activity to levofloxacin against MRSA strains that harbored up to four mutations in the quinolone-resistance–determining region (QRDR) if used in concentrations of 16–32 times the MIC, but both daptomycin and vancomycin were even more effective, requiring concentrations of approximately eight times the MIC (Remy *et al.*, 2016). However, no significant activity was observed against quinolone-resistant strains of *E. faecalis* or *E. faecium* (Almer *et al.,* 2004; Remy *et al.*, 2012)

ANAEROBIC BACTERIA

In vitro delafloxacin activity is considerably greater than those of many other quinolones against anaerobic bacteria, including against peptostreptococci, *Propionibacterium acnes*, *Clostridium perfringens*, *C. difficile*, *Bacteroides fragilis*, *Fusobacterium* spp., and *Prevotella* spp. (Andrews *et al.*, 2003; Sillerström *et al.,* 2004).

OTHER ORGANISMS

Delafloxacin is fourfold more potent than levofloxacin and ciprofloxacin against *M. pneumoniae*, and comparable to trovafloxacin in activity against *C. trachomatis* (Nilius *et al.,* 2003). The drug also has good activity against *Chlamydia pneumoniae*, *Mycoplasma fermentans*, *M. hominis*, and *Ureaplasma* spp. (Hammerschlag and Roblin, 2004; Waites *et al.*, 2003). The *in vitro* activity of delafloxacin against *M. tuberculosis* and *M. avium* complex isolates is greater than that of ciprofloxacin, and comparable to that of levofloxacin (Tomioka *et al.*, 2000).

2b. Emerging resistance and cross-resistance

There are currently few data regarding emerging resistance against delafloxacin. Due to its enhanced intrinsic activity against some organisms compared with other fluoroquinolones, isolates with resistance mutations that cause minor elevations in MIC remain susceptible to delafloxacin, despite being affected by target modifications/mutations (Van Bambeke, 2015). However, for many pathogens that exhibit high-level ciprofloxacin resistance, there is cross-class resistance to delafloxacin, as with other fluoroquinolones (see Chapter 101, Ciprofloxacin).

3. MECHANISM OF DRUG ACTION

Similar to other newer generation fluoroquinolones, delafloxacin inhibits both topoisomerase II (DNA gyrase) and topoisomerase IV, which are critical to DNA replication. In addition, it has been suggested that the improved activity of delafloxacin is in part related to the presence of a heteroaromatic substituent at position 1, a weak polarity associated with the presence of a chlorine in position 8, and a lack of basic group in position 7 (Duffy *et al.*, 2010). The absence of a protonatable substituent in position 7 gives delafloxacin an anionic character at neutral pH, which is unusual for a fluoroquinolone. Thus delafloxacin is predominantly found as an anion at physiological pH (~ 7–7.4), and mostly uncharged at more acidic pH (≤ 5.5), whereas moxifloxacin is present mainly as a cation at pH lower than 5.5 and as a zwitterion at higher pH (Van Bambeke, 2015). This specific characteristic may explain why delafloxacin appears to accumulate in bacteria at acidic pH, since the non-ionized form of a drug is more diffusible though biological membranes (Lemaire *et al.*, 2011). For a more detailed description of the action of fluoroquinolones, see Chapter 101, Ciprofloxacin and Chapter 104, Levofloxacin.

4. MODE OF DRUG ADMINISTRATION AND DOSAGE

4a. Adults

Delafloxacin has been used in both oral and intravenous preparations in clinical trials, but the details regarding proposed marketed formulations are not yet available. However, delafloxacin is generally administered twice daily, or once daily in some specific situations, with equivalence in exposure obtained for 300 mg intravenously and 450 mg orally (Van Bambeke, 2015).

The doses used in various clinical trials, particularly for ABSSSI, were 300 mg i.v. (infused over 1 hour) and 450-mg oral tablets twice daily for 5–14 days (O'Riordan *et al.*, 2015; Kingsley *et al.*, 2016) (see section 7, Clinical uses of the drug).

4b. Newborn infants and children

There are no data regarding appropriate doses for newborn infants and children.

4c. Pregnant and lactating mothers

There are no data regarding appropriate doses for pregnant women. However, fluoroquinolone use is generally discouraged in this population (see Chapter 101, Ciprofloxacin).

4d. Those requiring altered dosages

PATIENTS WITH IMPAIRED RENAL FUNCTION

Approximately 66% of intravenously administered delafloxacin is excreted in the urine, with the majority unchanged (Hoover *et al.*, 2016b). Systemic exposure to delafloxacin and the drug's AUC increases with decreased creatinine clearance, particularly in moderate to severe renal impairment (Hoover *et al.*, 2016b). A dose of 200 mg i.v. twice daily has been proposed in severe renal impairment (eGFR 15–29) or for patients undergoing dialysis (Hoover *et al.*, 2013; Hoover *et al.*, 2016a; Hoover *et al.*, 2016b).

PATIENTS WITH IMPAIRED HEPATIC FUNCTION

There are no data available regarding dosage changes in patients with impaired hepatic function.