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Direct Healthcare Professional Communication on the launch of Vibativ® ▼ (telavancin): recommendations for use and important risks (nephrotoxicity, QTc prolongation, reproductive toxicity and off-label use)

Dear Healthcare Professional,

Introduction

This letter is to inform you of important safety concerns associated with the use of Vibativ® and how to manage these in order to minimize the risk to the patient. Clinigen is providing this information as a requirement set by the European Medicines Agency; this letter is a mandatory condition of the marketing authorisation.

Summary

- Telavancin is a new antibiotic agent approved in the European Union for the treatment of nosocomial pneumonia (including ventilator-associated pneumonia), known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA) when alternative treatments are not appropriate or have failed.

- The benefit/risk balance of telavancin in treatment of complicated skin and soft tissue infections was assessed as negative by the CHMP, the EU committee providing scientific opinions on marketing authorisation applications for medicinal products. Therefore telavancin should not be used in this or other non-approved indications.

- In clinical studies, patients with preexisting acute renal failure receiving telavancin had an increased risk of death compared with those receiving vancomycin. The use of telavancin is therefore contraindicated in patients with severe renal impairment (CrCl <30 ml/min including patients undergoing haemodialysis). In all patients treated with telavancin, renal function should be monitored daily for at least the first 3-5 days of therapy and every 48 to 72 hours thereafter.

- QTc prolongation was observed in clinical trials. Use caution when administering telavancin with other QTc-prolonging medicines and in patients who are at high risk of QTc prolongation.

- The use of telavancin is contraindicated during pregnancy. There are no data on the use of telavancin in pregnant women. Studies in animals have shown reproductive toxicity (including teratogenic effects). Therefore a negative pregnancy status has to be confirmed and documented prior to administration of Vibativ® to women of child bearing potential.

Further information on correct use, safety concerns and recommendations

Telavancin is a new lipoglycopeptide antibiotic given as an intravenous infusion and indicated for the treatment of adults with nosocomial pneumonia (NP) including ventilator associated pneumonia, known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA).

Telavancin demonstrated efficacy against methicillin susceptible *Staphylococcus aureus* (MSSA) and MRSA in two randomized controlled studies in patients with NP, including ventilator associated pneumonia.

Nephrotoxicity

In clinical studies, patients with preexisting acute renal failure receiving telavancin had an increased risk of death compared with those receiving vancomycin. All-cause mortality was 32/73 (44%) in the telavancin group, and 16/64 (25%) in the vancomycin group. In patients without acute renal failure at baseline all-cause mortality was 118/678 (17%) and 124/688 (18%), respectively. Therefore, the use of **telavancin is contraindicated in patients with preexisting acute renal failure and in patients with severe renal impairment (CrCl <30 ml/min including patients undergoing haemodialysis).**

In pooled clinical studies (nosocomial pneumonia and complicated skin and soft tissue infection), renal adverse reactions were reported more frequently in patients receiving Vibativ® compared with vancomycin (3.8% vs. 2.2%, respectively). **In all patients treated with telavancin renal function (serum creatinine and urinary output for oliguria/anuria) should be monitored daily for at least the first 3 to 5 days of therapy and every 48 to 72 hours thereafter.** Initial dose and dosage adjustments should be made during treatment based on calculated or measured creatinine clearance according to the dosing regimen in section 4.2 of SmPC. **If renal function markedly decreases during treatment, the benefit of continuing telavancin should be assessed.**

Caution should be used when prescribing telavancin to patients receiving concomitant nephrotoxic medication, those with preexisting renal disease or with co- morbidity known to predispose to kidney dysfunction (e.g. diabetes mellitus, congestive heart failure, hypertension). If renal function is affected, take action as above.

QTc prolongation

In a clinical QT study, telavancin produced an average increase in QTcF of 4.1 to 4.5 ms above baseline at 7.5 mg/kg and 15 mg/kg respectively. **Caution is warranted when using telavancin to treat patients taking medicinal products known to prolong the QT interval and in patients with congenital long QT syndrome, known prolongation of the QTc interval, uncompensated heart failure or severe left ventricular hypertrophy.** Healthcare professionals should be alert to any symptoms of arrhythmias such as fainting, palpitations, shortness of breath or chest pain. If symptoms occur, stop telavancin treatment and investigate the symptoms.

Reproductive Toxicity

Telavancin is contraindicated during pregnancy. There are no data on the use of telavancin in pregnant women. Studies in animals have shown reproductive toxicity including teratogenic effects. Women of childbearing potential must take a pregnancy test before receiving telavancin. For documentation of this a checklist-sticker is included with each vial which should be completed and fixed to the patient chart prior to administration of telavancin. Where clinically appropriate, advise women of childbearing potential to use effective contraception during treatment. A pregnancy registry is in place to monitor the pregnancy outcomes of women inadvertently exposed to telavancin while pregnant. Information on this pregnancy registry can be obtained on the Clinigen website www.vibativ.eu. Information can also be obtained by calling **+44 (0)1748 828375** or by emailing clinigenEU@professionalinformation.co.uk.

Call For Reporting - suspected adverse reactions

Suspected adverse reactions should be reported to Clinigen by fax on **+44 (0) 1442 500615** or email pharmacovigilance@Aptivsolutions.com and to the MHRA through the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard.

Company Contact Point

Further information about Vibativ® can be obtained by visiting www.vibativ.eu or via the approved product information available at www.ema.europa.eu.

Yours sincerely,

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