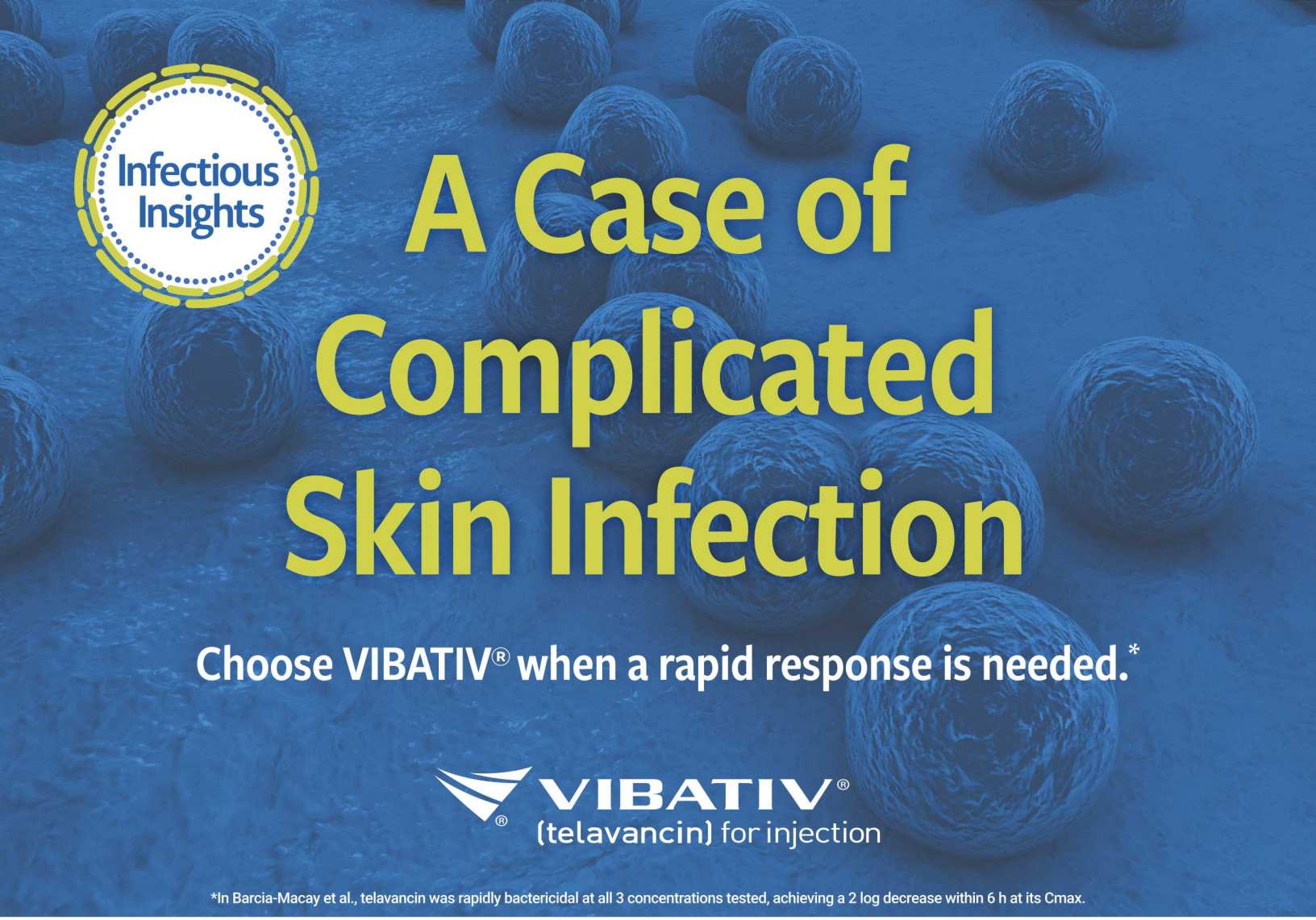


Vibativ® (telavancin) Injection

INDICATION: Vibativ is indicated in adults for the treatment of:

- complicated skin and skin structure infections (cSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-susceptible and -resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), or *Enterococcus faecalis* (vancomycin-susceptible isolates only).
- hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP), caused by susceptible isolates of *Staphylococcus aureus* (both methicillin-susceptible and -resistant isolates). Vibativ should be reserved for use when alternative treatments are not suitable.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vibativ and other antibacterial drugs, Vibativ should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

WARNING: INCREASED MORTALITY IN HABP/VABP PATIENTS WITH PRE-EXISTING MODERATE OR SEVERE RENAL IMPAIRMENT, NEPHROTOXICITY, and EMBRYO-FETAL TOXICITY

Patients with pre-existing moderate/severe renal impairment (CrCl ≤50 mL/min) who were treated with VIBATIV for hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia had increased mortality observed versus vancomycin. Use of VIBATIV in patients with pre-existing moderate/severe renal impairment (CrCl ≤50 mL/min) should be considered only when the anticipated benefit to the patient outweighs the potential risk.

- Nephrotoxicity: New onset or worsening renal impairment has occurred. Monitor renal function in all patients.
- Embryo-Fetal Toxicity: VIBATIV may cause fetal harm. In animal reproduction studies, adverse developmental outcomes were observed in 3 animal species at clinically relevant doses. Verify pregnancy status prior to initiating treatment and advise females of reproductive potential to use effective contraception.

Please see Important Safety Information throughout, and the accompanying full Prescribing Information, including Boxed Warning.

Why VIBATIV?

Infection may occur if planktonic bacteria comes into contact with an implanted device, including but not limited to a prosthetic joint, and adheres and colonizes the foreign material. Many of these bacteria form biofilm that protects the pathogen from both the host immune response and antibiotics, making prosthetic joint infections (PJI) difficult to treat.[5]

Ideal Anti-Biofilm Antibiotic Characteristics:[5]

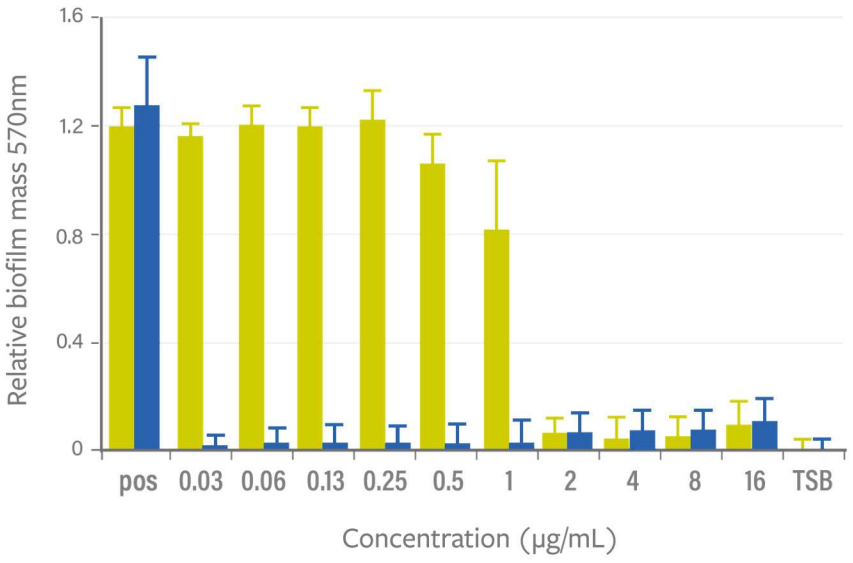
- ✓ Bactericidal mode of action
- ✓ Bactericidal activity against bacteria under the biofilm matrix-sessile state
- ✓ No inoculum effect
- ✓ Efficacy against biofilm-producing pathogens
- ✓ Ability to penetrate within biofilm

Staphylococcus aureus has been reported as one of the most common bacterial strains associated with knee and hip PJI, accounting for over 38% of joint infections.[6]

Infections caused by biofilm formation may lead to tissue destruction, systemic transmission of pathogens, severe systemic disease and even death.[7]

At clinically achievable concentrations, VIBATIV® (telavancin) was active against bacteria embedded in biofilm and bacteria seeding from a formed biofilm mass and inhibited biofilm development.[4]

Highly Effective Against: Biofilm-producing *Staphylococcus aureus* (ATCC 35556)



VIBATIV

Vancomycin

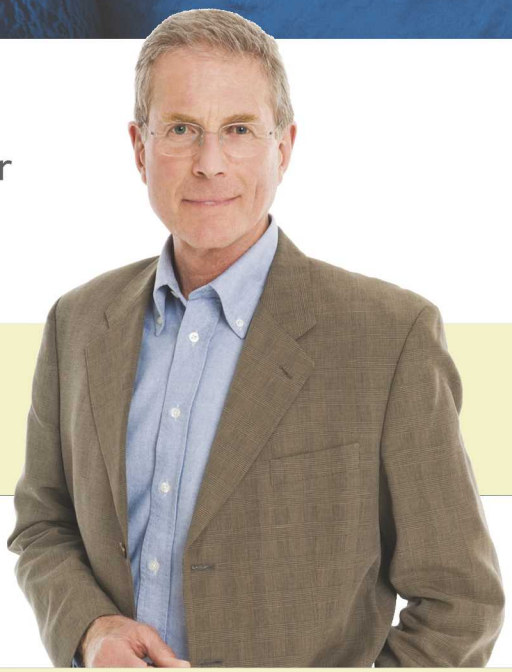
TSB = Tryptic soy broth
Biofilm-forming *S. aureus*, *S. epidermidis*, and *E. faecalis* strains were grown in 96-well polystyrene plates exposed to increasing concentrations of VIBATIV or vancomycin. Results are averages of four duplicates +/- the standard error of the mean. TSB, negative control wells containing TSB only; pos, positive control wells (no drug).

IMPORTANT DOSAGE AND ADMINISTRATION INSTRUCTIONS

Because telavancin is eliminated primarily by the kidney, a dosage adjustment is required for patients whose creatinine clearance is ≤50 mL/min. There is insufficient information to make specific dosage adjustment recommendations for patients with end-stage renal disease (CrCl <10 mL/min), including patients undergoing hemodialysis.

JOE M. | 65yo male, 82kg, Lawyer

(Not an actual patient. For illustration only.)



MEDICAL HISTORY

- History of osteoarthritis in right knee
- Baseline BUN 20 mg/dL, SCr 0.9 mg/dL

CURRENT MEDICATIONS

- Naproxen
- Acetaminophen

HISTORY OF PRESENT ILLNESS

- Patient underwent right total knee arthroplasty (TKA). On postoperative day 4, he experienced erythema, increased pain, swelling, and warmth around surgical incision with a subjective fever. JM was directed to report to the hospital and was subsequently admitted for intravenous antibiotics.

PHYSICAL EXAMINATION AT ADMISSION

- Tmax 38.5°C, BP 135/85, HR 95
- SCr 0.9 mg/dL
- WBC 14,000/mm^3, ESR 100 mm/hr, CRP 12.5 mg/L (normal < 1 mg/L)
- Right knee inflamed, red, tender to touch
- Blood and surgical site cultures from operating room wound debridement were obtained.

INITIAL TREATMENT

- Patient was started on Vancomycin to be dosed per local protocol + Cefepime 2g IV q12h
- On postoperative day 5 (hospital day 1), ID consult recommended to discontinue use of current antibiotic regimen and initiate VIBATIV (telavancin) 10 mg/kg daily for **better biofilm penetration**

TREATMENT TIMELINE

- Less than 48 hours later, the patient showed improvement in signs and symptoms - JM was afebrile, WBC normalized to 9,700/mm^3, and wound exudate no longer present
- Blood cultures resulted no growth. Wound culture revealed MRSA susceptible to vancomycin with MIC=0.5
- Patient received 3 doses of VIBATIV in the hospital setting and was discharged home on postoperative day 7 with OPAT therapy planned for 6 weeks of VIBATIV 820mg IV daily (10 mg/kg)

Once-daily dosing with no therapeutic drug-level monitoring required.[3]

Dosing Adjustments for Patients with Renal Impairment

Creatinine Clearance CrCl (mL/min)	VIBATIV Dosage Regimen
>50	10 mg/kg every 24 hours
30-50	7.5 mg/kg every 24 hours
10-<30	10 mg/kg every 48 hours

Calculate CrCl using the Cockcroft-Gault formula and ideal body weight (IBW). Use actual body weight if it is less than IBW.
Insufficient data are available to make a dosing recommendation for patients with CrCl < 10 mL/min, including patients on hemodialysis.

IMPORTANT SAFETY INFORMATION CONTINUED

CONTRAINDICATIONS

Vibativ should not be used with intravenous unfractionated heparin sodium because the activated partial thromboplastin time (aPTT) test results are expected to be artificially prolonged for 0 to 18 hours after Vibativ administration. Do not be use in patients with known hypersensitivity to Vibativ (telavancin).

WARNINGS AND PRECAUTIONS

- Decreased efficacy among patients treated for cSSSI with moderate/severe pre-existing renal impairment. Consider when selecting antibacterial therapy for patients with baseline CrCl ≤50 mL/min.
- Laboratory tests: interferes with some laboratory coagulation tests, including prothrombin time, international normalized ratio, and activated partial thromboplastin time.
- Serious and potentially fatal hypersensitivity reactions, including anaphylactic reactions, may occur after first or subsequent doses. Use with caution in patients with known hypersensitivity to vancomycin.
- Administer Vibativ over at least 60 minutes to minimize infusion-related reactions.
- Clostridium difficile-Associated Diarrhea; may range from mild diarrhea to fatal colitis. Evaluate if diarrhea occurs.
- Avoid use in patients at risk for QTc prolongation and who are taking drugs known to prolong the QT interval.

ADVERSE REACTIONS

The most common adverse reaction (≥10% of patients treated with Vibativ) in the HABP/VABP trials is diarrhea; in the cSSSI trials, the most common adverse reactions (≥10% of patients treated with Vibativ) include: taste disturbance, nausea, vomiting, and foamy urine.

USE IN SPECIAL POPULATIONS

Pediatric Use: Safety and efficacy have not been established. There is a concern for poor clinical outcomes in pediatric patients less than one year of age due to immature renal function.

References:

1. Ruggero MA, et al. Telavancin for refractory methicillin-resistant Staphylococcus aureus bacteremia and infective endocarditis. Infectious Dis. 2015; 1 – 6.
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3. Vibativ® [Package Insert]. Nashville, TN: Cumberland Pharmaceuticals Inc.; November 2023.
4. Chan C, et al. A review of telavancin activity in in-vitro biofilms and animal models of biofilm-associated infections. Future Microbiol. 2015; 10(8): 1325 –1338.
5. Jacqueline C, Caillon J. Impact of bacterial biofilm on the treatment of prosthetic joint infections. J Antimicrob Chemo. 2014; 69 Suppl 1: i37-i40.
6. Visperas A, et al. Current treatments for biofilm-associated periprosthetic joint infection and new potential strategies. J Orthop Res. 2022; 40: 1477-1491.
7. Xie H, et al. Recent advances in prevention detection and treatment in prosthetic joint infections of bioactive materials. Frontiers in Bioengineering and Biotechnology. 2022; Nov 10:10:1053399.

Please see Important Safety Information throughout,
and the accompanying full Prescribing Information, including Boxed Warning.

CUMBERLAND® PHARMACEUTICALS

POT1300124

Infectious Insights

A Case of Complicated Skin Infection

A short three-part video series with case study and commentary by Joseph Reilly, BS, PharmD, BCGP

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Infectious Insights is a case series designed to discuss challenges and offer solutions for difficult-to-treat gram-positive bacterial infections. These cases offer real-world examples of the use of telavancin as a treatment for complicated post-surgical infections, infections that involve biofilm-forming bacteria, and hospital-acquired infections.

VIBATIV® (telavancin) is a product of Cumberland Pharmaceuticals. Please see full Important Safety Information including Boxed Warning and full Prescribing Information at the links below.

VIBATIV® (telavancin)
vibativ.com

Important Safety Information
vibativ.com/#importantsafetyinformation

Clinical References
vibativ.com/references

Reference Request
vibativ.com/contact-us

Difficult-to-Treat Patient With a Heavy Burden of Biofilm

Clinical Options in Difficult-to-Treat Patients

Telavancin Utility in the Outpatient Setting

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