Category

Best Pharmaceutical Product

General Information

Company Name *

Innoviva Specialty Therapeutics

Product/Solution Name *

Zevtera

Compound/Tech Name*

ceftobiprole medocaril sodium for injection

Trade Name *

Zevtera

Corporate Name *

ceftobiprole medocaril sodium for injection

Date of Approval *

2024-04-03

Indications *

- Adult patients with Staphylococcus aureus bloodstream infections (bacteremia) (SAB), including those with right-sided infective endocarditis
- Adult patients with acute bacterial skin and skin structure infections (ABSSSI) and
- Adult and pediatric patients (3 months to less than 18 years old) with community-acquired bacterial pneumonia (CABP)

words remaining :

453

Therapeutic Areas *

Infectious Diseases, Antibiotic, Antibacterial

words remaining :

496

*Kindly clearly label your files with company name and asset name.

Background information and need for drug / device
(please be as specific as possible in your description; limit 500 words)

A Critical Need in emerging infections-

The Zevtera story can be summarized in three words: tenacity, creativity, and innovation.

Tenacity: the compound ceftobiprole has had many homes with several companies but finally found the commitment from Basilea: the team to bring it through development and ultimately into the hands of health care providers.

Creativity: the unique development plan centered on global programs targeting high need medical conditions treating complex infections, bacteremia, skin infections and community acquired pneumonia including infections caused by drug resistant bacteria.

Innovation: the team took a well-known class of antibiotics, with a well-established safety and efficacy profile that treats many infections and built on that by applying scientific principles to explore its utility in some of the most difficult-to-treat and deadly infections. Few have taken on the challenge of new treatments for infections caused by staphylococcus aureus including resistant strains.

Methicillin Resistant Staphylococcus Aureus (MRSA), one of the six top-priority AMR pathogen threats identified by the U.S. Centers for Disease Control and Prevention, is particularly concerning due it its resistance to many standard antibiotics. MRSA entering the bloodstream is especially problematic as this condition is associated with high mortality - up to 30% within 30 days. In addition to lethal bloodstream infections, MRSA can also form biofilms around commonly implanted medical devices like pacemakers and catheters which can severely complicate patient care with potentially life-threatening results. As a result of these challenges and the continued high mortality and morbidity associated there remains an unmet need for a new therapy to combat these infections present in just about every hospital in the US. In the United States, the prevalence of MRSA among S. aureus clinical isolates exceeds 50%, justifying empiric MRSA treatment in SAB.

Treating SAB requires careful clinical consideration due to the pathogen's potential to cause severe infections, its resistance to various antibiotics, its affinity to indwelling medical devices such as artificial heart valves, and the complexities involved in managing such conditions. The multifaceted nature of SAB treatment demands a comprehensive approach that addresses the diverse patient presentations and particularly the prevalence of MRSA. Early and optimized antimicrobial therapy is crucial to improving patient outcomes. This often includes the use of combination therapy to cover a broad spectrum of additional potential pathogens, especially in severe cases where there is persistent SAB or concern for antibiotic failure.

Recognizing the urgent need for effective treatments against resistant bacteria, ZEVTERA® (ceftobiprole medocaril sodium for injection) was developed to address these challenges.

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History of the development of the solution/product *
(please be as specific as possible in your description; 500 words)

The ERADICATE trial was a pivotal, phase 3, double-blind, noninferiority study comparing ZEVTERA with daptomycin for the treatment of complicated SAB, including both MRSA and MSSA infections. The trial was the largest trial ever in SAB with 390 patients and also the only double blind, randomized non inferiority trial ever done for this indication. This trial was conducted at 60 sites in 17 countries from August 2018 through March 2022. The objective of the trial was to evaluate the efficacy and safety of ZEVTERA in comparison to daptomycin in adult patients with complicated SAB. The primary outcome measure was overall treatment success at 70 days post-randomization, which was defined

by survival, clearance of bacteremia, symptom improvement, absence of new SAB-related complications, and no administration of other potentially effective antibiotics. Safety was also assessed.

The overall treatment success rate was found to be 69.8% in the ZEVTERA group compared to 68.7% in the daptomycin group, demonstrating noninferiority of ZEVTERA relative to daptomycin. Mortality rates were comparable between the two groups, with 9.0% for ZEVTERA and 9.1% for daptomycin. Microbiologic eradication was achieved in 82.0% of the ZEVTERA group and 77.3% of the daptomycin group. Adverse events were reported in 63.4% of patients receiving ZEVTERA and 59.1% of those receiving daptomycin. Serious adverse events were reported in 18.8% of patients in the ZEVTERA group and 22.7% in the daptomycin group.
These findings from ERADICATE published in 2023 in the New England Journal of Medicine, suggest that ZEVTERA may be a valuable treatment option for patients with complicated SAB, offering an alternative to daptomycin (especially in light of rising resistance to daptomycin) with comparable efficacy and safety profiles.

The pivotal trials for community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSIs) confirmed ceftobiprole's broad-spectrum activity and comparable efficacy and safety, supporting its potential as a viable treatment option for these indications.

The FDA agreed and approved ZEVTERA based on evidence from four clinical trials of 1,845 patients with SAB, ABSSSI, and CABP in adults and children (390 with SAB, 679 with ABSSSI, 638 with adult CABP, and 138 with pediatric CABP).

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Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition *

One of the ways to define innovation is to see it as applying new or improved solutions to an existing idea and creating new value. The ZEVTERA story is a classic example of that definition in action.

ZEVTERA's scientists created an advanced cephalosporin that covers both gram positive and gram-negative organisms and gained FDA approval for the challenging indication of Staphylococcus Aureus Bacteremia (SAB) including MRSA making ZEVTERA the first and only cephalosporin to achieve that feat. Physicians now have a new, innovative option to treat this lethal infection.

Adding to the innovation story are the attributes of tenacity and creativity.
Despite the first patient entering the initial trial way back in 2006 and the ownership of the compound passing through several developers, there was still the belief - a tenacious belief- among many of the scientists involved that this compound fulfilled an unmet need in MRSA therapy. Maintaining that passion and continuing to advocate for ZEVTERA's development, especially when many other big and small pharma companies exited the antibiotic R&D space was the definition of scientific tenacity
Cephalosporins are generally considered one of the safest and most preferred classes of antibiotics among providers due to their broad-spectrum activity, low toxicity, and efficacy against a wide range of bacterial infections. Zevtera's scientists recognized, however, that unlike earlier cephalosporin

generations ZEVTERA was unique in that it maintained efficacy against both gram positive and gram-negative bacteria, establishing it a potential new option to treat SAB as a monotherapy.

The next challenge was to creatively develop a clinical program to test that hypothesis despite the fact that no double blind, randomized non inferiority trial had ever been done for this indication. With ERADICATE the team succeeded in creating the largest trial that had ever been done in this area. Conducting the trial globally and including diverse patient groups was a further creative approach and added to the overall impact of the ERADICATE study.

A final creative step was to not choose the typical MRSA antibiotic vancomycin as the comparator. Going against the newer and more formidable daptomycin as the comparator in the ERADICATE study was the bolder and more innovative move and has resulted in data more reflective of clinical practice in treating persistent SAB here in the US.

The New England Journal of Medicine recognized the scientific importance of this study publishing the results in 2023. A further testament to the innovative and creative approach to the overall development of ZEVTERA.

Further research could delve into ZEVTERA's potential application in personalized medicine, paving the way for treatments tailored to individual patient needs.

The extraordinary journey of ZEVTERA from its inception to FDA approval marks a pivotal advancement in the treatment of serious bacterial infections, an area often overlooked by pharmaceutical companies. Its development reflects a steadfast commitment to innovation, resulting in a versatile therapy that not only meets urgent clinical needs but also paves the way for future breakthroughs in infectious disease research and development.

words remaining :
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Please provide appropriate references (PubMed, Abstract, Website) *

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