Access VIBATIV® (telavancin)

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Theravance Biopharma
Medicines That Make a Difference®

VIBATIV®
(telavancin) for injection

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VIBATIV® (telavancin) for injection, for intravenous use

Rx ONLY

BRIEF SUMMARY. See package insert available at www.vibativ.com for full Prescribing Information, including Boxed Warning and Medication Guide.

INDICATIONS AND USAGE: VIBATIV is a lipoglycopeptide antibacterial drug indicated for the treatment of the following infections in adult patients caused by designated susceptible bacteria:

- Complicated skin and skin structure infections (cSSSI)
- Hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) caused by susceptible isolates of *Staphylococcus aureus*. VIBATIV should be reserved for use when alternative treatments are not suitable.

CONTRAINDICATIONS:

- VIBATIV is contraindicated in patients who require intravenous unfractionated heparin sodium due to the potential of an artificially prolonged activated partial thromboplastin time (aPTT) up to 18 hours after VIBATIV administration.
- VIBATIV is contraindicated in patients with known hypersensitivity to telavancin.

WARNINGS: INCREASED MORTALITY IN HABP/VABP PATIENTS WITH PRE-EXISTING MODERATE OR SEVERE RENAL IMPAIRMENT, NEPHROTOXICITY, POTENTIAL ADVERSE DEVELOPMENTAL OUTCOMES

- **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 (HABP/VABP) 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.**
- **Women of childbearing potential should have a serum pregnancy test prior to administration of VIBATIV. Avoid use of VIBATIV during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus. Adverse developmental outcomes observed in 3 animal species at clinically relevant doses raise concerns about potential adverse developmental outcomes in humans.**

WARNINGS AND PRECAUTIONS: Increased Mortality in Patients with HABP/VABP and Pre-existing Moderate to Severe Renal Impairment (CrCl ≤50 mL/min): In the analysis of patients (classified by the treatment received) in the two combined HABP/VABP trials with pre-existing moderate/severe renal impairment (CrCl ≤50 mL/min), all-cause mortality within 28 days of starting treatment was 95/241 (39%) in the VIBATIV group, compared with 72/243 (30%) in the vancomycin group. All-cause mortality at 28 days in patients without pre-existing moderate/severe renal impairment (CrCl >50 mL/min) was 86/510 (17%) in the VIBATIV group and 92/510 (18%) in the vancomycin group. Therefore, VIBATIV use in patients with baseline CrCl ≤50 mL/min should be considered only when the anticipated benefit to the patient outweighs the potential risk. **Decreased Clinical Response in Patients with cSSSI and Pre-existing Moderate/Severe Renal Impairment (CrCl ≤50 mL/min):** In a subgroup analysis of the combined cSSSI trials, clinical cure rates in the VIBATIV-treated patients were lower in patients with baseline CrCl ≤50 mL/min compared with those with CrCl >50 mL/min. A decrease of this magnitude was not observed in vancomycin-treated patients. Consider these data when selecting antibacterial therapy for use in patients with cSSSI and with baseline moderate/severe renal impairment. **Nephrotoxicity:** In both the HABP/VABP trials and the cSSSI trials, renal adverse events were more likely to occur in patients with baseline comorbidities known to predispose patients to kidney dysfunction (pre-existing renal disease, diabetes mellitus, congestive heart failure, or hypertension). The renal adverse event rates were also higher in patients who received concomitant medications known to affect kidney function (e.g., non-steroidal anti-inflammatory drugs, ACE inhibitors, and loop diuretics). Monitor renal function (i.e., serum creatinine, creatinine clearance) in all patients receiving VIBATIV. Values should be obtained prior to initiation of treatment, during treatment (at 48- to 72-hour intervals or more frequently, if clinically indicated), and at the end of therapy. If renal function decreases, the benefit of continuing VIBATIV versus discontinuing and initiating therapy with an alternative agent should be assessed. In patients with renal dysfunction, accumulation of the solubilizer hydroxypropyl-betacyclodextrin can occur. **Pregnant Women and Women of Childbearing Potential:** Avoid use of VIBATIV during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus. VIBATIV caused adverse developmental outcomes in 3 animal species at clinically relevant doses. This raises concern about potential adverse developmental outcomes in humans. Women of childbearing potential should have a serum pregnancy test prior to administration of VIBATIV. If not already pregnant, women of childbearing potential should use effective contraception during VIBATIV treatment. **Coagulation Test Interference:** Although telavancin does not interfere with coagulation, it interfered with certain tests used to monitor coagulation, when conducted using samples drawn 0 to 18 hours after VIBATIV administration for patients being treated once every 24 hours. Blood samples for these coagulation tests should be collected as close as possible prior to a patient's next dose of VIBATIV. Blood samples for coagulation tests unaffected by VIBATIV may be collected at any time. No evidence of increased bleeding risk has been observed in clinical trials with VIBATIV. Telavancin has no effect on platelet aggregation. Furthermore, no evidence of hypercoagulability has been seen, as healthy subjects receiving VIBATIV have normal levels of D-dimer and fibrin degradation products. **Hypersensitivity Reactions:** Serious and sometimes fatal hypersensitivity reactions, including anaphylactic reactions, may occur after first or subsequent doses. Discontinue VIBATIV at first sign of skin rash, or any other sign of hypersensitivity. Telavancin is a semi-synthetic derivative of vancomycin; it is unknown if patients with hypersensitivity reactions to vancomycin will experience cross-reactivity to telavancin. VIBATIV should be used with caution in patients with known hypersensitivity to vancomycin. **Infusion-Related Reactions:** VIBATIV is a lipoglycopeptide antibacterial agent and should be administered over a period of 60 minutes to reduce the risk of infusion-related reactions. Rapid intravenous infusions of the glycopeptide class of antimicrobial agents can cause "Red-man Syndrome"-like reactions including: flushing of the upper body, urticaria, pruritus, or rash. Stopping or slowing the infusion may result in cessation of these reactions. ***Clostridium difficile*-Associated Diarrhea:** *Clostridium difficile*-associated diarrhea (CDAD) has been reported with nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the flora of the colon and may permit overgrowth of *C. difficile*. *C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin-producing strains of *C. difficile* cause increased morbidity and mortality, since these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated. **Development of Drug-Resistant Bacteria:** Prescribing VIBATIV in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. As with other antibacterial drugs, use of VIBATIV may result in overgrowth of nonsusceptible organisms, including fungi. Patients should be carefully monitored during therapy. If superinfection occurs, appropriate measures should be taken. **QTc Prolongation:** In a study involving healthy volunteers, doses of 7.5 and 15 mg/kg of VIBATIV prolonged the QTc interval. Caution is warranted when prescribing VIBATIV to patients taking drugs known to prolong the QT interval. Patients with congenital long QT syndrome, known prolongation of the QTc interval, uncompensated heart failure, or severe left ventricular hypertrophy were not included in clinical trials of VIBATIV. Use of VIBATIV should be avoided in patients with these conditions.

ADVERSE REACTIONS: In the cSSSI clinical trials, serious adverse events were reported in 7% (69/929) of patients treated with VIBATIV and most commonly included renal, respiratory, or cardiac events. Serious adverse events were reported in 5% (43/938) of vancomycin-treated patients, and most commonly included cardiac, respiratory, or infectious events. Treatment discontinuations due to adverse events occurred in 8% (72/929) of patients treated with VIBATIV, the most common events being nausea and rash (~1% each). Treatment discontinuations due to adverse events occurred in 6% (53/938) of vancomycin-treated patients, the most common events being rash and pruritus (~1% each). The most common adverse events occurring in ≥10% of VIBATIV-treated patients were taste disturbance, nausea, vomiting, and foamy urine. The following table displays the incidence of treatment-emergent adverse drug reactions reported in ≥2% of patients treated with VIBATIV possibly related to the drug.

	VIBATIV (N=929)	Vancomycin (N=938)
Body as a Whole		
Rigors	4%	2%
Digestive System		
Nausea	27%	15%
Vomiting	14%	7%
Diarrhea	7%	8%
Metabolic and Nutritional		
Decreased appetite	3%	2%
Nervous System		
Taste disturbance*	33%	7%
Renal System		
Foamy urine	13%	3%

*Described as a metallic or soapy taste.

In HABP/VABP clinical trials, serious adverse events were reported in 31% of patients treated with VIBATIV and 26% of patients who received vancomycin. Treatment discontinuations due to adverse events occurred in 8% (60/751) of patients who received VIBATIV, the most common events being acute renal failure and electrocardiogram QTc interval prolonged (~1% each). Treatment discontinuations due to adverse events occurred in 5% (40/752) of vancomycin-patients, the most common events being septic shock and multi-organ failure (<1%). The following table displays the incidence of treatment-emergent adverse drug reactions reported in ≥5% of HABP/VABP patients treated with VIBATIV possibly related to the drug.

	VIBATIV (N=751)	Vancomycin (N=752)
Nausea	5%	4%
Vomiting	5%	4%
Renal Failure Acute	5%	4%

OVERDOSAGE: In the event of overdosage, VIBATIV should be discontinued and supportive care is advised with maintenance of glomerular filtration and careful monitoring of renal function. The clearance of telavancin by continuous venovenous hemofiltration (CVVH) has not been evaluated in a clinical study.

Manufactured for:
Theravance Biopharma Antibiotics, Inc.

Marketed by:
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Medicines That Make a Difference®

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