The Medicines Company
8 Sylvan Way
Parsippany, NJ 07054 USA

February 2017

IMPORTANT PRESCRIBING INFORMATION

Subject: Updated Information Regarding the Concomitant Use of Warfarin with ORBACTIV® (oritavancin) for Injection

Dear Healthcare Provider,

The purpose of this letter is to inform you of updates to the Prescribing Information for ORBACTIV® (oritavancin), a semi-synthetic lipoglycopeptide antibacterial drug approved for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of certain gram-positive microorganisms.

Updates to the ORBACTIV® Prescribing Information

A pharmacokinetics study found no drug-drug interaction between ORBACTIV® and warfarin. Based on this study, the approved product labeling for ORBACTIV® has been updated regarding concomitant use of warfarin. The pharmacokinetics of S-warfarin, the more potent warfarin enantiomer, were evaluated following a single dose of warfarin 25 mg given alone or administered concomitantly with a single 1200 mg ORBACTIV® dose at 0, 24, or 72 hours and the results showed no pharmacokinetic effect of ORBACTIV® on S-warfarin C_{max} or AUC. The Warnings and Precautions section of the ORBACTIV® Prescribing Information regarding Potential Risk of Bleeding with Concomitant Use of Warfarin (now Section 5.5) has been updated to remove text that co-administration of ORBACTIV® and warfarin may result in higher exposure of warfarin, which may increase the risk of bleeding. Additional information on the study results has been added to Effect of ORBACTIV® on CYP Substrates (Section 7.1) and Pharmacokinetics (Section 12.3).

Prescriber Action

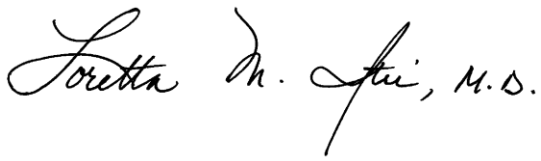
New drug interaction data indicate that ORBACTIV® does not affect the pharmacokinetics of warfarin. ORBACTIV® has been shown to artificially prolong PT/INR for up to 12 hours, therefore patients should be monitored for bleeding if concomitantly receiving ORBACTIV® and warfarin.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report suspected adverse events in patients taking ORBACTIV® to The Medicines Company at 1-888-977-6326. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

This letter is not intended as a complete description of the benefits and risks related to the use of ORBACTIV®. Please refer to the enclosed Full Prescribing Information. You may also contact our medical information department at 1-888-977-6326 if you have any questions about the information contained in this letter or the safe and effective use of ORBACTIV®.

Sincerely,



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Executive Vice President, Global Health Science & Regulatory Affairs
The Medicines Company

Enclosure: ORBACTIV® (oritavancin) Full Prescribing Information