and hyponatremia, which are more common at high doses. TMP-SMX has several important interactions with other drugs (Table 144-3), including warfarin, phenytoin, and methotrexate.

## FLUOROQUINOLONES

The fluoroquinolones include norfloxacin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin, and delafloxacin. Ciprofloxacin and levofloxacin have the broadest spectrum of activity against gram-negative bacteria, including *P. aeruginosa* (similar to that of third-generation cephalosporins). Because of the risk of selection of resistance during fluoroquinolone treatment of serious pseudomonal infections, these agents are usually used in combination with an antipseudomonal β-lactam. Levofloxacin, moxifloxacin, gemifloxacin, and delafloxacin have additional gram-positive activity, including that against *S. pneumoniae* and some strains of MSSA, and, with the exception of delafloxacin, these agents are used for treatment of community-acquired pneumonia. Strains of MRSA are commonly resistant to all fluoroquinolones except delafloxacin. Moxifloxacin is used as one component of second-line regimens for multidrug-resistant tuberculosis. Fluoroquinolones are no longer used for treatment of gonorrhea because of common resistance in *N. gonorrhoeae*. Fluoroquinolones exhibit concentration-dependent killing, are well absorbed orally, and have elimination half-lives that usually support once- or twice-daily dosing. Oral coadministration with compounds containing high concentrations of aluminum, magnesium, or calcium can reduce fluoroquinolone absorption. The penetration of fluoroquinolones into prostate tissue supports their use for bacterial prostatitis. Fluoroquinolones are generally well tolerated but can cause central nervous system (CNS) stimulatory effects, including seizures; peripheral neuropathy; glucose dysregulation; and tendinopathy associated with Achilles tendon rupture, particularly in older patients, organ transplant recipients, and patients taking glucocorticoids. Other potential effects on connective tissues include an association with increased risk of aortic aneurysm. Worsening of myasthenia gravis also has been associated with quinolone use. Moxifloxacin