



# CLINICAL COMMUNICATOR

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## SPECIAL POINTS OF INTEREST

*The manufacturer recommends that renal function be monitored in all patients on telavancin therapy*

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Review of Telavancin

## Vibativ™ (telavancin) New Antibiotic for Serious Skin Infections

*The following is a brief discussion of a newly approved drug. Please refer to the complete FDA-approved prescribing information for more complete information.*

Telavancin is a lipoglycopeptide, a semi-synthetic derivative of vancomycin. It is the first drug to be approved in this new class of antibiotics. Telavancin has rapid concentration-dependent bactericidal action against some gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). Telavancin is FDA-approved for treatment of adults with complicated skin and skin structure infections caused by susceptible gram-positive organisms. It is also under investigation for treatment of hospital acquired pneumonia. In comparison to vancomycin, telavancin had a similar cure rate for treatment of complicated skin and skin structure infections.

**Warning: Avoid use in pregnant women** as treatment could result in abnormal fetal development. A pregnancy test should be administered to female patients of child-bearing age prior to use of telavancin. If the patient is not pregnant, effective contraception should be used during treatment. A pregnancy registry has been established at 1-888-658-4228 to monitor the pregnancy outcome of any female exposed to telavancin during pregnancy.

**Mechanism of Action:** Like other kinds of glycopeptides, telavancin inhibits bacterial cell wall synthesis. A second mechanism involves disrupting the integrity of the bacterial cell membrane by incorporating part of the drug molecule into the membrane, causing depolarization and increased permeability.

**Pharmacokinetics:** Telavancin is administered intravenously. It is not metabolized in the liver and is not expected to be altered by liver enzyme inducers or inhibitors; the exact mechanism for metabolism is unknown. It is primarily eliminated by the kidneys. The elimination half-life in adults is 8-9 hours. Telavancin displays linear pharmacokinetic properties. It is 93% bound to human plasma proteins (primarily albumin); this protein binding has minimal impact on its efficacy.

**Indications:** Treatment of complicated skin and skin structure infections caused by susceptible bacteria, such as *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus* (methicillin resistant-MRSA), *Staphylococcus aureus* (methicillin susceptible-MSSA), *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, and certain other *Strep* species.

### Dosing:

**Adults:** 10 mg/kg by IV infusion over 60 minutes once every 24 hours for 7-14 days; actual duration of therapy to be determined by the patient's infection, clinical status, and progress.

**Renal dysfunction:** dose reductions are recommended for patients with renal impairment. Patients with baseline renal dysfunction have a decreased response to treatment with telavancin and drug-related nephrotoxicity was reported to occur more often in these patients. Refer to the complete prescribing information for guidance.

**Children and Adolescents:** safety and efficacy have not been established.



**Precautions:**

- Infusion-related reactions such as “red man syndrome” may occur if the dose is administered too rapidly. Infuse each dose over at least 60 minutes.
- Telavancin does not affect coagulation or platelet aggregation, but may interfere with the results of certain lab tests used to monitor coagulation status. It may also affect urine protein tests such as qualitative dipstick protein assays and quantitative dye methods. Refer to the complete prescribing information for details.
- *Clostridium* difficile-associated diarrhea (CDAD) has been reported with nearly all antibiotics and may range in severity from mild diarrhea to fatal colitis. Consider CDAD in all patients with diarrhea following antibiotic use.
- Telavancin has been associated with prolongation of the QT interval in clinical trials. Avoid use in patients with a history of congenital QT syndrome, known prolongation of the QTc interval, uncompensated heart failure, severe left ventricular hypertrophy, or receiving treatment with other drugs known to prolong the QTc interval.
- Avoid use with other potentially nephrotoxic drugs or monitor closely if such drugs must be used concurrently.
- Cross-sensitivity – use caution in patients with known hypersensitivity to vancomycin.

**Adverse Reactions:**

Compared to vancomycin, patients treated with telavancin in clinical trials experienced more serious adverse events (7% for telavancin – most commonly renal, respiratory, or cardiac vs. 4% for vancomycin – most commonly cardiac, respiratory or infectious). More patients in the telavancin group (8%) discontinued therapy compared to vancomycin (6%) due to an adverse event.

Nephrotoxicity occurred in 3% of patients in two clinical trials. Nephrotoxicity was more common in patients with baseline comorbid conditions and in patients receiving other medications that affect kidney function. Renal dysfunction was mild and reversible in most cases, but 6 patients discontinued telavancin due to adverse renal effects.

Other reported effects included abnormal or foamy urine (13%), chills or rigors (4%), dizziness (6%), fatigue (4%), headache (14%), and/or insomnia (10%). A soapy or metallic alteration in taste may occur (33%). Nausea/vomiting was reported but was usually mild (27%/14%). Constipation was also reported (10%). One patient developed temporary, mild hearing loss during telavancin treatment.

**Lab Monitoring:**

- **Renal function** – monitor in all patients. Obtain baseline serum creatinine concentrations prior to starting telavancin therapy, every 48-72 hours, and after treatment is completed.
- **Potassium** – Hyperkalemia (2%) or hypokalemia (2%) may occur in frequencies similar to that reported for vancomycin. Consider monitoring serum potassium.
- **Hepatic enzymes** – Elevated hepatic enzymes may occur with a frequency (2%) similar to vancomycin. Consider monitoring hepatic enzymes.
- **Hematologic changes** – Incidence is comparable to vancomycin and may include anemia (1-4%) eosinophilia (2%), leukopenia (1%), thrombocytopenia (<1%). Monitor for hematologic adverse events during therapy.

**Drug Mixing and Stability:**

Telavancin powder is mixed with 5% Dextrose, Sterile Water for Injection, or 0.9% Sodium Chloride to a concentration in the vial of 15 mg/mL. For doses of 150 – 800 mg, the dose should be further diluted in 100 – 250 mL of an appropriate infusion solution such as 5% Dextrose, 0.9% Sodium Chloride or Lactated Ringer’s. Doses less than 150 mg or greater than 800 mg should be diluted to achieve a final concentration of 0.6 – 8 mg/mL. The drug is stable in the vial or in the infusion bag for 4 hours at room temperature or 72 hours under refrigeration; the total time of mixed drug in the vial plus the time in the infusion bag should not exceed these time parameters.

**Full prescribing information and a patient Medication Guide to Vibativ™ are available at [www.vibativ.com](http://www.vibativ.com)**

**References:**

1. Prescribing information
2. Gold Standard, Inc, Clinical Pharmacology: Telavancin. Accessed on October 13, 2009.