of complicated skin and skin structure infections (cSSSi) in 2009 and for treatment of hospital-acquired and ventilator-associated pneumonia caused by *S. aureus* later in 2013 (Table 4.1).

4.5.2 Dalbavancin

Dalbavancin (**4**) is a semisynthetic derivative of the glycopeptide A40926 belonging to the teicoplanin family, which has been modified through the amidation of the C-terminal carboxyl group with a *N*,*N*-dimethylpropylamine group (Anderson and Keating 2009; Candiani et al. 1999). The terminally branched dodecyl fatty acid chain of dalbavancin connected through an amide linkage with the glucosamine moiety helps in membrane anchoring. Dalbavancin binds to D-Ala-D-Ala with higher affinity than its parent compound, by virtue of its ability to form dimers and membrane-anchoring property (Malabarba et al. 1995). This results in better potency than vancomycin and teicoplanin against MRSA and susceptible enterococci. The MIC of dalbavancin was approximately 0.1 $\mu g\,ml^{-1}$ against VRE (VanB phenotype), although it exhibited poor activity against VRE (VanA phenotype) (Candiani et al. 1999). It was approved by the FDA in 2014 for the treatment of acute skin and skin structure infections caused by MSSA, MRSA, streptococci, and vancomycin-sensitive *Enterococcus faecalis*. The half-life ranges from 149 to 250 hours in humans and requires a once-weekly intravenous injection (Zhanel et al. 2010).

4.5.3 Oritavancin

Oritavancin (**5**) is a derivative of chloroeremomycin with an acyl substitution and a lipophilic 4-chlorobiphenyl group attached to the amino group of the epivancosamine moiety (Bouza and Burillo 2010). The biphenyl moiety imparts membrane interaction properties leading to its permeabilization and promotes dimer formation prior to binding to the target peptides, resulting in enhanced binding affinity. Oritavancin has a significant inhibitory effect on transpeptidation in addition to inhibition of transglycosylation (Patti et al. 2009). Its activity against VRE results from its ability to bind the pentaglycyl bridging segment in the peptidoglycan. Its multiple modes of action result in enhanced antibacterial activity against MRSA, VRSA, and VRE (Arhin et al. 2009). This antibiotic exhibits strong bactericidal properties at concentrations where vancomycin had a static effect. It was approved by the FDA in 2014 for the treatment of acute skin and tissue infections caused by MRSA, MSSA, streptococci, and vancomycin-susceptible *E. faecalis*. It has a terminal half-life of approximately 393 hours, which enables treatment with just a single dose administered intravenously (Saravolatz and Stein 2015).