Macrolides are absorbed well into tissues, as seen in the case of telithromycin, where significantly higher concentrations are observed in the target tissues of the respiratory tract, which is similar to previous studies of other macrolides (Shain and Amsden 2002). Excellent tissue penetration is also seen for clarithromycin and azithromycin, where tissue concentrations are much higher than serum levels of macrolide, and azithromycin has a prolonged tissue half-life (Zuckerman 2000).

Contraindications for macrolides are varied, and some are restricted to the 15-membered macrolide azithromycin. Azithromycin has been shown to increase rates of cardiac arrhythmias in patients with coexisting risk factors (Albert and Schuller 2014). Telithromycin's use is restricted to treatment of mild to moderate community-acquired pneumonia due to its hepatotoxicity (Zuckerman et al. 2009). The imidazopyridyl side chain of telithromycin is thought to be associated with adverse health events including hepatic failure and exacerbation of myasthenia gravis (Fernandes et al. 2017).

Macrolides are often used to treat community-acquired pneumonia and other respiratory tract infections (both upper and lower) and are effective against both Gram-positive and Gram-negative bacteria. Generally, the 14-membered macrolides have similar activities to the prototypical erythromycin, while the 15-membered macrolide azithromycin shows less activity against Gram-positive bacteria, but higher activity against Gram-negative bacteria, and 16-membered macrolides are generally less active than erythromycin (Hardy et al. 1988). Ketolides have been shown to have better activity against many Gram-positive organisms than the other macrolides (Champney and Tober 2003). Macrolides such as dirithromycin are approved for acute exacerbations of chronic bronchitis and exacerbations of asthma and chronic obstructive pulmonary disease due to rhinoviruses and uncontrolled inflammatory pathways (FDA 1997; Porter et al. 2016). Roxithromycin has a similar profile to other macrolides for treatment of respiratory tract infections (Hayashi and Kawashima 2012).

Combination therapies that include macrolides have shown success in the treatment of pulmonary disease caused by nontuberculous mycobacteria, and azithromycin and clarithromycin are considered cornerstones of treatment for *M. avium* complex lung disease (van Ingen et al. 2013; Jeong et al. 2016). Macrolides are also currently recommended for treatment of pertussis (Hardy et al. 2016).

Macrolides are generally considered a first-line alternative to those allergic to beta-lactams. They are the first-line recommended treatment for *Legionella pneumophila* (Descours et al. 2017). Macrolides are the most effective treatment of *Helicobacter pylori* infection including duodenal ulcer disease in a standard sequential treatment along with a proton pump inhibitor and amoxicillin (Branquinho et al. 2017; Sivapalasingam and Neal 2015). Macrolides can be used with a potassium-competitive acid blocker to improve the efficacy of a