and clofazimine for lepromatous disease). Rifampin can be used alone for prophylaxis in close contacts of patients with *H. influenzae* or *N. meningitidis* meningitis. The drug has high oral bioavailability, which is further enhanced when it is taken on an empty stomach. Rifampin has several adverse effects, including elevated aminotransferase levels (14%), rash (1–5%), and gastrointestinal events such as nausea, vomiting, and diarrhea (1–2%). Its many clinically relevant interactions with other drugs mandate the clinician's careful review of the patient's medications before rifampin initiation to assess safety and the need for additional monitoring.

METRONIDAZOLE

Metronidazole is used in the treatment of anaerobic bacterial infections as well as infections caused by protozoa (e.g., amebiasis, giardiasis, trichomoniasis). It is the agent of choice as a component of combination therapy for polymicrobial abscesses in the lung, brain, or abdomen, the etiology of which often includes anaerobic bacteria, and for bacterial vaginosis, pelvic inflammatory disease, mild to moderate *C. difficile*–associated diarrhea, and anaerobic infections, such as those due to *Bacteroides*, *Fusobacterium*, and *Prevotella* species. Metronidazole is bactericidal against anaerobic bacteria and exhibits concentration-dependent killing. It has high oral bioavailability and tissue penetration, including penetration of the blood–brain barrier. The majority of *Actinomyces*, *Propionibacterium*, and *Lactobacillus* species are intrinsically resistant to metronidazole. The major adverse effects include nausea, diarrhea, and a metallic taste. Concomitant ingestion of alcohol may result in a disulfiram-like reaction, and patients are usually instructed to avoid alcohol during treatment. Long-term treatment carries the risk of leukopenia, neutropenia, peripheral neuropathy, and central nervous system toxicity manifesting as confusion, dysarthria, ataxia, nystagmus, and ophthalmoparesis. Through metronidazole's effect on the CYP2C9 drug-metabolizing enzyme, its coadministration with warfarin can result in decreased metabolism and enhanced anticoagulant effects that require close monitoring. Concomitant administration of metronidazole with lithium can result in increased serum levels of lithium and associated toxicity; coadministration with phenytoin can result in phenytoin toxicity and possibly decreased levels of metronidazole.

OXAZOLIDINONES

Linezolid is a bacteriostatic agent and is indicated for serious infections due to resistant gram-positive bacteria, such as MRSA and VRE. The intrinsic resistance of gram-negative bacteria is mediated primarily by endogenous efflux pumps. Linezolid has excellent oral bioavailability. Adverse effects include myelosuppression and ocular and peripheral neuropathy with prolonged therapy. Peripheral neuropathy may be irreversible. Linezolid is a weak, reversible monoamine oxidase inhibitor, and coadministration with sympathomimetics and foods rich in tyramine should be avoided. Linezolid has been associated with serotonin syndrome when coadministered with selective serotonin-reuptake inhibitors. Tedizolid has properties similar to those of linezolid, but with lower dosing it may be less likely to cause adverse hematologic and neuropathic effects.

NITROFURANTOIN

Nitrofurantoin's antibacterial activity results from the drug's conversion to highly reactive intermediates that can damage DNA and other macromolecules. Nitrofurantoin is bactericidal, and its action is concentration dependent. It displays activity against a range of gram-positive bacteria, including *S. aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *E. faecalis*, *Streptococcus agalactiae*, group D streptococci, viridans streptococci, and corynebacteria, as well as gram-negative organisms, including *E. coli* and *Enterobacter*, *Neisseria*, *Salmonella,* and *Shigella* species. Nitrofurantoin is used primarily in the treatment of urinary tract infections and is preferred in the treatment of such infections in pregnancy. It may be used for the prevention of recurrent cystitis. Recently, there has been interest in the use of nitrofurantoin for treatment of urinary tract infections caused by ESBL-producing Enterobacteriaceae such as *E. coli*, although resistance has been growing in Latin America and parts of Europe. Coadministration with magnesium should be avoided because of decreased absorption, and patients should be encouraged to take the drug with food to increase its bioavailability and decrease the risk of adverse effects, which include nausea, vomiting, and diarrhea. Nitrofurantoin may also cause pulmonary fibrosis and drug-induced hepatitis. Because the risk of adverse reactions increases with age, the use of nitrofurantoin in elderly patients is not recommended. Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency are at elevated risk for nitrofurantoin-associated hemolytic anemia.

POLYMYXINS

Colistin and polymyxin B act by disrupting cell membrane integrity and are active against the nonenteric pathogens *P. aeruginosa* and *A. baumannii* but not against *Burkholderia*. These drugs also exhibit activity against many Enterobacteriaceae,with the exceptions of *Proteus*, *Providencia*, and *Serratia* species. They lack activity against gram-positive bacteria. Polymyxins are bactericidal and are available in IV formulations. Colistimethate is converted to the active form (colistin) in plasma. Polymyxins are most often used for infections due to pathogens resistant to multiple other antibacterial agents, including urinary tract infections, hospital-acquired pneumonia, and bloodstream infections. Nebulized formulations have been used for adjunctive treatment of refractory ventilator-associated pneumonia. The most important adverse effect is dose-dependent reversible nephrotoxicity. Neurotoxicity, including paresthesias, muscle weakness, and confusion, is reversible and less common than nephrotoxicity.

QUINUPRISTIN-DALFOPRISTIN

Quinupristin-dalfopristin is a member of the streptogramin class of antibiotics and kills bacteria by inhibiting protein synthesis. The antibacterial spectrum of quinupristin-dalfopristin includes staphylococci (including MRSA), streptococci, and *E. faecium* (but not *E. faecalis*). This drug is also active against *Corynebacterium* species and *L. monocytogenes*. Quinupristin-dalfopristin is not reliably active against gram-negative organisms. It exhibits concentration-dependent killing, with an AUC/MIC ratio predicting efficacy. The clinical use of quinupristin-dalfopristin is largely for infections due to vancomycin-resistant *E. faecium* and other gram-positive bacterial infections. The drug has demonstrated efficacy in a variety of infections, including urinary tract infections, bone and joint infections, and bacteremia. Adverse effects associated with quinupristin-dalfopristin include infusion-related reactions, arthralgias, and myalgias. The arthralgias and myalgias may be severe enough to warrant drug discontinuation. Quinupristin-dalfopristin inhibits the CYP3A4 drug-metabolizing enzyme, with consequent drug interactions (Table 170-4).

FOSFOMYCIN

Fosfomycin is a phosphonic acid antibiotic that has greater activity in acidic environments and is excreted in its active form in the urine. Thus, its use is primarily for prophylaxis and treatment of uncomplicated cystitis. The drug is administered as a single 3-g dose that results in high urine concentrations for up to 48 h. Fosfomycin is active against *S. aureus*, vancomycin-susceptible and vancomycin-resistant enterococci, and a wide range of gram-negative organisms, including *E. coli*, *Enterobacter* species, *S. marcescens*, *P. aeruginosa*, and *K. pneumoniae*. Notably, the vast majority of ESBL-producing Enterobacteriaceae are susceptible to fosfomycin. *A. baumannii* and *Burkholderia* species are resistant. The emergence of resistance to fosfomycin has not been observed during treatment of cystitis but has been documented during treatment of respiratory tract infections and osteomyelitis. The few adverse effects that have been reported include nausea and diarrhea.

CHLORAMPHENICOL

The use of chloramphenicol is limited by its potentially serious toxicities. When other agents are contraindicated or ineffective, chloramphenicol represents an alternative treatment for infections, including meningitis caused by susceptible bacteria such as *N. meningitidis*,