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Editorial

New therapeutic alternatives to treat Acute Bacterial Skin and Skin Structure Infections (ABSSI)

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It has been a while since new alternatives to treat acute bacterial skin and skin structure infections (ABSSI) have been introduced in the market. Last year, FDA approved three new drugs: tedizolid phosphate (SIVEXTRO®), oritavancin (ORBACTIV™), and dalbavancin (DALVANCE®) for the treatment of ABSSI caused by Gram-positive microorganisms such as methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Streptococcus anginosus* group. While tedizolid phosphate (SIVEXTRO®) belongs to the class of Oxazolidinones, oritavancin (ORBACTIV™) and dalbavancin (DALVANCE®) are both lipoglycopeptides.

Tedizolid phosphate (SIVEXTRO®)

Tedizolid phosphate is a prodrug that is metabolically converted to the pharmacologically active tedizolid by the action of phosphatases following oral or intravenous administration. It belongs to the class of oxazolidinones and is structurally different to another member of its class linezolid. Once activated it acts as a protein synthesis inhibitor by binding to the 50S ribosomal subunit of the bacteria resulting in inhibition of protein synthesis. Although the mechanism of action is similar to the other member of its class (Linezolid), it has better ADME (absorption, distribution, metabolism, and excretion) and side effects profile as compared to Linezolid. Other side effect such as anemia, tachycardia, blurred vision, hypersensitivity reactions, pruritus, dermatitis, oral candidiasis, and clostridium difficile colitis have also been reported in a few patients. Tedizolid phosphate is also contraindicated in neutropenic patients. The active compound has a half-life of

approximately 12 hours. It is available in both oral as well as IV formulations where the IV formulations is restricted only for those who are 18 years and older.

Dalbavancin (DALVANCE®) and Oritavancin (ORBACTIV™)

Dalbavancin and Oritavancin are IV-only lipoglycopeptides indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates for the treatment of ABSSI caused by Gram-positive microorganisms such as methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Streptococcus anginosus* group. They act via interfering in the synthesis of bacterial cell wall by inhibiting the synthesis of peptidoglycan layer or by disrupting the bacterial membrane integrity, leading to depolarization, increased permeability and cell death. Dalbavancin and Oritavancin have the half-life of 170-210 and 245 hours respectively, making once a week dosing feasible as compared to vancomycin. Dalbavancin and Oritavancin are contraindicated in patients with known drug related hypersensitivity. Additional infusion-related reactions such as flushing, urticaria, pruritus, and rash can also show up. Similar to Tedizolid, mild to fatal colitis caused by *Clostridium difficile* has been reported with both Dalbavancin and Oritavancin. Oritavancin has shown some additional drug-drug interactions, co-administration of intravenous unfractionated heparin sodium and warfarin with Oritavancin due to the increased risk of bleeding. In Phase 3 clinical trials for the use of Oritavancin for ABSSI, more cases of osteomyelitis were

reported in the patients taking Oritavancin as compared to those taking vancomycin. These three new drugs provide an alternative to the current regime for the treatment for ABSSI. The current pharmacokinetics and pharmacodynamics of these drugs suggest that they might be better alternatives to the existing oxazolidinones and

lipoglycopeptides. However, only years of usage will provide us with more information regarding their application and toxicity profile.

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