions (≥ 2%) with Zevtera use in pediatric patients with CABP were vomiting, headache, increased hepatic enzyme, diarrhea, infusion site reaction, phlebitis and pyrexia.

- The recommended intravenous dosages of Zevtera for the treatment of pediatric and adult patients with SAB, ABSSSI and CABP are provided in the tables below.

Adult patients

Indication*	Dose	Frequency
SAB	667 mg	Every 6 hours on Days 1 to 8
		Every 8 hours from Day 9
ABSSSI	667 mg	Every 8 hours
CABP	667 mg	Every 8 hours

* Duration of treatment in adult patients is up to 42 days for SAB and 5 days to 14 days for ABSSSI and CABP.

Pediatric patients with CABP

Age group	Dose*	Frequency
12 years to less than 18 years old	13.3 mg/kg (up to 667 mg/dose)	Every 8 hours
3 months to less than 12 years old	20 mg/kg (up to 667 mg/dose)	Every 8 hours

* Duration of treatment for CABP in pediatric patients is 7 days to14 days.

- Basilea Pharmaceutica's launch plans for Zevtera are pending. Zevtera will be available as a 667 mg powder for reconstitution in a single-dose vial.

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