# Chapter 2

# Anti-infective Agents

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## Learning Objectives

- Identify current pharmacologic agents that are appropriate for each condition/diagnosis.
- Recommend optimal pharmacologic interventions based on patient-specific characteristics.
- Provide appropriate patient-specific counseling points and optimal overall medication management.

**Key Terms:** anthelmintics, antibacterials, aminoglycosides, cephalosporins, beta-lactams, carbapenems, cephamycins, monobactams, chloramphenicols, macrolides, erythromycins, ketolides, penicillins, aminopenicillins, penicillinase-resistant penicillins, extended-spectrum penicillins, quinolones, sulfonamides, tetracyclines, glycylcyclines, bacitracins, cyclic lipopeptides, glycopeptides, lincomycins, oxazolidinones, polymyxins, rifamycins, streptogramins, antifungals, allylamines, azoles, echinocandins, polyenes, pyrimidines, antimycobacterials, antituberculosis agents, antivirals, adamantanes, antiretrovirals, HIV entry and fusion inhibitors, HIV protease inhibitors, HIV integrase inhibitors, HIV non-nucleoside reverse transcriptase inhibitors, HIV nucleoside and nucleotide reverse transcriptase inhibitors, interferons, monoclonal antibodies, neuraminidase inhibitors, nucleosides and nucleotides, HCV antivirals, HCV polymerase inhibitors, HCV protease inhibitors, HCV replication complex inhibitors, antiprotozoals

## Overview of Anti-infective Agents

Antimicrobials are medications that prevent and treat infections; they are vital to the health and well-being of society. Often assisting the body's defenses, this wide variety of medications has been developed to manage infections caused by bacteria, viruses, and parasites. The clinical course of any infection is dependent on the interaction between the pathogen and a complex set of host defenses.

The first consideration in selecting antimicrobial therapy is whether an antimicrobial agent is truly needed. The differential diagnosis should indicate whether the cause requires treatment with an antimicrobial drug or whether the infection is self-limiting and will resolve without antimicrobial therapy. For self-limiting infections, supportive treatment and symptom management are recommended. If possible, antimicrobial use should be limited to highly suspicious, empiric, and definitive diagnoses of infection to avoid toxicity and the development of antimicrobial resistance.

Prior to beginning antimicrobial therapy, specimens for culture and sensitivity testing should be obtained. The exceptions to this care are septic patients, in whom prompt antimicrobial therapy should not be delayed if culture specimens cannot be obtained in a timely manner, because early administration of antibiotics in sepsis has shown to reduce mortality. Empiric antimicrobial therapy selection is based on the likely pathogens for the site or type of infection; the patient's medical, medication, and social history; prior antibiotic use; and local susceptibility patterns.

Monitoring includes assessing for resolution of signs and symptoms of infection (e.g., normalization of body temperature and white blood cell [WBC] count) and watching for adverse drug events. Ideally, the antibiotic with the narrowest effective spectrum of activity should be selected. The route of administration should be evaluated daily, and conversion to oral therapy should be made once the patient is clinically improving and able to tolerate it (i.e., functioning gastrointestinal [GI] tract; general exceptions are endocarditis and central nervous system [CNS] infections). Patients not responding to therapy within 2–3 days should be reevaluated to assess the diagnosis, determine whether therapeutic drug concentrations are being achieved, and identify if the patient is immunosuppressed. In addition, further investigation should be conducted to determine if there is an isolated infection (i.e., abscess, foreign body) or if resistance to the therapy has developed.

It is recommended that practitioners follow a systematic approach when selecting an antimicrobial regimen. This approach minimizes the development of resistance, the likelihood of superinfections, and the use of more expensive and potentially more toxic agents.

## Systematic Approach for Selection of Antimicrobials

- Confirm the presence of infection.
- Perform a careful history and physical examination.
- Identify signs and symptoms.
- Identify predisposing factors.
- Identify the pathogen.
- Collect infected material.
- Perform Gram stain.
- Perform serologies.
- Perform culture and sensitivity tests.
- Select an empiric therapy considering every infected site.
- Assess host factors.
- Assess drug factors.
- Monitor therapeutic response.
- Perform clinical assessment.
- Perform laboratory tests.
- Assess for therapeutic failure.

Initial selection of antimicrobial therapy is typically empiric, meaning before the causative pathogen has been identified. Infections are usually acute cases, and delaying treatment can result in serious morbidity or possibly death. Patient-specific factors such as allergy history, age, pregnancy, renal function, liver function, type of infection, infection site, and the cost of medication must be considered when deciding which antimicrobial agent to use. The classic signs and symptoms of infection include fever, elevated WBCs, and pain; however, they may not always be present. Older adults, for example, may experience altered mental status with a urinary tract infection (UTI), so clinicians must always look past the expected and seemingly obvious symptoms.

After beginning antimicrobial therapy, the patient must be monitored for a therapeutic response. Tissue and fluid cultures should be obtained for infections such as pneumonia, meningitis, bacteremia, and pyelonephritis. Cultures can take days to weeks for results to become available, depending on the pathogen. Once a pathogen is confirmed, the patient can be switched to narrower-spectrum antimicrobial therapy based on the susceptibility results. If anaerobic bacteria are suspected but not identified, anaerobic therapy should be continued, as commonly used laboratory culture techniques are often unsuccessful in isolating and identifying anaerobic organisms. Patient monitoring should include similar parameters used for diagnosis. The WBC count and temperature should begin to normalize within 24 to 48 hours. Physical complaints from the patient should also begin to diminish (i.e., decreased pain, shortness of breath, cough, or sputum production) and appetite (if reduced) should improve. Resolution of radiologic changes may lag behind the patient's clinical improvement.

Serum (or other fluid) concentrations of antimicrobials may guide efficacy assessments and prevent toxicity. Antimicrobials that require serum concentration monitoring in patient-specific situations include the aminoglycosides, vancomycin, flucytosine, and some azole antifungals. More efficacious outcomes have been associated with therapeutic aminoglycoside concentrations; for example, for a gram-negative infection, therapeutic peak concentrations have been correlated with better clinical outcomes.

Patient education is critical to optimize efficacy, minimize adverse effects, and prevent the development of antibiotic resistance. If the infection worsens, the patient should report this status to the prescriber, who will then determine whether a different therapy is needed. Patients should be instructed to finish the entire medication regimen, even if they are feeling better, to prevent recurrence and/or the development of antibiotic resistance. They should also report any significant effects or possible "new" secondary infections such as yeast infection or severe diarrhea. They should report serious adverse effects and not stop taking the medication unless instructed to do so. Excess medication should be disposed of properly and not shared or saved for later. Clinicians should explain to their patients that antibiotic resistance is an increasing societal problem and educate them on the rationale for using antimicrobials exactly as prescribed. In addition, they should explain why prescribers reserve the use of these medications for patients who have a suspected or documented bacterial infection and do not prescribe them for self-limiting viral infections.

Prescribing practices involving antibiotics have changed significantly with the rise of antibiotic resistance and the emergence of "superbugs." Clinicians have begun to reserve use of antibiotics for cases where bacterial infection is most likely, and to avoid indiscriminate use in a patient with a suspected viral infection. Because antibiotic resistance is a growing public health issue, prescribers should reserve use of these medications for patients with true infections to avoid contributing to this problem. Antimicrobial stewardship programs have been implemented at hospitals and some outpatient settings, with the goals of optimizing treatment of infections and reducing inappropriate use of antibiotics.

## 2.1 Anthelmintics

Infections with helminths or parasitic worms affect more than 2 billion people worldwide. Worms pathogenic for humans are classified as roundworms (intestinal and tissue nematodes) or as one of two types of flatworms, flukes (trematodes) and tapeworms (cestodes). Worldwide, several types of soil-transmitted helminths infect millions of people in developing countries and can negatively impact the health and well-being of school-aged children. Simultaneous infection with more than one type of helminth is common in tropical, poor, rural areas. In the United States, the most common helminthic infections are caused by intestinal nematodes: *Enterobius vermicularis* (pinworm), *Trichuris trichiura* (whipworm), *Ascaris lumbricoides* (roundworm), *Strongyloides stercoralis* (threadworm), and *Ancylostoma duodenale* and *Necator americanus* (hookworms). Anthelmintics are drugs that treat infections with parasitic worms.

Anthelmintics act either locally within the gut lumen to cause expulsion of worms from the GI tract or systemically against helminths residing outside the GI tract. Broad-spectrum anthelmintics, initially developed for veterinary use, are also used in humans. Unfortunately, treatment for many tissue-dwelling worms, such as filarial parasites, is not completely effective.

Anthelmintics are separated into classes on the basis of their chemical structure and mode of action. Anthelmintic resistance has been widely reported in livestock, and it may be only a matter of time before it emerges in human parasites.

### Ascariasis

Ascariasis is caused by *Ascaris lumbricoides*, a giant roundworm that can grow to be 35 cm long. Endemic areas in the United States include the southeastern parts of the Appalachian range, the Gulf Coast states, and areas with poor sanitation. Symptoms of ascariasis include abdominal discomfort, abdominal obstruction, vomiting, and appendicitis; many patients, however, are asymptomatic. During migration of the larvae through the lungs, patients can present with pneumonitis, fever, cough, eosinophilia, and pulmonary infiltrates on chest x-ray.

Diagnosis is made by identifying the characteristic egg in the stool. Because of a very high egg burden, sample concentration techniques are generally not needed to make the diagnosis. Eosinophilia is marked during worm migration but may be absent during intestinal infection. Treatment of ascariasis is one dose of albendazole or pyrantel pamoate (refer to companion drug grid for detailed drug regimens).

### Enterobiasis

Enterobiasis is caused by the small, threadlike pinworm, *Enterobius vermicularis*, which is approximately 1 cm long. It is a common helminthic infection and primarily affects children. Infection is manifested by a perianal cutaneous irritation caused by the migrating female worm or presence of eggs, which may result in dermatitis and secondary bacterial infections. Children may be restless and have difficulty sleeping. Appendicitis and intestinal perforation occur rarely.

Pinworm can be diagnosed by perianal swab using adhesive tape that is examined microscopically for eggs. Treatment includes two doses of pyrantel pamoate or albendazole with the second dose administered 2 weeks later. Following treatment, all bedding, underclothes, bathroom rungs, and toilet accessories should be sterilized by steaming or washing in the hot-water cycle of a regular washing machine to eradicate eggs. It is critical for all those in the household and those in close contact with the infected person be evaluated and also treated for infection.

## Trichuriasis

Infections caused by *Trichuris trichiura* (whipworm) are typically asymptomatic, but heavy infections may cause gastrointestinal symptoms, malnourishment, and rectal prolapse. Such infections are most common among poor children from resource-poor regions. *Trichuris* worms live in the colon and cecum. Lemon-shaped eggs are easily detected on stool examination. Adult worms, which are typically 3–5 cm long, may be seen on proctoscopy.

The treatment of choice in the United States is albendazole (400 mg daily for 3 doses), which produces cure rates of 70% to 90%. Ivermectin (200 μg/kg daily for 3 doses) may also be used, but has a lower cure rate.

## Anthelmintics

Albendazole
Ivermectin
Praziquantel
Pyrantel

## Case Studies and Conclusions

A 5-year-old boy presents for care, accompanied by his mother. The child is scratching between his legs and has been unable to sleep for the past 2 days. His perianal area is red and irritated and the prescriber has diagnosed the patient with pinworm (*Enterobius vermicularis*) infection. The mother describes she is experiencing similar symptoms.

1. What is the appropriate intervention for this mother once the pediatrician treats the child?

   a. One-time dose of pyrantel pamoate or albendazole
   b. One-time dose of mebendazole or albendazole
   c. One dose of pyrantel pamoate or albendazole, then a second dose 2 weeks later
   d. One dose of mebendazole or albendazole, then a second dose 2 weeks later

Answer C is correct. One dose of pyrantel pamoate or albendazole is given, then a second dose is administered 2 weeks later. Mebendazole is also an effective treatment but is no longer available in the United States.

2. The prescriber selects the optimal drug regimen. What common side effect should you warn the mother of?

   a. Confusion
   b. Behavior changes
   c. Abdominal pain
   d. Seizures

Answer C is correct. Patients on pyrantel pamoate commonly develop abdominal pain and nausea (mild adverse effects).

3. What administration recommendation would you make for taking the drug selected?

   a. May take with food or juice
   b. Must take on empty stomach
   c. Must take only at night
   d. Must take every other day

Answer A is correct. May take with food or juice and none of the other factors are required for appropriate medication administration.

4. Should anyone else be treated for pinworm infection?

   a. No one else needs to be treated.
   b. Only household contacts should be treated.
   c. All individuals in close contact with an infected person should be treated.
   d. All individuals with any contact with an infected person should be treated.

Answer C is correct. All individuals in close contact with the infected person should be treated, including family members.

A 23-year-old female has just returned from her visit to Panama City, Florida, after volunteering with a medical mission group for a month. She has abdominal discomfort and she reports that she ate some undercooked pork and also went swimming in dark, dirty (brackish) water. She is concerned she may have contracted an infection involving pork tapeworm (Taenia solium [*Ascaris lumbricoides*]), which is a fear that is confirmed upon diagnosis by her healthcare provider.

1. What is the appropriate treatment for this patient's condition?

   a. Albendazole 400 mg, single dose
   b. Mebendazole 500 mg, daily for 3 days
   c. Pyrantel pamoate 2 g, single dose
   d. Albendazole 400 mg once, then repeat 2 weeks later

Answer A is correct. Albendazole 400 mg as a single dose is the appropriate treatment in the United States.

2. The prescriber selects the optimal drug regimen. What common side effect would you want to prepare the family to observe for based on your previous answer?

   a. Confusion
   b. Behavior problems
   c. Abdominal pain
   d. Seizures

Answer C is correct. Patients on albendazole commonly develop abdominal pain and nausea (mild adverse effects). More common side effects include elevated liver enzymes and hepatotoxicity, which may also be associated with abdominal pain. Prescribers should monitor LFTS and discontinue therapy if liver enzymes are more than 2 times the upper limit of normal.

3. What administration recommendation would you make for taking the drug selected?

   a. Must take with high fat meal
   b. Must take on empty stomach
   c. Must take only at night
   d. Must take every other day

Answer A is correct. Optimal absorption of albendazole occurs in the presence of a high fat meal.

## 2.2 Antibacterials

The development of new antibiotics has also evolved to "keep up" with bacterial mutations; thus the different categories of antibiotics described in this section have different mechanisms of action that are responsible for their bactericidal (and sometimes bacteriostatic) effects. As is the case with the cephalosporin antibiotics, the mechanism of action may be similar for drug classes, but progressive "generations" of the antibiotic may be developed to increase potency and/or reduce chances of bacterial resistance through mutation of the organism. Antibiotics are unique in their concentration and in the time of exposure required for bacterial killing. While each antibiotic category has a somewhat unique mechanism of action, generally all of these drugs target critical survival mechanisms of the bacteria (such as altering the cell wall or disrupting protein synthesis), resulting in death of the pathogenic organism. One example of recent resistance includes the ability of some bacteria to produce the enzyme penicillinase, which destroys the chemical structure of certain antibiotics (β-lactam ring). Penicillinase-resistant penicillins are an effective tool in our clinical toolbox; however we are aware of current and evolving resistance to these agents. Penicillinase-resistant

penicillins include oxacillin, dicloxacillin, and nafcillin, and are the agents of choice for most staphylococcal disease. However, the recent emergence of methicillin-resistant (MRSA) organisms has reminded the clinical community of the need for heightened efforts to use antibiotics responsibly.

The absorption, distribution, metabolism, and elimination (ADME) of a medication are all critical elements for drug action with the body. One key aspect associated with the ADME process is the amount of drug found in the blood at any given time. Certain medications have a lower safety "tolerance" for large fluctuations of drug in the blood and are termed *narrow therapeutic* agents. Therapeutic drug monitoring is the process of using ADME predictions to estimate a safe range between efficacy and toxicity. It is critical that the ADME of antibacterial agents is accurately predicted to ensure the prescribed drug concentrations remain at therapeutic levels. Therapeutic levels of antibacterial agents are established during clinical trials and are based on specific microbiologic end points—including measurements such as the area under the curve (AUC):minimal inhibitory concentration (MIC) ratio, peak:MIC ratio, and time (T) that the concentration remains greater than MIC (T > MIC).

Aminoglycosides exhibit concentration-dependent bactericidal effects. High-dose, extended-interval aminoglycoside dosing maximizes the peak:MIC ratio through administration of a large dose once daily. Aminoglycosides have a postantibiotic effect (persistent suppression of organism growth after concentrations decrease to less than the MIC), which facilitates the efficacy of this regimen. Fluoroquinolones also exhibit concentration-dependent killing activity. For these antibiotics, the bactericidal effect is characterized by the AUC:MIC ratio. In contrast, beta-lactams (β-lactams) display time-dependent bactericidal effects. Bactericidal activity is most likely when the drug concentration is greater than the MIC (T > MIC) for at least 40% to 50% of the dosing interval. To achieve this effect, the antibiotic is typically administered as a continuous infusion, as a prolonged infusion, or as a series of small, frequent doses.

Many antimicrobials require dosage adjustment in patients with renal dysfunction (if the renal system is a substantial source of elimination) to minimize toxicity, and some may require dosage adjustment in patients with liver dysfunction. Food–drug or drug–drug interactions with certain antibacterial medications (such as occurs with the quinolones and calcium-containing foods or aluminum/magnesium-containing antacids) may decrease absorption of the antibacterial medication. This interaction is usually addressed by separating the administration times or avoiding the combination.

Patients with delayed dermatologic reactions (i.e., rash) to penicillin generally can receive cephalosporins without adverse effects. Patients with type I hypersensitivity reactions (i.e., anaphylaxis) to penicillins should not receive cephalosporins. Although the likelihood of cross-reactivity is low, the severe consequences of an anaphylactic reaction outweigh the benefits of using another β-lactam antibiotic. Non-β-lactam options (depending on the targeted pathogen) include aztreonam, quinolones, sulfonamides, and vancomycin.

Renal function (typically creatinine clearance or estimated glomerular filtration rate) should be calculated for each patient receiving antibiotics; for renally eliminated antibiotics, the dose amount or dosing interval should be adjusted accordingly. Hepatic function should be assessed in each patient receiving medications metabolized via the hepatobiliary system, such as clindamycin, erythromycin, and metronidazole. All concomitant drugs and nutritional supplements should be reviewed to avoid drug–drug interactions. Combination antibiotic therapy may be indicated for polymicrobial infections (e.g., intra-abdominal, gynecologic infections), to produce synergistic killing (such as β-lactam plus aminoglycoside regimens in enterococcal endocarditis), or to prevent the emergence of resistance.

## Aminoglycosides

Amikacin
Gentamicin
Neomycin
Streptomycin
Tobramycin
Paromomycin *(see also the Antiprotozoals section)*

## Cephalosporins

### *First-Generation Cephalosporins*

Cefadroxil
Cefazolin
Cephalexin

### *Second-Generation Cephalosporins*

Cefaclor
Cefprozil
Cefuroxime
Cefotetan *(see also the Cephamycins section)*
Cefoxitin *(see also the Cephamycins section)*

### *Third-Generation Cephalosporins*

Cefdinir
Cefditoren
Cefixime
Cefotaxime
Cefpodoxime
Ceftazidime
Ceftazidime and avibactam
Ceftibuten
Ceftolozane and tazobactam
Ceftriaxone

### *Fourth-Generation Cephalosporins*

Cefepime

### *Fifth-Generation Cephalosporins*

Ceftaroline

## Miscellaneous Beta Lactams

### *Carbapenems*

Doripenem
Ertapenem
Imipenem and cilastatin sodium
Meropenem

### *Cephamycins*

Cefotetan
Cefoxitin

### *Monobactams*

Aztreonam

## Chloramphenicols

Chloramphenicol

## Macrolides

### *Erythromycins*

Erythromycin
Erythromycin estolate
Erythromycin ethylsuccinate
Erythromycin lactobionate
Erythromycin stearate

### *Ketolides*

Telithromycin

### *Other Macrolides*

Azithromycin
Clarithromycin
Fidaxomicin

## Penicillins

### *Natural Penicillins*

Penicillin G (benzathine, potassium, procaine)
Penicillin V potassium

### *Aminopenicillins*

Amoxicillin
Amoxicillin and clavulanate
Ampicillin
Ampicillin and sulbactam

### *Penicillinase-Resistant Penicillins*

Dicloxacillin
Nafcillin
Oxacillin

### *Extended-Spectrum Penicillins*

Piperacillin and tazobactam

## Quinolones

Ciprofloxacin
Finafloxacin
Gemifloxacin
Levofloxacin
Moxifloxacin
Ofloxacin

## Sulfonamides

Co-trimoxazole
Sulfadiazine
Sulfamthoxazole/Trimethoprim
Sulfasalazine

## Tetracyclines

Demeclocycline
Doxycycline
Minocycline
Tetracycline

## Glycylcyclines

Tigecycline

## Antibacterials: Miscellaneous Agents

### *Bacitracins*

Bacitracin

### *Cyclic Lipopeptides*

Daptomycin

### *Glycopeptides*

Dalbavancin
Oritavancin
Telavancin
Vancomycin

### *Lincomycins*

Clindamycin
Lincomycin

### *Oxazolidinones*

Linezolid
Tedizolid

### *Polymyxins*

Colistimethate/colistin
Polymyxin B

### *Rifamycins*

Rifaximin
Rifabutin *(see also the Antimycobacterials section)*
Rifampin *(see also the Antimycobacterials section)*
Rifapentine *(see also the Antimycobacterials section)*

### *Streptogramins*

Quinupristin and dalfopristin

### *Miscellaneous Urinary Anti-infectives*

Fosfomycin
Methenamine
Nitrofurantoin
Trimethoprim

## Case Studies and Conclusions

A 56-year-old man diagnosed with a MRSA infection expresses concern that he has never "not finished" an antibiotic and has always followed the instructions.

1. Why is he now experiencing antibiotic resistance?

   a. He shares the societal problem of progressive mutation.
   b. His body must just be "born" to be resistant.
   c. He may grow out of resistance, so keep trying penicillin.
   d. He may never use penicillin again.

Answer A is correct. Antibacterial resistance is on the rise. The mechanism of penicillin resistance is as follows: β-Lactam antibiotics are capable of being inactivated by β-lactamases that are present in large quantities. The β-lactamases are grouped into four classes. Some Class A and D enzymes are inhibited by β-lactamase inhibitors such as clavulanate and tazobactam. Bacterial resistance to the β-lactam antibiotics may also develop by mechanisms other than destruction by β-lactamases.

A 68-year-old woman has contracted an *S. epidermidis* infection that is methicillin sensitive. An infectious diseases consultant recommends the use of a penicillinase-resistant penicillin. The patient wants to know which medications are included in this category so she can determine if they are "covered by her health plan."

1. Which of the following agents do you advise as being the list of potential penicillinase-resistant penicillins?

   a. Amoxicillin
   b. Dicloxacillin
   c. Moxifloxacin
   d. Azithromycin

Answer B is correct. The penicillinase-resistant penicillins (oxacillin, dicloxacillin, and nafcillin) are resistant to hydrolysis by staphylococcal penicillinase. These semisynthetic penicillins are effective against penicillinase-producing strains of *Staphylococcus*.

Your patient inquires further about which types of infections might be resistant to dicloxacillin.

2. Which infection type is resistant to penicillinase-resistant penicillins?

   a. *Candida* infections
   b. MSSA infections
   c. MRSA infections
   d. *C. difficile* infections

Answer C is correct. The role of these penicillins as the agents of choice for most staphylococcal disease is changing with the increasing incidence of isolates of MRSA microorganisms. MRSA strains demonstrate resistance to all penicillinase-resistant penicillins and cephalosporins. Hospital-acquired strains usually are resistant to the aminoglycosides, tetracyclines, erythromycin, and clindamycin as well. Vancomycin is considered the drug of choice for hospital-acquired resistant strains, although resistance to vancomycin is also emerging.

## 2.3 Antifungals

Fungal infections are becoming more common. Organ and bone marrow transplantation, cytotoxic chemotherapy, long-term indwelling IV catheters, and the increased use of potent broad-spectrum antibiotic agents have contributed to the increase in fungal infections. Immunocompromised patients are at increased risk for fungal infections.

Systemic fungal infections include histoplasmosis, coccidioidomycosis, cryptococcosis, blastomycosis, paracoccidioidomycosis, and sporotrichosis. Most systemic fungal infections are acquired via inhalation. Fungi are eukaryotes with unique cell walls containing glucans and chitin, and their eradication requires different strategies than those used for treatment of bacterial infections. Antifungals work by inhibiting synthesis of cell wall components, synthesis of nucleic acids, or microtubule/mitotic spindle function. As with most infections, host factors contribute greatly to the clinical outcome for patients with fungal infections. An antifungal agent may provide for cure of an infection despite in vitro resistance because the immune system may eradicate the infection, or the antifungal agent may achieve high concentrations at the infection site, allowing the drug to overcome high MICs.

Resistance can be categorized as clinical or microbiological. Clinical resistance refers to treatment failure because of factors other than microbial resistance; microbial resistance can refer to either primary or secondary resistance, as determined by in vitro susceptibility testing using standardized methodology. Primary (intrinsic) resistance is present prior to drug exposure. Secondary (acquired) resistance develops after exposure to an antifungal agent; it can be reversible in some cases. The clinical consequences of antifungal resistance can take the form of treatment failure and changes in the prevalence of the fungal species causing disease. Antifungal resistance has been reported in *Candida albicans* as well as *C. glabrata*, *C. tropicalis*, and *C. krusei* isolates.

Several antifungal classes are available. Amphotericin B, a polyene, binds to sterols in the fungal cell membrane, leading to alterations in cell permeability and cell death. It is available in four formulations; each has relative advantages and disadvantages. Newer liposomal formulations are associated with less toxicity than the older ones, however, renal toxicity remains one of the most prominent clinical concerns. Imidazoles and triazoles have a similar spectrum of activity and mechanism of action. The azoles are agents that require significant hepatic metabolism and often strongly compete with other drugs using the same pathway through the liver. For this reason, these agents are associated with drug–drug interactions that may limit their use. The echinocandins are used primarily for invasive candidiasis and aspergillosis. Griseofulvin is used for mycotic disease of the skin, hair, and nails due to *Microsporum, Trichophyton*, or *Epidermophyton* species. Topical antifungal treatment is useful for superficial infections that are confined to the stratum corneum, squamous mucosa, or cornea. In addition, creams for vaginal use are available to treat vaginal candidiasis.

## Allylamines

Terbinafine

## Azoles

Efinaconazole
Fluconazole
Isavuconazonium sulfate
Itraconazole
Ketoconazole
Luliconazole
Posaconazole
Voriconazole

## Echinocandins

Anidulafungin
Caspofungin
Micafungin

## Oxaboroles

Tavaborole

## Polyenes

Amphotericin B
Nystatin

## Pyrimidines

Flucytosine

## Miscellaneous Antifungal Agents

Griseofulvin
Potassium iodide *(see also the Thyroid Hormones section in the Hormones and Synthetic Substitutes chapte)*

## Case Studies and Conclusions

A 56-year-old woman is diagnosed with mucormycoses involving the maxillary sinuses. An infectious diseases consultant recommends that she be treated with amphotericin B.

1. Which formulations of amphotericin B are available for her treatment?

   a. C-AMB, L-AMB, ABLC, ABCD
   b. C-AAB, L-AAB, ABBC, AAAD
   c. C-BBA, LBBB, ABBA, ADDA
   d. CAAA, LAAB, ABBL, ADDD

Answer A is correct. Four formulations of amphotericin B are commercially available: conventional amphotericin B (C-AMB), liposomal amphotericin B (L-AMB), amphotericin B lipid complex (ABLC), and amphotericin B colloidal dispersion (ABCD).

2. The patient requests more information about the amphotericin options available to her. What would you advise her about the major difference in these formulations?

   a. Degree of infusion reaction
   b. Blood concentration achieved
   c. Indications for use
   d. All of these are major differences.

Answer D is correct. C-AMB is insoluble in water, but is formulated for intravenous use by complexing it with a bile salt, deoxycholate. ABCD forms a colloidal solution when dispersed in water and is present in much lower blood concentrations than C-AMB. Infusion reactions of chills and fever are more commonly noted with ABCD than with C-AMB. L-AMB is supplied as a lyophilized powder and achieves blood concentrations equivalent to those for C-AMB. L-AMB is approved for empirical therapy of fever in the neutropenic host not responding to appropriate antibacterial agents, as well as for salvage therapy in patients with aspergillosis and candidiasis. ABLC provides blood concentrations of amphotericin B that are much lower than those achieved with the same dose of C-AMB. ABLC is approved for salvage therapy of deep mycoses. The lipid formulations appear to reduce the risk of nephrotoxicity during therapy. The costs of the lipid formulations of amphotericin B greatly exceed the cost of C-AMB.

3. The patient requests information on how these medications will "fight her infection." How would you describe the mechanism of action of amphotericin?

   a. Binds to the membranes of fungi, increasing permeability
   b. Decreases permeability of the fungal membrane, causing fungal dehydration
   c. Forms a calcified cell membrane
   d. Triggers preprogrammed cell death

Answer A is correct. The antifungal activity of amphotericin B depends principally on its binding to a sterol moiety, primarily ergosterol, in the membrane of sensitive fungi. By virtue of their interaction with these sterols, polyenes appear to form pores or channels that increase the permeability of the membrane, allowing the outward leakage of a variety of small molecules.

4. The patient is concerned about side effects of amphotericin B. Which serious, untoward effects should be watched for in this patient?

   a. Hepatic impairment
   b. Renal impairment
   c. Hair loss
   d. Constipation

Answer B is correct. Major untoward effects of amphotericin B are infusion-related reactions such as fever and chills. These are most severe with ABCD, slightly less severe with C-AMB, even less severe with ABLC, and least severe with L-AMB. Nephrotoxicity, a major concern with amphotericin B use, is dose dependent, usually transient, and increased by concurrent therapy with other nephrotoxic agents such as aminoglycosides or cyclosporine. Permanent functional renal impairment is uncommon in adults with normal renal function prior to treatment. Hypochromic, normocytic anemia commonly occurs during treatment with C-AMB.

A 19-year-old woman with coccidioidal meningitis is being treated with fluconazole. Her parents (who have received HIPAA clearance from the patient) and she request information about why fluconazole was chosen instead of amphotericin B.

1. Which of the following statements is the best response?

   a. Fluconazole is the least expensive antifungal drug available.
   b. Fluconazole is the drug of choice for this type of fungal infection.
   c. Fluconazole has less potential to cause stomach irritation.
   d. Fluconazole will not interfere with the patient's oral contraceptive.

Answer B is correct. Fluconazole is the drug of choice for the treatment of coccidioidal meningitis because of its good penetration into cerebrospinal fluid and its much lower morbidity compared to intrathecal amphotericin B.

2. The patient is a new pharmacy technician and is learning about medication side effects as she works in the pharmacy. She wants to know which major issues and limitations are involved with the use of fluconazole, an azole antifungal. What do you tell her?

   a. There are none; fluconazole is 100% safe to use.
   b. Fluconazole has numerous drug interactions that must be considered.
   c. Fluconazole should not be used in patients older than age 50.
   d. Fluconazole is not covered by most insurance plans and is expensive.

Answer B is correct. Fluconazole competes with other drugs that are metabolized through the liver and for this reason drug–drug interactions limit its use.

## 2.4 Antimycobacterials

Agents used for the treatment of mycobacterial infections, including tuberculosis (TB), leprosy, and infections due to nontuberculous mycobacteria (NTM), are administered in multiple-drug regimens for prolonged courses. Because these pathogenic organisms grow slowly, treatment requires a much longer course of therapy compared with most bacterial infections. Combination therapy is needed because of the high rate of intrinsic resistance mutations as well as mutations that develop during treatment.

The incidence of TB (i.e., *Mycobacterium tuberculosis* infection) has been declining in the United States; however, TB remains a leading cause of morbidity and mortality in developing countries. In addition to effective drug regimens, a well-organized infrastructure for diagnosis and treatment of TB, including both therapeutic and control efforts, is needed to ensure successful individual and public health outcomes. Infections with NTM have become more common because of the increased number of immunocompromised hosts and persons with structural lung disease.

Even though a multiple-drug regimen is used, typically 3–6 months of treatment is required to eradicate drug-susceptible TB. Latent TB infection (LTBI) and active TB disease are diagnosed based on the patient's history, physical examination, radiographic imaging, tuberculin skin test (TST), interferon-γ release assays (IGRA), acid-fast staining, and/or mycobacterial cultures. Active TB disease is treated with regimens that include an initial phase of 2 months (daily isoniazid, rifampin, pyrazinamide and ethambutol), followed by a choice of several options for the continuation phase—either 4 or 7 months (typically the combination of isoniazid and rifampin is used for drug susceptible TB) for a total of 6 or 9 months of treatment. Multiple drug combination treatment has decreased the risk of resistance and has also led to a reduction in total treatment duration. LTBI is treated with isoniazid (optimally given daily or twice weekly for 6–9 months), rifampin (daily for 4 months), or isoniazid plus rifapentine (weekly for 3 months). Any regimen with weekly or twice-weekly dosing (anything less frequent than daily) requires directly observed therapy (DOT) to ensure adequate adherence to the regimen. If significant clinical improvement does not occur or the patient's clinical status worsens, then treatment failure due to nonadherence, poor medication absorption, or development of resistance should be considered. If resistance is documented or strongly suspected, at least two efficacious drugs to which the isolate is susceptible or which the patient has not already taken should be added to the therapeutic regimen. Due to the high risk of drug–drug interactions with both isoniazid and rifamin, any exaggerated side effects or suboptimal therapeutic responses should be evaluated based on the potential for interaction in light of other medications the patient is taking.

Multidrug-resistant TB (MDR-TB) is caused by a strain of *M. tuberculosis* that is resistant to both isoniazid and rifampin. The risk of MDR-TB is elevated in patients presenting from specific geographic areas in which 5% or

more of incident cases involve MDR-TB and in patients previously treated for TB. Treatment regimens for MDR-TB generally include a susceptible fluoroquinolone and an injectable second-line agent (such as capreomycin or amikacin). Regimens of at least five drugs are recommended for the treatment of MDR-TB. Extensively drug-resistant TB (XDR-TB) is MDR-TB with additional resistance to any fluoroquinolone and at least one of the second-line injectable agents. Treatment of XDR-TB is individualized on the basis of complete phenotypic and, if possible, genotypic antimicrobial susceptibility testing. Therapeutic regimens for either MDR-TB or XDR-TB should be constructed with input from experienced clinicians, who should continue the management of the disease.

## Antimycobacterial Agents

### *Antituberculosis Agents*

Aminosalicylic acid
Bedaquiline
Capreomycin
Cycloserine
Ethambutol
Ethionamide
Isoniazid
Pyrazinamide
Rifabutin
Rifampin
Rifapentine
Amikacin *(see also the Antibacterials section)*
Ciprofloxacin *(see also the Antibacterials section)*
Clarithromycin *(see also the Antibacterials section)*
Levofloxacin *(see also the Antibacterials section)*
Moxifloxacin *(see also the Antibacterials section)*
Streptomycin *(see also the Antibacterials section)*

## Miscellaneous Antimycobacterial Agents

Dapsone

## Case Studies and Conclusions

A 55-year-old male has returned from traveling to India for 3 months. He returns with a productive cough and chest x-ray indicative of TB.

1. Which medication(s) should be initiated in this patient?

   a. Isoniazid for 9 months
   b. Isoniazid and rifampin for 6 months
   c. Isoniazid, rifampin, and pyrazinamide for 6 months
   d. Isoniazid, rifampin, pyrazinamide, and ethambutol for up to 9 months

Answer D is correct. Regimens for treating TB disease are based on an initial phase lasting 2 months (daily isoniazid, rifampin, pyrazinamide, and ethambutol), followed by a choice of several options for the continuation phase—either 4 or 7 months (typically the combination of isoniazid and rifampin is used for drug-susceptible TB), for a total of 6 or 9 months for treatment. Combination anti-TB therapy is recommended for treatment of TB because resistance quickly develops when these medications are used alone. The probability that resistance will emerge when the regimen includes more than 2 drugs is small. Multidrug therapy has also led to a reduction in the length of therapy to 6–9 months.

When TB bacteria become active (multiplying in the body) and the immune system cannot stop the bacteria from growing, the condition is called TB disease. People with TB disease may spread the bacteria to people with whom they spend many hours. TB medication adherence is important to prevent treatment failure, TB spread, and resistance. MDR-TB is more difficult and more expensive to treat compared with susceptible strains.

2. Which drug interaction education should this patient be warned about with isoniazid?

   a. Isoniazid is a potent competitor (inhibitor) of drug metabolism and is responsible for many drug interactions.
   b. Isoniazid is not metabolized by the liver and therefore is not subject to drug interactions.
   c. Isoniazid is only a potential drug interaction problem when taken with rifampin.
   d. Isoniazid should never be taken with any other drug because it is dangerous to do so.

Answer A is correct. Isoniazid is a potent inhibitor of specific liver enzymes well known to be responsible for numerous drug interactions. Drugs metabolized by competing liver enzymes will potentially be affected by the patient's use of isoniazid.

A 37-year-old respiratory therapist with no past medical history has a positive (more than 10 mm) tuberculin skin test (TST) and normal chest x-ray. She is employed full time at the university hospital.

1. Which medication therapy, if any, should this patient receive?

   a. Isoniazid for 3 months
   b. Isoniazid for 9 months or rifampin for 4 months
   c. Isoniazid, rifampin, and pyrazinamide for 6 months
   d. No therapy is needed since TST < 15 mm.

Answer B is correct. People with latent TB infection do not have symptoms, and they cannot spread TB bacteria to others. These individuals should receive treatment to prevent them from developing active TB disease—a step that is essential for controlling and eliminating TB. Groups who should be given high priority for latent TB infection treatment (not a complete list) include HIV-infected persons, organ transplant recipients, and persons with a positive IGRA result or a TST reaction of 10 mm or more, including residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other healthcare facilities). Persons with no known risk factors for TB may be considered for treatment of LTBI if they have a positive IGRA result or if their reaction to the TST is 15 mm or greater. For patients with a positive TST, no symptoms, and normal chest x-ray, drug therapy with isoniazid for 6–9 months, rifampin for 4 months, or combination isoniazid plus rifapentine for 3 months is appropriate for treatment of their latent TB.

2. What is a potential adverse effect of isoniazid therapy in this otherwise healthy woman with adequate nutrition?

   a. Nephrotoxicity
   b. Cardiac toxicity
   c. Hepatotoxicity
   d. Peripheral neuropathy

Answer C is correct. Isoniazid is converted to acetyl isoniazid, which can be converted to acetyl hydrazine and hepatotoxic metabolites. Rapid acetylators will form diacetyl hydrazine, which is nontoxic; slow acetylators or CYP2E1 induction will lead to more hepatotoxic metabolites. Rifampin, a potent inducer of CYP2E1, potentiates isoniazid hepatotoxicity. Isoniazid also can cause a peripheral neuropathy in patients who are deficient in vitamin $B_6$ (pyridoxine).

3. Which adverse effect(s) from rifampin use should this patient be warned about?

   a. Orange-tan discoloration of skin, urine, and contact lenses
   b. Peripheral neuritis
   c. Cardiac toxicity
   d. Nephrotoxicity

Answer A is correct. Orange-tan discoloration of the skin, urine, feces, saliva, tears, and contact lenses is possible with rifampin.

## 2.5 Antivirals

Viruses replicate intracellularly and often use host cell enzymes, macromolecules, and organelles to make viral particles. Therefore, useful antiviral compounds must discriminate between host and viral functions with a high degree of specificity; agents without such selectivity would be too toxic for clinical use.

Viruses are simple microorganisms made up of double- or single-stranded DNA or RNA enclosed in a protein coat (capsid). Effective antiviral agents inhibit virus-specific replicative events or inhibit virus-directed nucleic acid or protein synthesis. Nonspecific antiviral agents (e.g., interferons) have multiple mechanisms of action that include modulation of the host's immune responses. DNA viruses include poxviruses (smallpox), herpesviruses (chickenpox, shingles, herpes), adenoviruses (conjunctivitis, sore throat), hepadnaviruses (hepatitis B [HBV]), and papillomaviruses (warts). Antiviral agents work best when administered early (when infection is first recognized). As is the case with antibiotics, antiviral agents are also susceptible to mutation and resistance. For example, with some miscellaneous antivirals, such as foscarnet, resistant clinical isolate of herpes viruses have emerged during therapeutic use and may be associated with poor clinical response.

## Interferons

Interferons (IFNs) are biological response modifiers with antiviral and immunomodulatory activity. IFN-α (leukocyte interferon) and IFN-β (fibroblast interferon) are released by human cells infected with certain viruses, whereas IFN-γ (immune interferon) is produced by natural killer cells (T-cell lymphocytes) in response to antigen exposure. These cytokines then act on uninfected host tissue cells to induce a state of relative resistance to viral infections. IFNs bind to cell-surface receptors that initiate the induction of certain enzymes, inhibition of cell proliferation, enhancement of immune activities (including increased phagocytosis by macrophages), and augmentation of cytotoxicity by T cells. IFNs are not absorbed orally because of their large amino acid sequence, which is digested by proteolytic enzymes in the digestive tract.

IFN-α is rapidly absorbed after both intramuscular and subcutaneous injection, and frequent injections are needed to maintain adequate serum concentrations. The available products are now chemically modified with polyethylene glycol (PEG) to extend their half-life and allow for once-weekly dosing. In addition, adverse effects are reduced because of the lowered peak concentration. IFN-α is used to treat chronic hepatitis C infections.

IFN-β products have antiviral properties but are used for multiple sclerosis, not infections. IFN-γ1b injection is used for prevention of infections in patients with chronic granulomatous disease in combination with antibacterials and antifungals. In rare cases, IFN-γ is used as salvage therapy for mycobacterial infections.

Topical imiquimod creams do not have inherent antiviral activity alone, but instead induce IFN-α, IFN-β, and IFN-γ plus tumor necrosis factor alpha (TNF-α). Local application of these medications to external genital and perianal warts stimulates an immunomodulatory response that produces cytokines, which have antiviral action and reduce viral load and wart size.

## Monoclonal Antibodies

Antibodies (immunoglobulins) are produced by B cells of the immune system. Antibodies neutralize and eliminate the infectious agents and toxins produced by pathogens. They are found in blood, plasma, and extracellular fluids. Antibodies' Y-shaped structures contain two identical variable-region antigen binding sites, with the lower (constant) region being responsible for the initiation of effector functions that lead to the removal and destruction of the pathogen or cells harboring the pathogen. The antigen binding sites on an antibody can bind to and neutralize bacterial toxins and viruses, thereby preventing them from binding to their target cells or receptors and thereby causing toxic effects or spread of the infection.

Antibodies being developed for treatment of diseases in humans are highly purified and are mostly fully human monoclonal antibodies. The term *monoclonal antibody* (mAb) refers to the cell cultures used—that is, a single cell line that produces one specific antibody. Antibodies are specific to a single virus, bacterium, or bacterial subtype. Mutations can render the antibody ineffective; however, the mutation would not affect other similar agents and would not cause resistance to spread. Only one monoclonal antibody, palivizumab, is approved for treatment of infection—that is, for the prevention and treatment of respiratory syncytial virus (RSV) infection in high-risk children.

## Antiretroviral Agents

Infection with human immunodeficiency virus (HIV) may occur through a sexual, parenteral, or perinatal route. Sexual intercourse, primarily receptive anal and vaginal intercourse, is the most common method for HIV transmission. HIV infects cells expressing cluster of differentiation 4 (CD4) receptors, such as T-helper lymphocytes, monocytes, macrophages, dendritic cells, and brain microglia. Untreated HIV infection leads to depletion of CD4 T lymphocytes and immunosuppression that increases the patient's risk of opportunistic infections (OIs). Untreated OIs and a lack of effective antiretroviral therapy (ART) are the main causes of HIV morbidity and mortality.

The current goal of ART is to achieve maximum and durable suppression of HIV replication or a level of HIV RNA in plasma (viral load) less than the lower limit of quantification. Another, equally important outcome is an increase in CD4 lymphocytes, as their number closely correlates with the risk for developing OIs. Prophylaxis with antiretroviral agents in at-risk persons lowers HIV acquisition risk.

Clinical use of antiretroviral agents is complicated by drug–drug interactions. Some interactions are beneficial and used purposely; others may be harmful, leading to dangerously elevated or inadequate drug concentrations. For these reasons, clinicians involved in the pharmacotherapy of HIV infection must exercise constant vigilance and maintain a current knowledge of drug interactions. Current recommendations for the initial treatment of HIV advocate the use of a minimum of three active antiretroviral agents from at least two drug classes.

The typical HIV regimen consists of two nucleoside/nucleotide analogues plus either a "boosted" protease inhibitor (PI)—utilizing a purposeful drug interaction that results in an increased blood concentration of the PI—a non-nucleoside reverse transcriptase inhibitor, or an integrase strand transfer inhibitor (InSTI). Inadequate suppression of viral replication allows HIV to select for antiretroviral-resistant HIV variants; this possibility is a major factor limiting the ability of antiretroviral drugs to inhibit virus replication. Current recommendations for treating drug-resistant HIV include choosing at least two drugs (preferably three) to which the patient's virus is susceptible. Susceptibility can be assessed using either virtual genotypic or phenotypic resistance testing.

The longer life span conferred by antiretroviral treatment has given rise to other medical issues. Complications associated with older age have become common, some of which are adverse effects from antiretroviral drugs. Hepatitis C virus (HCV) coinfection is an important cause of morbidity and mortality in these patients. Medical management of these contemporary HIV complications is constantly evolving.

## Adamantanes

Amantadine
Rimantadine

## Antiretrovirals

### *HIV Entry and Fusion Inhibitors*

Enfuvirtide
Maraviroc

### *HIV Protease Inhibitors*

Atazanavir
Darunavir
Fosamprenavir
Indinavir
Lopinavir and ritonavir
Nelfinavir
Ritonavir
Saquinavir
Tipranavir

### *HIV Integrase Inhibitors*

Dolutegravir
Elvitegravir and cobicistat
Raltegravir

### *HIV Non-nucleoside Reverse Transcriptase Inhibitors*

Delavirdine
Efavirenz
Etravirine
Nevirapine
Rilpivirine

### *HIV Nucleoside and Nucleotide Reverse Transcriptase Inhibitors*

Abacavir
Didanosine
Emtricitabine
Lamivudine
Stavudine
Tenofovir
Zidovudine

## Interferons

Interferon alfa
Peginterferon alfa

## Neuraminidase Inhibitors

Oseltamivir
Peramivir
Zanamivir

## Nucleosides and Nucleotides

Acyclovir
Adefovir
Cidofovir
Entecavir
Famciclovir
Ganciclovir
Ribavirin
Telbivudine
Valacyclovir
Valganciclovir

## HCV Antivirals

### *NS5B Polymerase inhibitors*

Dasabuvir
Sofosbuvir

### *NS3/4A Protease Inhibitors*

Grazoprevir
Paritaprevir
Simeprevir

### *NS5A Replication Complex Inhibitors*

Daclatasvir
Elbasvir
Ledipasvir
Ombitasvir

## Antivirals: Miscellaneous

Foscarnet

## Case Studies and Conclusions

A 73-year-old man with no other health issues developed a rash on his back yesterday. He now complains of considerable pain in the area. You suspect varicella zoster virus (VZV) infection (shingles).

1. What is the best treatment option for this patient?

   a. Acyclovir within 7 days of rash presentation
   b. Valacyclovir within 24 hours of rash presentation
   c. Penciclovir within 5 days of rash presentation
   d. Famciclovir within 3 days of rash presentation

Answer B is correct. The two drugs most commonly used for VZV infections are acyclovir and penciclovir, or their prodrugs, valacyclovir and famciclovir, respectively. Both drugs are most effective if started within 24 hours of the rash's appearance.

A 23-year-old man with AIDS has begun to develop blurred vision in his left eye. The diagnosis of cytomegalovirus (CMV) retinitis is made. The patient is started on intravenous foscarnet.

1. Regardless of the initial choice of IV foscarnet, which treatment option is not recommended for the treatment of CMV retinitis?

   a. Ganciclovir
   b. Famciclovir
   c. Fomivirsen
   d. Cidofovir

Answer B is correct. The treatment options for CMV retinitis include foscarnet, ganciclovir, fomivirsen, and cidofovir. Fomivirsen is given by intravitreal injection for patients intolerant of or unresponsive to other therapies.

2. Which of the following statements is true regarding development of resistance to foscarnet?

   a. Resistant clinical isolates of adenoviruses have emerged during therapeutic use of foscarnet and may be associated with poor clinical response.
   b. CMV strains that are resistant to foscarnet have point mutations in the viral DNA polymerase and are associated with 3- to 7-fold reductions in foscarnet activity in vitro.
   c. Herpesviruses that are resistant to foscarnet have point mutations in the viral DNA polymerase and are associated with 3- to 7-fold reductions in foscarnet activity in vitro.
   d. Resistant clinical isolates of noroviruses have emerged during therapeutic use of foscarnet and may be associated with poor clinical response.

Answer C is correct. Resistant clinical isolates of herpesviruses have emerged during therapeutic use of foscarnet and may be associated with poor clinical response. Herpesviruses resistant to foscarnet have point mutations in the viral DNA polymerase and are associated with 3- to 7-fold reductions in foscarnet activity in vitro.

3. This patient should be monitored for which major adverse effects while on foscarnet?

   a. Nephrotoxicity and symptomatic hypocalcemia
   b. Nephrotoxicity and hyponatremia
   c. Hepatoxicity and hyponatremia
   d. Hepatoxicity and symptomatic hypocalcemia

Answer A is correct. The dose-limiting toxicities associated with foscarnet are nephrotoxicity and symptomatic hypocalcemia. Acute tubular necrosis, crystalline glomerulopathy, nephrogenic diabetes insipidus, and interstitial nephritis have been described. Saline loading may reduce the risk of nephrotoxicity. Foscarnet is highly ionized at physiological pH, and metabolic abnormalities are common—for example, increases or decreases in calcium and phosphate, hypomagnesemia, and hypokalemia. Decreased serum ionized calcium may cause paresthesia, arrhythmias, tetany, seizures, and other CNS disturbances.

## 2.6 Antiprotozoals

Antiprotozoal drugs are a class of medications used to treat infections caused by protozoa (single-cell organisms) that can act as parasites. Amebiasis, giardiasis, trichomoniasis, toxoplasmosis, cryptosporidiosis, trypanosomiasis, and leishmaniasis are common protozoal infections seen worldwide. Protozoa multiply rapidly, and effective vaccines against them are not available. Therapy of protozoal infections often requires multiple drugs, but antiprotozoal drugs have severe toxicities that require careful monitoring.

Giardiasis is the most commonly reported protozoal infection in the United States. Trichomoniasis is a sexually transmitted disease that is common in the United States. Treatment of patients with giardiasis or trichomoniasis using either metronidazole or tinidazole is usually successful.

Malaria is transmitted by the bite of an infected *Anopheles* mosquito that introduces the sporozoites (tissue parasites) of the plasmodia (*Plasmodium falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*) into the bloodstream. *P. vivax* and *P. ovale* have life stages that can remain in the liver, and specific antiparasitic drugs are necessary to treat the liver stages of these organisms.

### Giardiasis

The acute presentation of giardiasis is characterized by diarrhea, cramping abdominal pain, bloating, flatulence, malaise, anorexia, nausea, and belching. Chronic presentation includes diarrhea (foul-smelling, copious, light-colored, fatty stools) and weight loss. Periods of diarrhea may alternate with constipation. Steatorrhea, lactose intolerance, and vitamin $B_{12}$ and fat-soluble vitamin deficiencies may also be present. For patients with prolonged diarrhea and malabsorption with a history of recent travel to an endemic area, rapid identification based on ova and parasites examination or an antigen detection test should be performed so as to institute appropriate therapy.

Giardiasis can be prevented with good personal hygiene and avoiding potentially contaminated food and drink. All symptomatic adults and children (older than 8 years) with giardiasis can be treated with metronidazole 250 mg 3 times daily for 5–10 days or tinidazole 2 g once or nitazoxanide 500 mg twice daily for 3 days. Metronidazole cures 80% to 90% of cases and is the agent most commonly used to treat giardiasis. This treatment regimen also prevents the infected person from shedding infection to others which is described as the development of a carrier state. Diarrhea should cease within 2–3 days, although it may take as long as 2 weeks to end. Patients who do not respond to the initial therapy with metronidazole should be switched to a drug from a different class, such as nitazoxanide (500 mg twice daily for 3 days).

### Malaria

Malaria is a devastating disease in terms of its burden of human suffering and economics. As many as 500 million new infections and 2 million deaths are reported annually worldwide. Deaths occur in patients because of lack of access to or failure to take chemoprophylaxis, inappropriate chemoprophylaxis, delay in seeking medical care, or misdiagnosis. In the United States, most cases of malaria are reported in immigrants from endemic areas and in travelers to these areas.

Symptoms of malaria vary based on the course of the disease. At their initial presentation, patients may complain of nonspecific fever, chills, rigors, diaphoresis, malaise, vomiting, and lightheadedness. During the erythrocytic phase (when the plasmodia attack erythrocytes), patients may complain of headache, anorexia, malaise, fatigue, and myalgia as well as abdominal pain, diarrhea, chest pain, and arthralgia. Complications such as hypoglycemia, pulmonary edema, and renal failure are associated with increased mortality. Blood smears should be obtained every 12–24 hours for 3 consecutive days. The presence of parasites in the blood 3–5 days after initiation of therapy suggests drug resistance. Recent advances in detecting malaria parasite have included DNA or RNA probes that utilize polymerase chain reaction (PCR) and rapid dipstick tests. The dipstick is reported to have a sensitivity of 88% and a specificity of 97%; however, microscopy is still considered the optimal test.

Chemoprophylaxis has traditionally consisted of chloroquine phosphate 300 mg (base) once weekly beginning 1–2 weeks prior to departure to the endemic areas and continued for 4 weeks after leaving the endemic area. When departing an area where *P. vivax* or *P. ovale* is endemic, primaquine phosphate 30 mg (base) daily for 14 days, beginning during the last 2 weeks of chloroquine prophylaxis, should be added to the regimen. When advising potential travelers on prophylaxis for malaria, be aware of the incidence of chloroquine-resistant *P. falciparum* (CRPF) and the countries where in which this variant is prevalent. In these areas, commonly recommended drugs for malaria prophylaxis include mefloquine, atovaquone/proguanil, or doxycycline.

The adult dose of mefloquine is 250 mg once weekly, beginning 1 week prior to departure and continuing for the full period of exposure, followed by 250 mg for 4 weeks after last exposure. Treatment regimens require different

doses and schedules, however, chloroquine is still currently the recommended drug of choice for most cases of uncomplicated malaria (refer to drug grid for further detail). All patients receiving mefloquine should receive the FDA Medication Guide; note that this agent is contraindicated in patients with a history of cardiac conduction problems. Patients may experience neuropsychiatric reactions (seizures, psychosis, anxiety, sleep disturbances, insomnia, and dizziness) from mefloquine and should be monitored closely.

Doxycycline is an alternative option for chemoprophylaxis that avoids the central nervous system side effects. However, it requires daily dosing, can increase sun sensitivity, and should be avoided in children and pregnant women.

Atovaquone/proguanil is generally well tolerated and preferred by many travelers. This regimen is more expensive than most malaria prophylaxis medications, which may be a barrier to its use.

Detailed recommendations for prevention of malaria may be obtained by checking the Centers for Disease Control and Prevention's (CDC) website: www.cdc.gov/travel.

## Amebicides

Iodoquinol
Paromomycin
Metronidazole (*see also Miscellaneous Antiprotozoals section*)

## Antimalarials

Artemether and lumefantrine
Atovaquone and proguanil
Chloroquine
Hydroxychloroquine
Mefloquine
Primaquine
Pyrimethamine
Quinine
Quinidine *(see also the Cardiac Drugs section in the Cardiovascular Agents chapter)*

## Miscellaneous Antiprotozoals

Atovaquone
Metronidazole
Nitazoxanide
Pentamidine
Tinidazole
Co-trimoxazole *(see also the Antibacterials section)*
Dapsone *(see also the Antimycobacterials section)*

## Case Studies and Conclusions

A 35-year-old woman presents with a history of diarrhea and abdominal pain for the past 3 days. She recently returned from a whitewater rafting trip. During the trip, she fell out of the boat; although she had a life preserver on, she swallowed considerable amounts of river water. She is diagnosed with giardiasis, and treatment should begin after obtaining appropriate specimens.

1. How is the diagnosis of giardiasis made?

   a. Identification of cysts or trophozoites in feces
   b. Based on history and clinical presentation
   c. Microscopic analysis of blood sample
   d. Identification of cysts in duodenal contents

Answer A is correct. Giardiasis, which is caused by the protozoan *Giardia lamblia*, is prevalent worldwide and is the most common intestinal protozoal infection in the United States. *Giardia* is a zoonosis, and cysts shed in the feces of animals and humans can contaminate recreational and drinking water supplies. Infection with *Giardia* results in an asymptomatic carrier state, acute self-limited diarrhea, or chronic diarrhea. The diagnosis of giardiasis is made by identification of cysts or trophozoites in fecal specimens or of trophozoites in duodenal contents.

2. What is the most appropriate therapy to limit the acute diarrhea, prevent the development of chronic diarrhea, and prevent the development of a "carrier state" in patients with giardiasis?

   a. Nitazoxanide
   b. Pentamidine
   c. Metronidazole
   d. Co-trimoxazole

Answer C is correct. Chemotherapy with a 5-day course of metronidazole or a single dose of tinidazole is usually successful in eradicating giardiasis. Paromomycin has been used to treat pregnant women to avoid any possible mutagenic effects of the other drugs.

A 38-year-old male with no significant past medical history has returned from traveling to Nicaragua. He forgot to take chemoprophylaxis for malaria and now presents with fever, chills, rigors, and diaphoresis.

1. Which therapy should be initiated in this patient?

   a. Chloroquine 600 mg
   b. Quinine 648 mg
   c. Mefloquine 250 mg
   d. Quinidine 300 mg

Answer A is correct. In an uncomplicated attack of malaria (for all plasmodia except CRPF), the recommended regimen is chloroquine 600 mg (base) initially, followed by 300 mg (base) 6 hours later, and then 300 mg (base) daily for 2 days.

## Tips from the Field

### Worms

1. Diagnosis of tape worms and pinworms is generally made by detection of eggs in stool. Stool should be analyzed for the characteristic eggs, such as for the Ascaris lumbricoides-"round worm." Because of a very high egg burden, sample concentration techniques are generally not needed to make the diagnosis.

2. Patients may assist in diagnosis of pinworms with cellophane tape used to collect the eggs from the perianal area and collected in the morning before bathing or using the toilet. The tape is removed and brought in for examination under a microscope. The sensitivity of the tape test is about 50% for a one-time collection and 90% for three collections.

### Other Pearls

1. Remember:
   - Systematic Approach for Selection of Antimicrobials (details provided earlier in this chapter).
   - Refer to guidelines prior to ordering/administering subacute bacterial endocarditis (SBE) prophylaxis to patients as the criteria for use have become more restrictive in order to reduce the overuse and unnecessary use of antibiotics.

2. If a bacterial otitis media infection is established:
   - Watchful waiting is encouraged for uncomplicated cases for which reliable follow-up is available.
   - Amoxicillin or amoxicillin/clavulanate is the recommended first-line therapy.
   - Macrolides, such as azithromycin, are not recommended due to high levels of *Streptococcus pneumoniae* antibiotic resistance (approximately 40%).
   - For penicillin-allergic patients, doxycycline or a respiratory fluoroquinolone (levofloxacin or moxifloxacin) are recommended alternative agents.

3. Routine treatment of uncomplicated acute bronchitis with antibiotics is not recommended, regardless of cough duration. Options for symptomatic therapy include:
   - Cough suppressants (codeine, dextromethorphan)
   - First-generation antihistamines (diphenhydramine)

- Decongestants (phenylephrine)
- Beta agonists (i.e., albuterol).
- Decongestants (pseudoephedrine and phenylephrine) combined with a first-generation antihistamine—may provide short-term symptom relief of nasal symptoms and cough
- Non-steroidal anti-inflammatory drugs—can be given to relieve symptoms

Evidence is lacking to support antihistamines (as monotherapy), opioids, intranasal corticosteroids, and nasal saline irrigation as effective treatments for cold symptom relief.

4. Providers and patients must weigh the benefits and harms of symptomatic therapy.
   - Antibiotic treatment for pharyngitis is NOT recommended unless the patient has a positive rapid antigen detection test (RADT) or culture with group A streptococci (GAS).
   - Amoxicillin and penicillin V remain first-line therapy due to their reliable antibiotic activity against GAS.
   - For penicillin-allergic patients, cephalexin, cefadroxil, clindamycin, or macrolides are recommended.
   - GAS antibiotic resistance to azithromycin and clindamycin are increasingly common.
   - Recommended treatment course for all oral β-lactams is 10 days.
5. For acute uncomplicated cystitis in healthy adult non-pregnant, premenopausal women:
   - Nitrofurantoin, trimethoprim/sulfamethoxazole (TMP-SMX)—where local resistance is <20%—and fosfomycin are appropriate first-line agents.
   - Fluoroquinolones (e.g., ciprofloxacin) should be reserved for situations in which other agents are not appropriate.
6. For most agents that require nebulized inhalation administration (such as tobramycin):
   - The solution for nebulization is administered by inhalation only. Do not administer subcutaneously, intravenously, or intrathecally. Use care when ordering and administering.
   - Do not dilute or mix with other medicines in the nebulizer (unless there are specific manufacturer's directions that offer these administration alternatives).
   - Administer *nebulized solution for inhalation* while the patient is sitting or standing upright and breathing normally through the mouthpiece of the nebulizer.
   - Encourage gradual inhalation over approximately 15 minutes, using a hand-held nebulizer as recommended by the specific product manufacturer. Full treatment dose has been administered when the mouthpiece makes a spitting noise for at least 1 minute and the nebulizer cup is empty.
7. For most agents that require administration of the powder for inhalation:
   - Capsules are for oral inhalation only; do not swallow the capsules.
   - Devices to use for powder inhalation are specific to product used.
   - Clean, store, and/or replace device according to manufacturer recommendations.
   - Encourage your patients to have a spare device as a backup in case of loss, breakage, or dysfunction of primary device currently in use. Do not remove capsules from original package until ready to use.
   - Become familiar with stewardship programs and appropriate prescribing (refer to http://www.cdc.gov/getsmart/community/improving-prescribing/outpatient-stewardship.html).
8. For most agents that require reconstitution prior to use:
   - Many of these anti-infective agent injections are supplied as powder that must be reconstituted prior to administration.
   - It is important to read instructions on the specific diluent to use, and how long the product is good for once reconstituted.
   - Keep in mind that refrigerated storage of reconstituted injections often allows a longer beyond use date.
   - Always label and indicate date of reconstitution.

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## Symbols

- Renal impairment: Dose adjustment is recommended.
- Hepatic impairment: Dose adjustment is recommended.
- Black box warning exists for this drug.
- QTc prolongation effects have been reported.
- Beers list criteria (avoid in elderly).
- FDA-approved pediatric doses are available.
- FDA-approved geriatric doses are available.
- See primary body system.

# Anti-infective Agents

## Universal prescribing alerts:

- Known serious hypersensitivity to the specific drug or any other component of the product/formulation selected warrants a contraindication for use.
- Adverse reactions associated with the use of some **anti-infective agents** include dizziness, drowsiness, vertigo, or fatigue; these agents may also impair the ability to perform tasks requiring mental alertness. Caution should always be recommended when using any new drug for the first time, when there is a dose change, and for continued use of known offending agents.
- Doses expressed are for usual adult dosage ranges only. "Geriatric doses" are assumed to be the same as adult doses unless otherwise noted with a symbol. Where FDA approved geriatric or pediatric dosing is available, a symbol will guide the reader to additional prescribing references. Refer to real-time prescribing references for these age specific doses.
- Use of anti-infective agents in pregnancy is based on clinical risk versus benefit; safety concerns are not represented in this grid. Refer to the package insert (PI) for more information. Clinicians should continue to provide education about the reproductive risks of any medication and offer risk reduction strategies (which may include contraceptive use) to women of childbearing age and understand that these reproductive risks may also extend to males. Anti-infective agents, as well as a number of other medications, may decrease the effectiveness of oral contraceptives. Where necessary, an alternative means of birth control should be explored.
- Brand names are provided for those agents that are still available on the market. Due to the ever-changing product availability, refer to Food and Drug Administration (FDA) resources to confirm the actual brands available. This drug summary is for educational purposes only. Prescribing decisions should be based on real-time, comprehensive drug databases that are updated on a regular basis.

## Anthelmintics

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Albendazole<br><br>**Brand Name**<br>Albenza<br><br>PD | Parenchymal neurocysticercosis<br>*Taenia solium*<br>(pork tapeworm)<br><br>Cystic hydatid disease of the liver, lung, or peritoneum<br>*Echinococcus granulosus*<br>(dog tapeworm) | **Usual oral dose:**<br>Patients weighing less than 60 kg:<br>15 mg/kg per day in 2 divided doses (max 800 mg per day)<br><br>Patients weighing 60 kg or more:<br>800 mg per day in 2 divided doses | • Can cause severe bone marrow suppression, especially in hepatic impairment; discontinue if clinically significant decreases in complete blood count (CBC) occur<br>• May elevate liver function tests (LFTs); discontinue if LFTs rise to more than 2 times the upper limit of normal<br>• Take with high-fat meal for optimal bioavailability<br>• When treating neurocysticercosis, use anticonvulsants and corticosteroids during first week<br>• Monitor: fecal specimens for ova and parasites 3 weeks after treatment, LFTs, CBC with differential, and perform ophthalmic exam if treating neurocysticercosis to determine eye involvement |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Ivermectin<br><br>**Brand Name**<br>Stromectol<br>Soolantra<br>Sklice | Strongyloidiasis of intestinal tract<br>*Strongyloides stercoralis* (nematode)<br><br>Onchocerciasis<br>*Onchocerca volvulus* (immature nematode)<br><br>Head lice<br>*Pediculus capitis*<br><br>Rosacea | **Usual oral dose for onchocerciasis:**<br>150 mcg/kg single dose<br><br>**Usual oral dose for strongyloidiasis:**<br>200 mcg/kg single dose (alternatively, once daily for 2 days per CDC)<br><br>**Topical lotion (head lice):** apply enough to cover dry scalp and hair for single use<br><br>**Topical cream (rosacea):** apply to affected area daily | • Systemic exposure can cause cutaneous and systemic reactions, especially in hyper-reactive onchodermatitis<br>• Assess for loiasis if has traveled to West and Central Africa, and pretreat before systemic exposure (serious/fatal encephalopathy has been reported in patients with *Loa loa* infection)<br>• Take oral on empty stomach with water for optimal bioavailability (bioavailability increased 2.5-fold when administered with a high-fat meal)<br>• No activity against adult *Onchocerca volvulus*<br>• Monitor (systemic): skin and eye microfilarial counts, ophthalmologic exams, stool exam post treatment<br>• Leave lotion on for 10 minutes, then rinse out; recommend washing clothing, bedding, and hair accessories |
| **Generic Name**<br>Praziquantel<br><br>**Brand Name**<br>Biltricide | Treatment of all species of *Schistosoma* (blood flukes)<br><br>*Clonorchis sinensis* (liver fluke)<br><br>*Opisthorchis viverrini* (liver fluke) | **Usual oral dose for schistosomiasis:**<br>20 mg/kg per dose 3 times per day separated by 4 to 6 hours for 1 day<br><br>**Usual oral dose for clonorchiasis/ opisthorchiasis:**<br>25 mg/kg per dose 3 times per day separated by 4 to 6 hours for 1 day | • Use with caution in patients with cardiac abnormalities<br>• Systemic exposure can increase in patients with moderate to severe hepatic impairment<br>• Not recommended for use if patient has a history of seizures or infection involves the CNS<br>• Swallow tablets quickly with water to avoid potent bitter taste<br>• Caution patients about driving and operating machinery (adverse effects may last for 2 days)<br>• Drug interactions may require dose adjustments<br>• Patients with cerebral cysticercosis should be hospitalized during treatment<br>• May not be effective in migrating schistosomiasis and can potentiate severe reactions caused by a sudden inflammatory immune response<br>• Monitor: LFTs, seizures, patients with cardiac abnormalities, and a feces exam for ova prior to use |

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|---|---|---|---|
| **Generic Name**<br>Pyrantel<br><br>**Brand Name**<br>Pamix<br>Pin-X<br>Reese's Pinworm Medicine | Pinworms<br>*Enterobius vermicularis* | **Usual oral dose:**<br>11 mg/kg single dose (max 1 g per dose) | • Use with caution in patients with hepatic impairment owing to risk of increased exposure<br>• Alternative agent; not first-line therapy<br>• Treat family members who were in close contact with the patient<br>• Monitor: feces for eggs, worms, and occult blood<br>• Usual oral dose is based on pyrantel base |

## Antibacterial

### Aminoglycosides

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Amikacin<br><br>**Brand Name**<br>Amikin<br>(See also Antituberculosis Agents)<br>  | Treatment of serious gram-negative bacilli bacteria that cause bone infections, respiratory tract infections, endocarditis, and septicemia that is resistant to gentamicin and tobramycin *(for example: Pseudomonas, Proteus, Serratia)* | **Usual parenteral dose:**<br>IM, IV: 5 to 7.5 mg/kg per dose every 8 hours | • Low therapeutic index: individualize dosing<br>• Use with caution if patient has low calcium<br>• Monitor: urinalysis, blood urea nitrogen (BUN), serum creatinine (SCr), peaks and troughs (usually after third dose), vital signs, temperature, weight, input and output (I&O); audiograms at baseline, during, and after treatment if used for an extended period of time<br>Associated with:<br>• Nephrotoxicity; use caution when using with other nephrotoxic agents<br>• Neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Neurotoxicity; ototoxicity can occur with high doses at extended use and is irreversible |
| **Generic Name**<br>Gentamicin<br><br>**Brand Name**<br>Garamycin<br>  | Treatment of susceptible bacteria that cause bone infections, respiratory tract infections, skin and soft-tissue infections, abdominal and urinary tract infections, septicemia, and endocarditis *(for example: Pseudomonas, Proteus, Serratia, Staphylococcus)* | **Usual parenteral dose:**<br>IM, IV:<br>Conventional: 1 to 2.5 mg/kg per dose every 8 to 12 hours<br><br>Extended dosing interval: 4 to 7 mg/kg per dose once daily<br><br>Intrathecal: 4 to 8 mg per day | • May cause neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Low therapeutic index: individualize dosing<br>• Decreased absorption in atrophic muscles<br>• Suitable solutions for administration are clear to slight yellow<br>• Use with caution if patient has low calcium<br>• Monitor: urinalysis, urine output, BUN, SCr, troughs and peaks (usually after third dose); audiograms at baseline, during, and after treatment if using for 2 weeks or more<br>• Inconclusive data show certain penicillins, when administered with gentamicin, may result in loss of efficacy |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| | | | Associated with:<br>• Nephrotoxicity; use caution when using with other nephrotoxic agents<br>• Neurotoxicity; ototoxicity can occur with high doses at extended use and is irreversible |
| **Generic Name**<br>Neomycin<br><br>**Brand Name**<br>Neo-Fradin<br><br>■ | Portal-systemic encephalopathy as adjunct<br><br>Perioperative prophylaxis as adjunct with erythromycin EC | **Usual oral dose for perioperative prophylaxis:** 1 g at 1:00 pm, 2:00 pm, and 11:00 pm on the day before 8:00 am surgery as an adjunct<br><br>**Usual oral dose for hepatic encephalopathy:** 4 to 12 g daily in divided dose every 4 to 6 hours for 5 to 6 days<br><br>**Chronic hepatic insufficiency:** 4 g daily | • Doses greater than 12 g per day may cause malabsorption of certain nutrients, fats, and glucose<br>• Do not administer parenterally or as surgical irrigation due to toxicity from increased systemic absorption<br>• Monitor: SCr and BUN at baseline and throughout therapy; audiograms if symptoms develop<br>• Contraindicated in intestinal obstruction, inflammatory or ulcerative bowel disease<br>Associated with:<br>• Nephrotoxicity; use caution when using with other nephrotoxic agents<br>• Neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Neurotoxicity; ototoxicity can occur with high doses at extended use and is irreversible |
| **Generic Name**<br>Streptomycin<br><br>■ PD | Treatment of tuberculosis in combination with other antibiotic agents<br>Treatment of numerous infections involving the following susceptible bacteria: plague *(Yersinia pestis)*, tularemia *(Francisella tularensis), Brucella, K. granulomatis, Haemophilus ducreyi, H. influenza, K. pneumoniae, E. coli, Proteus, E. aerogenes, E. faecalis, S. viridans, E. faecalis* | **Usual parenteral dose:**<br>IM: 15 to 30 mg/kg per day in divided doses or 1 to 2 g daily | • Adjusted doses for renal impairment are suggested, although the manufacturer does not provide specific dosing recommendations, refer to PI<br>• Specific dosing recommendations for patients undergoing intermittent dialysis, refer to PI<br>• Often used as second-line therapy due to the high risk of toxicities<br>• Administer in mid lateral thigh muscle or upper gluteal muscle<br>• Exposure to light can darken the solution without loss of efficacy<br>• Monitor: audiograms at baseline and periodically during treatment; BUN, SCr, troughs and peaks after third dose<br>Associated with:<br>• Nephrotoxicity; use caution when using with other nephrotoxic agents<br>• Neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Neurotoxicity; ototoxicity can occur with high doses at extended use and is irreversible<br>• Parenteral infusions: need appropriate audiometric and laboratory testing facility in place |

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|---|---|---|---|
| **Generic Name**<br>Tobramycin<br><br>**Brand Name**<br>Tobi<br>Tobi Podhaler<br>Kitabis Pak<br>Bethkis<br>  | Treatment of infections by gram-negative bacilli<br>*P. aeruginosa*<br>Cystic fibrosis with *P. aeruginosa*<br>Treatment of susceptible bacteria that cause brucellosis, cholangitis, complicated diverticulitis, meningitis, pelvic inflammatory disease, plague *(Yersinia pestis),* pneumonia, tularemia, urinary tract infections, ocular infections<br>Prophylaxis against endocarditis | **Usual parenteral dose:**<br>IM, IV:<br>Conventional dosing: 1 to 2.5 mg/kg per dose every 8 to 12 hours<br><br>Extended interval dosing: 4 to 7 mg/kg per dose daily<br><br>**Usual nebulized dose for cystic fibrosis:**<br>300 mg of solution for inhalation nebulized every 12 hours in 28-day cycles<br>**Usual oral inhalation dose for cystic fibrosis**<br>(powder for inhalation): 112 mg (four 28mg capsules) every 12 hours in 28-day cycles<br>**Usual ophthalmic dose:**<br>Ointment: ½ inch, 2 to 6 times per day<br>Solution: 1 to 2 drops every 2 to 4 hours | • May cause neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Low therapeutic index: individualize dosing<br>• Specific dosing recommendations for patients undergoing intermittent dialysis, refer to PI<br>• Use caution if patient has low calcium<br>• If patient uses a multiple dose inhaler for cystic fibrosis, use tobramycin last: 15 to 90 minutes after bronchodilator<br>• Exposure of drug to light can darken the solution without loss of efficacy: normal solution for inhalation is clear to pale yellow<br>• Monitor: urinalysis, urine output, BUN, SCr, peaks and troughs after third dose; audiograms at baseline and during treatment if used for extended period of time<br>• Inconclusive data show certain penicillins, when administered with tobramycin, may result in loss of efficacy<br>• Injectable aminoglycoside dosing is highly variable and dependent on several factors<br>Associated with:<br>• Nephrotoxicity; use caution when using with other nephrotoxic agents<br>• Neuromuscular blockade and paralysis; do not give after using anesthesia or a muscle relaxant<br>• Neurotoxicity; ototoxicity can occur with high doses at extended use and is irreversible |
| Paromomycin | Refer to the Antiprotozoals section. | | |

## Cephalosporins

Universal prescribing alerts:

- Known serious allergic reaction: use with caution if the patient is allergic to penicillin agents due to cross-reaction
- Cephalosporins have been associated with seizures, especially in patients with renal impairment given unadjusted doses. Dosage reductions are recommended in these patients for certain cephalosporin agents.
- Can cause false-positive urinary glucose if the patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

### *First-Generation Cephalosporins*

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefadroxil<br><br>**Brand Name**<br>Duricef<br>  | Pharyngitis or tonsillitis<br>*Streptococcus pyogenes*<br><br>Skin and skin structure infections caused by staphylococci or streptococci<br><br>Urinary tract infection *(for example: E. coli, Proteus mirabilis, Klebsiella)* | **Usual oral dose:**<br>1 to 2 g daily as single dose or 2 divided doses | • Use with caution in patients with colitis due to increased absorption<br>• Monitor: renal function |
| **Generic Name**<br>Cefazolin<br><br>**Brand Name**<br>Ancef<br>  | Treatment of susceptible bacteria that cause biliary tract infections, bone and joint infections, endocarditis, genital infections, respiratory tract infections, septicemia, skin and skin structure infections, and urinary tract infections *(for example: E. coli,* streptococci, *P. mirabilis, Klebsiella, S. aureus, H. influenza)*<br><br>Perioperative prophylaxis | **Usual parenteral dose for treatment of endocarditis:**<br><br>IM, IV:<br>1 to 1.5 g every 6 hours (max of 12 g per day)<br><br>**Perioperative prophylaxis:** 1 g, 30 to 60 minutes prior to surgery. Additional doses are often required postoperatively depending on type of surgery (refer to PI for specific details) | • May increase international normalized ration (INR)<br>• High levels in patients with poor renal function can increase risk for seizures<br>• Reconstitution of powder formulation is required prior to administration<br>• Stability of reconstituted solution vary based on storage location (longer beyond use date when refrigerated; refer to PI<br>• Suitable solutions for administration range in color from light yellow to yellow<br>• Monitor: renal function, LFTs, CBC |

| | | | |
|---|---|---|---|
| **Generic Name**<br>Cephalexin<br><br>**Brand Name**<br>Keflex<br><br>▲ PD | Treatment of susceptible gram-positive bacteria that cause respiratory tract infections, otitis media, skin and skin structure infections, bone infections, and genitourinary tract infections<br><br>Prophylaxis for acute infective endocarditis | **Usual oral dose:**<br>250 to 1000 mg every 6 hours (max 4 g per day) | • May increase INR<br>• Store suspension in the refrigerator<br>• Monitor: renal, hepatic, and hematologic function with extended use |

*Second-Generation Cephalosporins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Some cephalosporins have been associated with seizures, especially in patients with renal impairment given unadjusted doses. Dosage reductions are recommended in these patients for certain cephalosporin agents.
- Can cause false-positive urinary glucose if the patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefaclor<br><br>**Brand Name**<br>Ceclor<br><br>PD | Treatment of susceptible bacteria that cause exacerbations of chronic bronchitis (ER only), lower respiratory tract infections (capsules and suspension only), otitis media (capsules and suspension only), pharyngitis and tonsillitis, secondary infection of acute bronchitis (ER only), skin and skin structure infections, urinary tract infections (for example: *H. influenza, M. catarrhalis, S. pneumoniae, S. pyogenes, E. coli, P. mirabilis, Klebsiella,* coagulase-negative staphylococci) | **Usual oral dose:**<br>Immediate release (IR): 250 to 500 mg every 8 hours<br><br>Extended release (ER): 500 mg every 12 hours | • Use with caution in patients with colitis due to increased absorption<br>• Use with caution in patients with poor renal function<br>• Beta-lactamase–negative, ampicillin-resistant (BLNAR) strains of *H. influenza* should be considered resistant to cefaclor<br>• Administer ER tablets with food or within 1 hour of food<br>• Extended release (ER) 500 mg can be ordered 2 times per day as an alternative to immediate release (IR) 250 mg 3 times per day<br>• Monitor: renal function |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefprozil<br><br>**Brand Name**<br>Cefzil<br>  | Treatment of susceptible bacteria that cause pharyngitis/tonsillitis, otitis media, acute bronchitis secondary infection or exacerbation, skin and skin structure infections *(for example: S. pyogenes, S. pneumoniae, H. influenza, M. catarrhalis, S. aureus)* | **Usual oral dose for uncomplicated skin infections:**<br>250 to 500 mg every 12 to 24 hours for 10 days | • Use with caution in patients with colitis due to increased absorption<br>• Store reconstituted suspension in a refrigerator<br>• Monitor: renal function |
| **Generic Name**<br>Cefuroxime<br><br>**Brand Name**<br>Ceftin<br>Zinacef<br>  | Treatment of susceptible bacteria that cause bone and joint infections, lower respiratory infections, septicemia, skin and skin structure infections, urinary tract infections, and early Lyme disease *(for example: S. pneumoniae, H. influenza, Klebsiella, S. aureus, S. pyogenes, E. coli, Enterobacter)*<br><br>Perioperative prophylaxis | **Usual oral dose for uncomplicated skin infections:**<br>250 to 500 mg every 12 hours for 10 days<br><br>**Usual parenteral dose for uncomplicated skin infections:**<br>IM, IV: 750 mg every 8 hours<br><br>**Perioperative prophylaxis:** IV: 1.5 g 30 to 60 minutes prior to procedure. Additional doses are often required postoperatively depending on type of surgery (refer to PI for specific details) | • May increase INR<br>• Use with caution in patients with colitis due to increased absorption<br>• High levels in patients with poor renal function can increase risk for seizures<br>• Swallow tablets whole due to potent bitter taste<br>• Administer suspension with food and store reconstituted suspension in a refrigerator<br>• Tablets and suspension are not bioequivalent and not equal on a milligram-to-milligram basis<br>• Transition patients to oral administration as soon as medically appropriate.<br>• Monitor: renal, hepatic, and hematologic function with extended use; prothrombin time if extended use, poor renal or hepatic function, or malnourished |
| **Generic Name**<br>Cefoxitin | Refer to the Cephamycins section. | | |

| | |
|---|---|
| **Generic Name**<br>Cefotetan | Refer to the Cephamycins section. |

*Third-Generation Cephalosporins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution).
- Some cephalosporins have been associated with seizures, especially in patients with renal impairment given unadjusted doses. Dosage reductions are recommended in these patients for certain cephalosporin agents.

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefdinir<br><br>**Brand Name**<br>Omnicef<br>▲ PD | Treatment of susceptible bacteria that cause acute otitis media, acute exacerbations of chronic bronchitis, sinusitis, community-acquired pneumonia, pharyngitis/tonsillitis, and skin and skin structure infections *(for example: H. influenza, S. pneumoniae, M. catarrhalis, H. parainfluenzae, S. pyogenes, S. aureus)* | **Usual oral dose for acute sinusitis:**<br>300 mg twice daily for 5 to 10 days or<br>600 mg once daily for 10 days | • Use with caution in patients with colitis due to increased absorption<br>• Administer 2 hours before or after antacids or iron supplements<br>• Monitor: renal function<br>• Specific recommendations provided for patients undergoing dialysis |
| **Generic Name**<br>Cefditoren<br><br>**Brand Name**<br>Spectracef<br>▲ | Treatment of susceptible bacteria that cause exacerbation of chronic bronchitis or community-acquired pneumonia, pharyngitis, tonsillitis, and skin and skin structure infections *(for example: H. influenzae, H. parainfluenzae, S. pneumoniae, M. catarrhalis, S. pyogenes, S. aureus)* | **Usual oral dose for community acquired pneumonia:** 400 mg twice daily for 14 days | • Contraindicated if patient is carnitine deficient due to worsening of condition<br>• May increase INR<br>• Use with caution in patients with hepatic impairment; cefditoren has not been studied in patients with severe hepatic disease. No dose adjustment is required with mild hepatic impairment (Child-Pugh Class A or B) per PI<br>• High levels in patients with poor renal function can increase risk for seizures<br>• Administer with food to increase absorption<br>• Monitor: renal function |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefixime<br><br>**Brand Name**<br>Suprax<br>  | Treatment of susceptible bacteria that cause uncomplicated urinary tract infections (UTI), otitis media, pharyngitis/tonsillitis, acute exacerbations of chronic bronchitis, and uncomplicated cervical/urethral gonorrhea *(for example: E. coli, P. mirabilis, H. influenzae, M. catarrhalis, S. pyogenes, S. pneumoniae, N. gonorrhoeae)* | **Usual oral dose for uncomplicated UTI:**<br>400 mg daily in divided doses every 12 to 24 hours | • Chewable tablets and suspensions achieve higher peak blood concentrations compared with an equivalent dose of the capsule; otitis media should be treated with the chewable tablet or suspension<br>• No longer considered first-line therapy for uncomplicated gonorrhea in the United States because of resistance; ceftriaxone is preferred<br>• Monitor: renal and hepatic function with prolonged therapy<br>• Specific recommendations for patients undergoing dialysis, refer to PI |
| **Generic Name**<br>Cefotaxime<br><br>**Brand Name**<br>Claforan<br>  | Treatment of susceptible bacteria that cause bacteremia/septicemia, bone and joint infections; CNS infections, genitourinary infections, gynecologic infections, intra-abdominal infections, lower respiratory tract infections, and skin and skin structure infections *(for example: E. coli, Klebsiella, S. marcescens, S. aureus, Streptococcus, Pseudomonas, P. mirabilis, N. meningitides, H. influenzae, S. pneumoniae, Enterococcus, S. epidermidis, Citrobacter, P. vulgaris, P. stuartii, M. morganii, P. rettgeri, S. marcescens, N. gonorrhoeae, Enterobacter, Bacteroides, Clostridium,* anaerobic cocci, *Fusobacterium, S. pyogenes, H. parainfluenzae)*<br><br>Surgical prophylaxis for contaminated or potentially contaminated procedure | **Usual parenteral dose for severe infection:**<br>IM, IV: 1 to 2 g every 8 hours | • Infuse bolus slowly; arrhythmias have been reported when infusing the bolus in less than 1 minute<br>• May cause granulocytopenia with extended use greater than 10 days<br>• Use with caution in patients with colitis due to increased absorption<br>• If administering 2 g, divide into 2 doses and give into different IM injection sites<br>• To limit inflammation. change infusion sites when applicable<br>• Monitor: CBC with differential and renal function |

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|---|---|---|---|
| **Generic Name**<br>Cefpodoxime<br><br>**Brand Name**<br>Vantin<br>  | Treatment of susceptible bacteria that cause chronic bronchitis exacerbations, gonorrhea, otitis media, pharyngitis/tonsillitis, community-acquired pneumonia, sinusitis, skin and skin structure infections, and uncomplicated urinary tract infections *(for example: S. pneumoniae, H. influenzae, M. catarrhalis, N. gonorrhoeae, S. pyogenes, S. aureus, E. coli, K. pneumoniae, P. mirabilis, S. saprophyticus)* | **Usual oral dose for community acquired pneumonia:** 200 mg every 12 hours for 14 days | • Administer tablets with food to increase bioavailability<br>• Monitor: renal function<br>• Specific recommendations for patients undergoing dialysis, refer to PI |
| **Generic Name**<br>Ceftazidime<br><br>**Brand Name**<br>Fortaz<br>Tazicef<br>  | Treatment of susceptible bacteria that cause septicemia, bone and joint infections, CNS infections, gynecologic infections, intra-abdominal infections, lower respiratory infections, skin and skin structure infections, and urinary tract infections (complicated and uncomplicated) *(for example: P. aeruginosa, Klebsiella, H. influenzae, E. coli, Serratia, S. pneumoniae, S. aureus, Enterobacter, N. meningitides, Bacteroides, P. mirabilis, Serratia, Citrobacter, S. pyogenes, Proteus)*<br><br>Empiric treatment in immunocompromised patients | **Usual parenteral dose for uncomplicated lower respiratory tract infections:**<br>IM/IV: 500mg to 1000mg every 8 hours | • May increase INR<br>• Neurotoxicity can develop in patients with poor renal function due to increased levels: decrease dose<br>• Use with caution in patients with history of seizures; high levels can increase risk for seizure<br>• With some organisms (such as *Enterobacter* and *Serratia*), resistance can develop during treatment; consider combination therapy or intermittent susceptibility testing for bacteria with inducible resistance<br>• Monitor: renal function<br>• Specific recommendations for patients undergoing dialysis, refer to PI |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Ceftazidime with avibactam<br><br>**Brand Name**<br>Avycaz | Treatment of susceptible bacteria that cause complicated intra-abdominal infections (when used with metronidazole) and complicated urinary tract infections *(for example: C. freundii, C. koseri, E. aerogenes, E. cloacae, E. coli, K. pneumoniae, Proteus* species, *P. aeruginosa, K. oxytoca, P. mirabilis, P. stuartii)* | **Usual parenteral dose for complicated urinary tract infections:**<br>IV: 2.5 g every 8 hours for 7 to 14 days | • May cause neurotoxicity, such as seizures and encephalopathy: may worsen in renal impairment<br>• Infuse over 2 hours<br>• Suitable solutions for administration range in color from clear to light yellow<br>• Monitor: renal function<br>• Specific recommendations for patients undergoing dialysis, refer to PI |
| **Generic Name**<br>Ceftibuten<br><br>**Brand Name**<br>Cedax<br>PD | Treatment of susceptible bacteria that cause exacerbations of chronic bronchitis, otitis media, and pharyngitis/tonsillitis | **Usual oral dose for otitis media:** 400 mg daily for 10 days | • Use with caution in patients with colitis due to increased absorption<br>• Administer suspension 2 hours before or 1 hour after meals (empty stomach)<br>• Refrigerate suspension<br>• Monitor: renal, hepatic, and hematologic function with extended use<br>• Specific recommendations for patients undergoing dialysis, refer to PI |
| **Generic Name**<br>Ceftolozane and tazobactam<br><br>**Brand Name**<br>Zerbaxa | Treatment of susceptible bacteria that cause complicated intra-abdominal infections (when used with metronidazole) and complicated UTI including pyelonephritis *(for example: B. fragilis, S. anginosus, S constellatus, S. salivarius, E. cloacae, E. coli, K. pneumoniae, P. aeruginosa, K. oxytoca, P. mirabilis)* | **Usual parenteral dose for complicated UTI**:<br>IV: 1.5 g every 8 hours for 7 days | • Administer suspension 2 hours before or 1 hour after meals<br>• Suitable solutions for administration range in color from clear to slight yellow<br>• Monitor: renal function<br>• Specific recommendations for patients undergoing dialysis, refer to PI |

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|---|---|---|---|
| **Generic Name**<br>Ceftriaxone<br><br>**Brand Name**<br>Rocephin<br>PD | Treatment of susceptible bacteria that cause lower respiratory tract infections, otitis media, skin and skin structure infections, bone and joint infections, intra-abdominal infections, urinary tract infections, pelvic inflammatory disease, uncomplicated gonorrhea, septicemia, and meningitis<br><br>Perioperative prophylaxis | **Usual parenteral dose for skin and skin structure infections:**<br>IM, IV: 1 to 2 g every 12 to 24 hours | • Contraindicated in IV solutions with lidocaine<br>• May increase INR<br>• Rarely causes hemolytic anemia<br>• Use with caution if patient has biliary stasis or sludge; can cause pancreatitis<br>• Use with caution in patients with colitis due to increased absorption<br>• Do not administer concurrently with calcium due to precipitation; flush lines before and after infusion<br>• In patients with renal and hepatic impairment, do not use doses greater than 2 g daily<br>• Monitor: prothrombin time and INR |

*Fourth-Generation Cephalosporins*

Universal prescribing alerts:

- Cephalosporins have been associated with seizures, especially in patients with renal impairment given unadjusted doses. Dosage reductions are recommended in these patients for certain cephalosporin agents.

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefepime<br><br>**Brand Name**<br>Maxipime<br>▲ PD | Treatment of susceptible bacteria that cause intra-abdominal infections, pneumonia, skin and skin structure infections, and complicated and uncomplicated urinary tract infections *(for example: E. coli, viridans group streptococci, P. aeruginosa, K. pneumoniae, Enterobacter, B. fragilis, S. pneumoniae, S. aureus, S pyogenes, P. mirabilis)*<br><br>Empiric treatment of febrile neutropenia | **Usual parenteral dose for moderate to severe pneumonia:**<br>IV: 1 to 2 g every 12 hours for 10 days | • May increase INR<br>• Neurotoxicity can develop in patients with poor renal function due to increased levels: decrease dose<br>• Use with caution in patients with colitis due to increased absorption<br>• Use with caution in patients with history of seizures; high levels can increase risk for seizure<br>• Decrease dose in elderly patients, who often have impaired renal function; increased risk of encephalopathy, myoclonus, and seizures<br>• The intramuscular (IM) administration is only indicated by the FDA for UTI due to *E. coli* when the IM route is considered a more appropriate route of administration<br>• Monitor: renal function<br>• Specific recommendations for patients undergoing dialysis, refer to PI |

### *Fifth-Generation Cephalosporins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Cephalosporins have been associated with seizures, especially in patients with renal impairment given unadjusted doses. Dosage reductions are recommended in these patients for certain cephalosporin agents.

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Ceftaroline<br><br>**Brand Name**<br>Teflaro | Community-acquired pneumonia *(for example those caused by: S. pneumoniae, S. aureus, H. influenzae, K. pneumoniae, K. oxytoca, E. coli)* | **Usual parenteral dose for skin and skin structure infections:**<br>IV: 600 mg every 12 hours for 5 to 14 days | • Rarely can cause hemolytic anemia<br>• Administer by slow infusion over 5 to 60 minutes<br>• Suitable solutions for administration range in color from clear to dark yellow<br>• Monitor: renal function and for allergic reaction<br>• Specific recommendations for patients undergoing dialysis, refer to PI |
| | Complicated skin and skin structure infections *(for example those caused by: S. aureus* (MSSA and MRSA), *S. pyogenes, S. agalactiae, E. coli, K. pneumoniae, K. oxytoca)* | | |

## Miscellaneous Beta-Lactams

### *Carbapenems*

Universal prescribing alerts

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Contraindicated if patient has a known serious allergic reaction to carbapenems; use caution if patient is allergic to beta-lactams

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Doripenem<br><br>**Brand Name**<br>Doribax | Treatment of susceptible bacteria that cause complicated intra-abdominal infections, and complicated urinary tract infections<br><br>Aerobic gram-positive, aerobic gram-negative *(P. aeruginosa)*, and anaerobic organisms | **Usual parenteral dose for complicated intra-abdominal infections:**<br>IV: 500 mg every 8 hours for 5 to 14 days | • Can cause confusion and seizures in high doses; use with caution in patients with poor renal function and CNS disorders<br>• Monitor: renal function; hematologic function with extended use<br>• Switch to oral therapy when clinical improvement is appropriate for conversion. |

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|---|---|---|---|
| **Generic Name**<br>Ertapenem<br><br>**Brand Name**<br>Invanz<br>  | Treatment of susceptible bacteria that cause pelvic infections, community-acquired pneumonia, complicated intra-abdominal infections, complicated skin and skin structure infections, and complicated UTI<br>Colorectal surgery prophylaxis *(for example: S. agalactiae, E, coli, Bacteroides, P. asaccharolytica, Peptostreptococcus, P. bivia, S. pneumoniae, H. influenzae, M. catarrhalis, C. clostridioforme, E. lentim, S. aureus, S pyogenes, K. pneumoniae, P. mirabilis* sensitive to beta-lactamase–producing bacteria) | **Usual parenteral dose for complicated UTI:**<br>IV: 1 g daily for 10 to 14 days<br>IM administration may be used as an alternative to IV, however only administer IM injection for 7 days<br><br>**Usual dose for surgical prophylaxis:** IV: 1 g 1 hour before surgery | • Can cause confusion and seizures in high doses; use with caution in patients with poor renal function and CNS disorders<br>• IM is diluted with lidocaine<br>• Can increase risk of breakthrough seizures if used with valproic acid and derivatives: avoid combination use if possible<br>• Monitor: renal, hepatic, and hematologic function with extended use; conduct neurologic assessment before use |
| **Generic Name**<br>Imipenem and cilastatin sodium<br><br>**Brand Name**<br>Primaxin<br>  | Treatment of susceptible bacteria that cause lower respiratory tract infections, urinary tract infections, intra-abdominal infections, gynecologic infections, bone and joint infections, skin and skin structure infections, endocarditis, polymicrobic infections, and septicemia *(for example: S. aureus, Streptococcus, E. coli, Klebsiella, Enterobacter, P. aeruginosa,* anaerobes Sensitive to beta-lactamase–producing bacteria) | **Usual parenteral dose for UTI:**<br>IV: 250 to 500 mg every 6 hours. Duration of treatment is based on severity of the infection | • Can cause confusion and seizures in high doses; use with caution in patients with poor renal function and CNS disorders<br>• Do not administer IV push<br>• If nausea/vomiting develops during administration, lower the infusion rate<br>• May cause glucose monitoring by Clinitest to be inaccurate<br>• Monitor: renal, hepatic, and hematologic function throughout therapy<br>• Specific recommendations for patients undergoing dialysis, refer to PI<br>• Adults with lower body weight require dose adjustments (less than 70 kg) |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Meropenem<br><br>**Brand Name**<br>Merrem<br><br>▲ (PD) | Treatment of infections caused by susceptible bacteria such as: meningitis, complicated skin and skin structure infections, and intra-abdominal infections *(for example: S. pneumoniae, H. influenzae, N. meningitides, S. aureus, S. pyogenes, S. agalactiae, E. faecalis, viridans group streptococci, P. aeruginosa, E. coli, P. mirabilis, B. fragilis, Peptostreptococcus, K. pneumoniae, B. thetaiotaomicron)* | **Usual parenteral dose for complicated skin and skin structure infections:**<br>IV: 500 to 1000mg daily every 8 hours. Duration of treatment is based on severity of infection | • Can cause confusion and seizures in high doses; use with caution in patients with poor renal function and CNS disorders<br>• Outpatients should not operate machinery or drive until it is determined that the patient can tolerate the therapy<br>• Monitor: renal and liver function and CBC during extended use<br>• Specific recommendations for patients undergoing dialysis; refer to PI<br>• Age-specific dose/indications; refer to PI |

## *Cephamycins*

Universal prescribing alerts:

- Known serious allergic reaction: contraindicated if patient has had an allergic reaction to a cephalosporin agent; use caution if patient has had an allergic reaction to a penicillin agent due to cross-reaction
- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Cefotetan<br><br>**Brand Name**<br>Cefotan<br><br>▲ | Treats susceptible bacteria that cause respiratory tract infections, skin and skin structure infections, bone and joint infections, UTI and gynecologic infections, septicemia, intra-abdominal infections, and mixed infections<br><br>Active against gram-negative bacilli: *E. coli, Klebsiella, Proteus;* anaerobes<br><br>Less active against staphylococci and streptococci<br><br>Perioperative prophylaxis | **Usual parenteral dose for complicated UTI:**<br>IM, IV: 1 to 2g every 12 hours | • Alcohol use may cause a disulfiram-like reaction<br>• Monitor: renal, hepatic, and hematologic function with extended use; prothrombin time if poor renal/hepatic function, nutritionally deficient, or extended use of treatment; for hemolytic anemia<br>• Specific recommendations for patients undergoing dialysis; refer to PI<br>• Perioperative doses are given 30 to 60 minutes prior to surgery<br>Contraindications:<br>• Previous cephalosporin-associated hemolytic anemia (threefold increased risk compared to other cephalosporins) |

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|---|---|---|---|
| **Generic Name**<br>Cefoxitin<br><br>**Brand Name**<br>Mefoxin<br><br>PD | Treatment of susceptible bacteria that cause bone and joint infections, gynecologic infections, intra-abdominal infections, lower respiratory tract infections, septicemia, skin and skin structure infections, and urinary tract infections *(for example: S. aureus, E. coli, N. gonorrhoeae, B. fragilis, Clostridium, P. niger, Peptostreptococcus, S. agalactiae, Klebsiella, S. pneumoniae, H. influenzae, S. epidermidis, S. pyogenes, P. mirabilis, Morganella morganii, P. vulgaris, Providencia)*<br><br>Perioperative prophylaxis for uncontaminated GI surgery, hysterectomy, and cesarean section | **Usual parenteral dose for lower respiratory infection:**<br>IV or IM: 1 to 2 g every 6 to 8 hours (max 12 g per day) | • Use with caution in patients with colitis due to increased absorption<br>• Powder for solution requires reconstitution prior to use<br>• Cephalosporin agents, including cefoxitin, have been associated with seizures, especially in patients with renal impairment given unadjusted doses<br>• High levels in patients with poor renal function can increase risk for seizures<br>• IV is preferred route since IM is painful<br>• Solution for injection can darken depending on storage conditions with no loss in efficacy<br>• Monitor: renal function and prothrombin time<br>• Specific recommendations for patients undergoing dialysis; refer to PI |

*Monobactams*

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Aztreonam<br><br>**Brand Name**<br>Azactam<br>Cayston<br><br>PD | Treatment of susceptible gram-negative bacilli bacteria that cause urinary tract infections, lower respiratory tract infections, septicemia, skin and skin structure infections, intra-abdominal infections, and gynecologic infections<br><br>Inhalation via nebulizer improves respiratory symptoms in cystic fibrosis (CF).<br><br>*P. aeruginosa* | **Usual parenteral dose for lower respiratory infections:**<br>IM/IV: 1 to 2 g every 8 to 12 hours<br>(max 8 g per day)<br><br>**Usual nebulized dose for CF:**<br>75 mg 3 times per day for 28 days | • Rarely can cause toxic epidermal necrolysis (TEN): use with caution in bone marrow transplant patients who have risks for TEN<br>• Suitable solutions for administration range in color from clear to light yellow to pink<br>• Administer a bronchodilator before using the nebulizer to prevent bronchospasm<br>• Special pharmacies distribute Cayston; contact Cayston Access Program<br>• Monitor: liver function periodically<br>• Specific recommendations for patients undergoing dialysis; refer to PI |

## Chloramphenicols

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Chloramphenicol<br><br>**Brand Name**<br>Chloromycetin<br><br>■ | Treatment of severe infections when other antibiotics are unable to eradicate the bacteria *(for example: Bacteroides, H. influenzae, N. meningitides, Salmonella, Rickettsia)*<br><br>Active against most vancomycin-resistant enterococci | **Usual parenteral dose for CNS infections:**<br>IV: 50 to 100 mg/kg per day in divided doses every 6 hours | • Drug interactions may require dose adjustment<br>• May cause gray syndrome, which causes circulatory collapse: do not let blood levels reach or exceed 50 mcg/mL; use with caution in patients with poor renal or hepatic function<br>• Use with caution in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency: greater risk for hemolytic anemia<br>• Can deplete vitamin B in patients: may need to supplement<br>• Use caution in preparing and disposing of infusion<br>• Aplastic anemia may develop weeks or months after use: caution patients on symptoms<br>• Monitor: CBC with differential at baseline and every 2 days during treatment; renal and liver function periodically; chloramphenicol blood levels (greater risk of high levels with poor renal or hepatic function)<br>Contraindicated:<br>• In patients with viral infections or mild or moderate bacterial infections<br>• When used for bacterial prophylaxis and other minor infections due to potential for toxicity<br>Associated with:<br>• Serious and fatal blood dyscrasia events when used on a short-term or long-term basis |

## Macrolides

### *Erythromycins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Drug interactions may require dose adjustments

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Erythromycin<br><br>**Brand Name**<br>Ery-Tab (delayed release) | Treatment of infections caused by susceptible bacteria *(for example: S. pyogenes, S. pneumoniae, S. aureus, M. pneumoniae, L. pneumophila,* diphtheria, pertussis, *Chlamydia, erythrasma, N. gonorrhoeae, E. histolytica,* | **Usual oral dose:** 250 to 500 mg every 6 to 12 hours (max 4 g per day)<br>Delayed release tablet/capsule | • Rarely can cause QTc prolongation and ventricular arrhythmias: use with caution in patients who already have prolongation, hypokalemia, or hypomagnesemia<br>• Can cause hepatic impairment: use with caution in patients with existing poor hepatic function |

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| PCE Dispertab (delayed release, contains polymer-coated particles)<br>ERYC (delayed release)<br>Ilotycin (ophthalmic)<br>Romycin (ophthalmic)<br>Erygel<br>Akne-Mycin<br>Ery | syphilis, *Campylobacter)*<br>Nongonococcal urethritis<br>Colorectal preoperative prophylaxis in combination with neomycin<br><br>Conjunctivitis (ophthalmic only)<br><br>Acne (topical only) | **Ophthalmic:** ½ inch, 2 to 6 times per day on the underlid of the eye<br><br>**Gel (for acne):** apply 1 to 2 times daily; response should be seen in 6 to 8 weeks<br><br>**Ointment, solution, pads (for acne):**<br>Apply 2 times daily | • High doses may cause ototoxicity<br>• Do not administer with milk or acidic beverages<br>• Administer with food if nausea/vomiting develops<br>• May worsen weakness caused by myasthenia gravis<br>• Elderly patients are at increased risk of adverse events<br>• Alcohol may decrease absorption: avoid use<br>• Gel is flammable: do not put near heat source<br>• Monitor: for adverse events |
| **Generic Name**<br>Erythromycin estolate<br><br>**Brand Name**<br>Ilosone<br>QT PD | See Erythromycin | **Usual oral dose:**<br>250 mg every 6 hours<br>500 mg every 12 hours | • See Erythromycin<br>• More acid-stable compared to base<br>• Available as capsules, tablets and suspension |
| **Generic Name**<br>Erythromycin ethylsuccinate<br><br>**Brand Name**<br>E.E.S. granules<br>EryPed<br>E.E.S. Liquid<br>E.E.S. Filmtab<br>QT PD | See Erythromycin | **Usual oral dose for moderately severe lower respiratory tract infections:**<br>400 to 800 mg every 6 to 12 hours (max 4 g erythromycin base per day) | • See Erythromycin<br>• Refrigerate after reconstituting<br>• More acid-stable compared to base<br>• 400mg EES is roughly equal to 250mg base/stearate<br>• Available as a tablet and suspension |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Erythromycin lactobionate<br>QT PD | See Erythromycin | **Usual parenteral dose for lower respiratory tract infections:**<br>IV: 15 to 20 mg/kg per day in divided doses every 6 hours<br>(max 4 g erythromycin base per day) | • See Erythromycin<br>• Administer IV slowly to minimize irritation to the vein |
| **Generic Name**<br>Erythromycin stearate<br><br>**Brand Name**<br>Erythrocin Filmtab<br>QT PD | See Erythromycin | **Usual oral dose for lower respiratory tract infections:**<br>250 to 500 mg every 6 to 12 hours<br>(max 4 g erythromycin base per day) | • See Erythromycin<br>• More acid-stable than base<br>• Better bioavailability on empty stomach; however, most people take it with food to avoid nausea |

*Ketolides*

Universal prescribing alerts

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Telithromycin<br><br>**Brand Name**<br>Ketek<br>▲ ■ QT | Treatment of infections caused by susceptible bacteria that cause community-acquired pneumonia *(for example: S. pneumoniae, H. influenzae, M. catarrhalis, Chlamydophila pneumoniae, M. pneumoniae)* | **Usual oral dose for community acquired pneumonia:**<br>800 mg once daily for 7 to 10 days | • Rarely can cause QTc prolongation and ventricular arrhythmias: use with caution in patients with existing prolongation, hypokalemia, or hypomagnesemia<br>• Can cause hepatic impairment: use with caution in patients with existing poor hepatic function and discontinue therapy if signs and symptoms of liver damage occur<br>• Can cause syncope, loss of consciousness, and visual disturbances: caution patients about operating machinery and driving until tolerance of the therapy is established<br>• Monitor: hepatic function including liver enzymes and signs and symptoms of liver failure, visual changes<br>• Drug interactions may require dose adjustments<br>Contraindications:<br>• Myasthenia gravis<br>• History of hepatitis with macrolide use<br>• Associated with life-threatening respiratory failure in myasthenia gravis; avoid use in patients with this condition |

## *Other Macrolides*

Universal prescribing alerts:

- Drug interactions may require dose adjustments

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Azithromycin<br><br>**Brand Name**<br>Zithromax<br>Tri-Pak<br>Zithromax Z-Pak<br>Zmax<br>AzaSite<br><br>QT PD | Treatment of susceptible bacteria that cause infections such as: otitis media, pharyngitis/tonsillitis, community-acquired pneumonia (CAP), pelvic inflammatory disease, genital ulcer disease in males, exacerbations of chronic obstructive pulmonary disease, sinusitis, uncomplicated skin and skin structure infections, urethritis, and cervicitis *(for example: H. influenzae, M. catarrhalis, S. pneumoniae, Chlamydia pneumoniae, S. pyogenes, M. pneumoniae, C. trachomatis, N. gonorrhoeae, M. hominis, H. ducreyl, S. aureus, S. agalactiae)*<br><br>Prophylaxis against and treatment of Mycobacterium avium complex in HIV patients<br><br>Conjunctivitis | **Usual oral dose for CAP:**<br>500 mg day 1, then 250 mg daily on days 2 through 5.<br>Alternatively may give ER: 2 g once as a single dose<br>Alternatively may give Usual parenteral dose for CAP:<br>IV: 500 mg daily for at least 2 days then convert to oral dose to complete 7 to 10 day course<br><br>***M. avium* complex disease prophylaxis in HIV patients:**<br>1200 mg once weekly<br>600 mg twice weekly<br>500 to 600 mg daily with ethambutol<br>**Ophthalmic:** 1 drop into affected eye 2 times per day for 2 days, then once daily for 5 days | • Rarely can cause QTc prolongation and ventricular arrhythmias: use with caution in patients with existing prolongation, hypokalemia, or hypomagnesemia<br>• Use with caution in patients with hepatic impairment: can cause cholestatic hepatitis and hepatic dysfunction<br>• Can delay or mask symptoms of gonorrhea or syphilis; assess for these diseases before initiating treatment<br>• Use with caution if GFR less than 10 mL/min; increased gastrointestinal side effects are possible in such cases<br>• Immediate-release forms are not interchangeable with the extended-release suspension<br>• Administer extended-release suspension on an empty stomach<br>• May cause worsening of existing myasthenia gravis symptoms or create new symptoms<br>• Increased macrolide resistance is occurring in syphilis; macrolides are not recommended for early syphilis<br>• Monitor: hepatic function, CBC with differential; if used for gonorrhea, test for cure 7 days after treatment<br><br>Contraindications:<br>• Prior azithromycin use was associated with cholestatic jaundice or hepatic dysfunction |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Clarithromycin<br><br>**Brand Name**<br>Biaxin<br>  | Treatment of susceptible bacteria that cause infections such as: pharyngitis/tonsillitis, sinusitis, chronic bronchitis, community-acquired pneumonia (CAP), uncomplicated skin and skin structure infections, and duodenal ulcer disease<br><br>Prophylaxis against and treatment of *Mycobacterium avium* complex in HIV patients *(for example: H. influenzae, S. pneumoniae, M. catarrhalis, M. pneumoniae, Chlamydophila pneumoniae, S. pyogenes, H. parainfluenzae, S. aureus, H. pylori)* | **Usual oral dose for CAP:**<br>250 every 12 hours for 7 to 14 days<br>Alternatively may give<br>1000 mg ER once daily for 7 days | • Rarely can cause QTc prolongation and ventricular arrhythmias: use with caution in patients with existing prolongation, hypokalemia, or hypomagnesemia<br>• Can cause hepatic impairment: use with caution in patients with existing poor hepatic function and discontinue therapy if signs and symptoms of liver damage occur<br>• Can cause TEN, Stevens–Johnson syndrome (SJS), and drug reaction with eosinophilia and systemic symptoms (DRESS): discontinue if patient develops rash or other symptoms<br>• Administer ER formulation with food<br>• ER tablets may appear in stools: consider alternative dosage form<br>• May cause worsening of existing myasthenia gravis symptoms or create new symptoms<br>• Use with caution in patients with coronary artery disease: associated with an increase in cardiovascular mortality<br>• Do not use with ranitidine if patient has a history of porphyria or if CrCl less than 25 mL/min<br>• Monitor: CBC with differential, BUN, SCr<br>Contraindications:<br>• History of QTc prolongation or ventricular arrhythmias<br>• Prior clarithromycin use was associated with cholestatic jaundice or hepatic dysfunction |
| **Generic Name**<br>Fidaxomicin<br><br>**Brand Name**<br>Dificid | Treatment of *C. difficile*-associated diarrhea (CDAD) | **Usual oral dose for CDAD:**<br>200 mg 2 times per day for 10 days | • Minimal absorption: not effective against systemic infections |
| **Penicillins** | | | |
| *Natural Penicillins* | | | |
| Universal prescribing alerts:<br>• Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use<br>• May cause false-positive or negative urinary glucose if patient is using Clinitest | | | |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Penicillin G<br><br>**Brand Name**<br>Benzathine<br>Bicillin L-A<br><br>■ PD | Treatment of susceptible bacteria that cause respiratory tract infections caused by streptococci<br><br>Treatment of syphilis, yaws, bejel, and pinta<br><br>Secondary prophylaxis against glomerulonephritis, rheumatic fever, chorea, and rheumatic heart disease | **Usual parenteral dose for upper respiratory tract infections:**<br>IM: 600,000 to 1.2 million units once daily for at least 10 days (duration is based on severity of infection) | • Use with caution in patients with poor renal function<br>• May increase risk of seizures in patients with history of seizure disorder<br>• To reduce the pain of injection, warm the medication to room temperature<br>• Inject in the upper outer quadrant of the gluteal muscle; avoid injecting near an artery or nerve to prevent neurologic damage<br>• Not recommended to treat congenital syphilis and neurosyphilis due to treatment failures<br>• Assess the patient's renal function and identify any history of seizures<br>• Associated with cardiopulmonary arrest and death with IV use (never administer IV)<br>• May be give every 1 to 4 weeks for secondary prevention or latent syphilis<br>• Benzathine recommended for syphyllis |
| **Generic Name**<br>Penicillin G<br><br>**Brand Name**<br>Potassium<br>Pfizerpen-G<br><br>▲ PD | Treatment of susceptible bacteria that cause infections such as sepsis, pneumonia, pericarditis, endocarditis, meningitis, anthrax, botulism, gas gangrene, and tetanus | **Usual parenteral dose for pneumonia:**<br>IV: 5 to 24 million units per day in divided doses every 4 to 6 hours | • High levels may increase risk of seizures: use with caution in patients with history of seizures<br>• Neurovascular damage may occur if administered via an artery or near peripheral nerves or blood vessels<br>• May increase potassium in serum<br>• 1 million units is approximately equal to 625 mg<br>• Monitor: electrolytes periodically; hepatic, renal, cardiac, and hematologic function if extended use or high doses |
| **Generic Name**<br>Penicillin G<br><br>**Brand Name**<br>Procaine<br>Wycillin<br><br>PD | Treatment of susceptible bacteria that cause infections such as: anthrax, diphtheria, endocarditis, erysipeloid, fusospirochetosis, respiratory tract infections, rat-bite fever, skin and soft-tissue infections, syphilis, yaws, bejel, and pinta<br><br>Prophylaxis against anthrax<br><br>Treatment of susceptible streptococci and staphylococci | **Usual parenteral dose for upper respiratory tract infections:**<br>IM: 600,000 to 1.2 million units once daily for at least 10 days (duration is based on severity of infection) | • May cause fibrosis and atrophy with repeated injections in the anterolateral thigh<br>• Transient neuropsychiatric reactions such as confusion and hallucinations have occurred after receiving a large dose; they typically last for 15 to 30 minutes<br>• Use with caution in patients with poor renal function or history of seizures<br>• Neurovascular damage may occur if administered via the intra-arterial, intravascular, or IV route<br>• If the patient has an allergy to procaine, test with 0.1 mL of procaine to determine if there is an allergic reaction; do not use if an allergic reaction occurs<br>• Monitor: injection-site reactions; mental status after injection; renal and hematologic function with extended use |

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| **Generic Name**<br>Penicillin V potassium<br><br>**Brand Name**<br>Potassium<br>Pen-Vee K<br>Veetids<br>PD | Treatment of susceptible bacteria that cause respiratory tract infections, otitis media, sinusitis, and skin and soft-tissue infections<br><br>Prophylaxis in rheumatic fever<br><br>Strong activity in streptococcal species | **Usual oral dose for upper tract infections:**<br>250 to 500 mg every 6 hours | • Use with caution in patients with poor renal function or history of seizures<br>• Administer on an empty stomach to increase absorption<br>• Store reconstituted suspension in the refrigerator<br>• Monitor: renal and hematologic function periodically with extended use<br>• Treatment duration depends on severity of infection |

*Aminopenicillins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Amoxicillin<br><br>**Brand Name**<br>Moxatag<br>PD | Treatment of susceptible bacteria that cause genitourinary tract infections, *H. pylori* infections, lower respiratory infections, pharyngitis/tonsillitis, otitis media, rhinosinusitis, and skin and skin structure infections *(for example: E. coli, P. mirabilis, E. faecalis, Streptococcus, S. pneumoniae, Staphylococcus, H. influenzae)*<br><br>ER: *S. pyogenes* | **Usual oral dose for upper respiratory tract infections:**<br>250 to 500 mg every 8 hours<br>Alternatively may give:<br>500 to 875 mg twice daily<br>ER: 775 mg once daily | • Administer extended-release tablets within 1 hour after a meal<br>• Monitor: renal, hepatic, and hematologic function with extended use |
| **Generic Name**<br>Amoxicillin and clavulanate<br><br>**Brand Name**<br>Augmentin<br>Amoclan | Treatment of susceptible bacteria that cause community-acquired pneumonia (XR only), otitis media, lower respiratory tract, sinusitis, skin and skin structure infections, and urinary tract infections | **Usual oral dose for acute otitis media:**<br>500 mg every 8 to 12 hours<br>Alternatively may give<br>875 mg every 12 hours<br>For sinusitis and other | • More likely to cause diarrhea than amoxicillin due to the amounts of clavulanic acid used<br>• Can cause hepatic dysfunction (though rare)<br>• Dosed based on the amoxicillin component<br>• Administer XR tablets with food; may administer other formulations with food to decrease stomach upset<br>• Refrigerate suspension after reconstitution |

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| PD | *(for example: H. influenzae, M. catarrhalis, H. parainfluenzae, K. pneumoniae, S. aureus, S. pneumoniae, E. coli, Klebsiella, Enterobacter)*<br><br>Sensitive to beta-lactamase–producing bacteria | infections may alternatively give: XR: 2000 mg every 12 hours | • Different formulations may contain different amounts of clavulanic acid and are not interchangeable<br>• Monitor: renal, hepatic, and hematologic function with extended use<br>• Specific recommendations for patients undergoing dialysis; refer to PI<br>Contraindications:<br>• Prior use caused hepatic dysfunction<br>• XR tablets are contraindicated if CrCl less than 30 mL/min |
| **Generic Name**<br>Ampicillin<br><br>**Brand Name**<br>Principen<br><br>PD | Treatment of susceptible bacteria that cause the following infections:<br><br>Oral: genitourinary tract infections, gastrointestinal tract infections, respiratory tract infections<br><br>Parenteral (IM, IV): meningitis, gastrointestinal infections, respiratory tract infections, septicemia, endocarditis, urinary tract infections *(for example: E. coli, P. mirabilis,* enterococci*, Shigella, Salmonella, N. gonorrhoeae, H. influenzae,* staphylococci, streptococci*, L. monocytogenes, N. meningitides, S. pneumoniae, S. aureus)* | **Usual oral dose for respiratory tract infections:** 250 to 500 mg every 6 hours<br><br>**Usual parenteral dose for respiratory tract infections:**<br>IM, IV: 250 to 500 mg every 6 hours | • May cause a rash that is not associated with hypersensitivity reaction; appears 3 to 14 days after first dose<br>• Rapid infusion may cause seizures: infuse slowly<br>• Administer on an empty stomach to increase absorption<br>• Monitor: renal, hepatic, and hematologic function with extended use<br>• Specific recommendations for patients undergoing dialysis<br>Contraindications:<br>• Infection with penicillinase-producing bacteria |
| **Generic Name**<br>Ampicillin and sulbactam<br><br>**Brand Name**<br>Unasyn<br><br>PD | Treatment of susceptible bacteria that cause skin and skin structure infections, intra-abdominal infections, and gynecologic infections *(for example: S. aureus, H. influenzae, E. coli, Klebsiella, Acinetobacter, Enterobacter,* anaerobes)<br><br>Sensitive to beta-lactamase–producing bacteria | **Usual parenteral dose for skin and skin structure infections:**<br>IM, IV: 1.5 to 3 g every 6 hours (max 12 g per day) | • May cause hepatic dysfunction: use with caution in patients with hepatic impairment<br>• May cause a rash that is not associated with hypersensitivity reaction; appears 3 to 14 days after first dose<br>• Dose represents the combination of ampicillin and sulbactam<br>• Monitor: renal, hepatic, and hematologic function with extended therapy; if hepatic impairment exists, monitor LFTs periodically<br>Contraindications:<br>• Prior use caused hepatic dysfunction |

## *Penicillinase-Resistant Penicillins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using cupric sulfate (Benedict's solution, Clinitest, Fehling's solution)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Dicloxacillin<br><br>**Brand Name**<br>Dynapen<br><br>PD | Treatment of susceptible bacteria that cause pneumonia, skin and soft-tissue infections, and osteomyelitis<br><br>Sensitive to penicillinase-producing staphylococci | **Usual oral dose:**<br>125 to 500 mg every 6 hours for 7 to 14 days | • Administer on an empty stomach |
| **Generic Name**<br>Nafcillin<br><br>**Brand Name**<br>Nallpen<br><br>PD | Treatment of susceptible bacteria that cause osteomyelitis, bacteremia, septicemia, endocarditis, and CNS infections<br><br>*Staphylococcus* | **Usual parenteral dose for osteomyelitis:**<br>IV: 1 to 2 g every 4 hours<br>Treatment duration based on severity of infection | • Can cause neurotoxic effects: use caution when giving large doses or if patient has renal/hepatic impairment<br>• Administer IM injections deep in the gluteal muscle<br>• IV formulation is a vesicant: avoid extravasation; if extravasation occurs, stop the infusion immediately and give hyaluronidase<br>• Monitor: CBC with differential at baseline and throughout treatment, urinalysis, BUN, SCr, aspartate transaminase (AST), alanine aminotransferase (ALT)<br>• May administer for a longer period of time for more serious infections (6 weeks) |
| **Generic Name**<br>Oxacillin<br><br>**Brand Name**<br>Bactocill<br><br>PD | Treatment of infections caused by penicillinase-producing staphylococci<br>Not for use if organism is susceptible to penicillin G | **Usual parenteral dose for mild to moderate severity skin infections:**<br>IM, IV: 250 to 500 mg every 4 to 6 hours | • Can cause acute (but reversible) hepatitis 2 to 3 weeks after first dose<br>• Use with caution in patients with poor renal function, although no specific dosage reductions are recommended<br>• May contain a significant amount of sodium: use with caution in elderly patients and patients on salt-restricted diets<br>• Can cause false-positive results for urinary and serum proteins<br>• Monitor: CBC, urinalysis, BUN, renal and liver function |

## *Extended-Spectrum Penicillins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive urinary glucose if patient is using copper reduction (Clinitest)

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Piperacillin and tazobactam<br><br>**Brand Name**<br>Zosyn<br>▲ PD | Treatment of susceptible bacteria that cause community-acquired pneumonia, intra-abdominal infections, nosocomial pneumonia, pelvic infections, and skin and skin structure infections *(for example: H. influenzae, P. aeruginosa, E. coli, B. fragilis, B. ovatus, B. thetaiotaomicron, B. vulgatus, S. aureus, Acinetobacter baumanii, K. pneumoniae)*<br><br>Treatment of moderate to severe susceptible infections<br><br>Sensitive to beta-lactamase–producing bacteria | **Usual parenteral dose for skin and skin structure infections:**<br>IV: 3.375 g every 6 hours<br><br>Higher dose recommendations for more severe infections<br>(max 18 g per day) | • May cause severe skin reactions such as TEN, SJS, or DRESS; discontinue if rash progresses<br>• Monitor electrolytes, especially if patient has low potassium<br>• Abnormal prothrombin time, platelet aggregation, and clotting times have occurred: use with caution in patients with renal impairment; discontinue if bleeding occurs<br>• Use with caution in patients with cystic fibrosis: increases the risk of fever and rash<br>• Use with caution in patients with renal impairment<br>• May increase risk of seizures: use with caution in patients with preexisting seizure disorders or renal impairment<br>• Specific recommendations for patients undergoing dialysis<br>• Ratio of piperacillin to tazobactam is 8:1<br>• 1 g contains 2.79 mEq of sodium<br>• Can cause false-positive results with the Platelia *Aspergillus* enzyme immunoassay<br>• Monitor: SCr, BUN, CBC with differential, prothrombin time (PT), partial thromboplastin time (PTT), serum electrolytes, LFTs, urinalysis, signs of bleeding |

## Quinolones

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause false-positive results with commercially available immunoassay kits for opioids
- May cause photosensitivity
- May cause QTc prolongation: use with caution in patients at high risk for arrhythmias
- May cause CNS effects such as tremor, restlessness, confusion, hallucinations, seizures, and pseudotumor cerebri: discontinue if severe adverse effects occur
- Because of the risk for serious and potentially permanent side effects associated with fluoroquinolone antibiotics, it is recommended that these agents be used only when alternative treatment options cannot be used
- Pediatric dose symbols are not included for these agents. Specific cautions are noted in the PI for anyone under the age of 18. Refer to additional references when treating this population

Associated with:

- Tendon inflammation or rupture: increased risk with concurrent corticosteroids, organ transplant, and age greater than 60 years
- Worsening weakness in myasthenia gravis: avoid use in patients with this condition

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Ciprofloxacin<br><br>**Brand Name**<br>Cipro<br>Ciloxan<br>Cextraxal<br>  | Treatment of susceptible bacteria that cause plague, UTI, uncomplicated cystitis in females, chronic prostatitis, lower respiratory tract infections, sinusitis, skin and skin structure infections, bone and joint infections, complicated intra-abdominal infections, infectious diarrhea, typhoid fever, uncomplicated cervical and urethra gonorrhea, and nosocomial pneumonia<br><br>To prevent anthrax or prevent progression of disease<br><br>Empiric treatment of febrile neutropenic patients<br><br>Ophthalmic: bacterial conjunctivitis and corneal ulcer<br><br>Otic: otitis externa | **Usual oral dose for complicated UTI:**<br>250 to 500 mg every 12 hours<br><br>Alternatively may give:<br>Usual ER dose: 1000 mg once daily<br>Alternatively may give:<br>Usual IV dose:<br>200 to 400 mg every 12 hours<br>Duration 7 to 14 days depending on severity of UTI infection<br><br>**Usual ophthalmic dose:**<br>Solution: 1 to 2 drops every 15 minutes to 4 hours<br><br>**Usual topical dose:**<br>Ointment: Apply ½ inch under eye 2 to 3 times per day<br><br>**Usual otic dose: instill contents of "single dose" container** twice per day for 7 days | • Rarely causes crystalluria: keep patient well hydrated<br>• May cause serious hypoglycemia: greater risk in diabetes and elderly<br>• Can cause hepatotoxicity: discontinue if signs of hepatitis occur<br>• Rarely can cause peripheral neuropathy: discontinue if symptoms occur<br>• Use with caution in patients with rheumatoid arthritis or seizure disorder<br>• Hemolytic anemia is more likely to occur with G6PD deficiency<br>• Immediate-release and extended-release tablets are not interchangeable<br>• Administer IV via slow infusion over 60 minutes and in a large vein to reduce venous irritation<br>• Administer at least 2 hours before or 6 hours after using antacids, calcium, iron, zinc, and dairy products<br>• Do not administer suspension through feeding tubes to avoid adherence to the tube<br>• Drug interactions may require doses adjustments or avoidance of certain drug combinations<br>• May mask symptoms of syphilis: test patients for syphilis when treating them for gonorrhea<br>• Warm the otic solution to room temperature before use<br>• Monitor: CBC, renal and hepatic function with extended use |
| **Generic Name**<br>Finafloxacin<br><br>**Brand Name**<br>Xtoro | Treatment of susceptible bacteria that cause acute otitis externa<br><br>*P. aeruginosa*, *S. aureus* (including MRSA) | **Usual otic dose:** 4 drops twice daily for 7 days<br>May increase dose to 8 drops for first dose with use of otowick | • Before instilling drops into affected ears, warm the bottle by holding it in the hand for 1 to 2 minutes<br>• Shake well before administration |

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| **Generic Name**<br>Gemifloxacin<br><br>**Brand Name**<br>Factive | Treatment of susceptible bacteria that cause exacerbation of chronic bronchitis and community-acquired pneumonia<br><br>Treatment of multidrug-resistant strains of *S. pneumoniae* | **Usual oral dose:**<br>320 mg once daily | • May cause serious hypoglycemia: greater risk in patients with diabetes and elderly patients<br>• Rarely can cause peripheral neuropathy: discontinue if symptoms occur<br>• Use with caution in patients with rheumatoid arthritis or seizure disorder<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Administer 3 hours before or 2 hours after using iron, zinc, or magnesium supplements<br>• May cause photosensitivity<br>• Monitor: WBC, renal function<br>• Specific recommendations for patients undergoing dialysis |
| **Generic Name**<br>Levofloxacin<br><br>**Brand Name**<br>Levaquin<br>Quixin<br><br>(See also Antituberculosis Agents) | Treatment of susceptible bacteria that cause community-acquired pneumonia, nosocomial pneumonia, chronic bronchitis exacerbation, rhinosinusitis, prostatitis, urinary tract infections (complicated and uncomplicated), pyelonephritis, and skin and skin structure infections (complicated and uncomplicated)<br><br>Reduce progression of anthrax<br><br>Treatment and prophylaxis of plague<br><br>Treatment of multidrug-resistant strains of *S. pneumoniae*<br><br>Ophthalmic: bacterial conjunctivitis | **Usual dose for sinusitis:**<br>PO, IV: 500 mg every 24 hours for 10 to 14 days<br>Alternatively may give 750 mg daily for 5 days<br><br>**Usual ophthalmic dose:**<br>1 to 2 drops 4 to 8 times per day | • May cause serious hypoglycemia: greater risk in patients with diabetes and elderly patients<br>• Can cause hepatotoxicity: discontinue if signs of hepatitis occur<br>• Rarely can cause peripheral neuropathy: discontinue if symptoms occur<br>• Use with caution in patients with rheumatoid arthritis or seizure disorder<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Infuse slowly to prevent hypotension<br>• Keep patients well hydrated to prevent crystalluria or cylindruria<br>• Administer oral medication 1 hour before or 2 hours after meals<br>• Administer 2 hours before or after antacids, magnesium, aluminum, iron, and zinc supplements<br>• Monitor: renal, hepatic, and hematopoietic function periodically during therapy; WBC<br>• Specific recommendations for patients undergoing dialysis. |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Moxifloxacin<br><br>**Brand Name**<br>Avelox<br>Vigamox<br>Moxeza<br><br>■ QT | Treatment of susceptible bacteria that cause community-acquired pneumonia, chronic bronchitis exacerbation, sinusitis, complicated and uncomplicated skin and skin structure infections, and complicated intra-abdominal infections<br><br>Treatment of multidrug-resistant *S. pneumoniae*<br><br>Prophylaxis and treatment of plague<br><br>Ophthalmic: conjunctivitis | **Usual dose for sinusitis:**<br>PO, IV: 400 mg every 24 hours for 10 days<br><br>**Usual ophthalmic dose:**<br>1 drop 2 to 3 times per day for 7 days | • May cause serious hypoglycemia: greater risk in patients with diabetes and elderly patients<br>• Can cause hepatotoxicity: discontinue if signs of hepatitis occur<br>• Rarely can cause peripheral neuropathy: discontinue if symptoms occur<br>• Use with caution in patients with rheumatoid arthritis or seizure disorder<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Administer 4 hours before or 8 hours after antacids, magnesium, aluminum, iron, and zinc supplements<br>• Infusion contains 34.2 mEq of sodium<br>• Monitor: WBC, ECG in patients with cirrhosis of the liver |
| **Generic Name**<br>Ofloxacin<br><br>**Brand Name**<br>Oflox<br>Ocuflox<br>Floxin<br><br>▲ ■<br>■ QT | Treatment of susceptible bacteria that cause chronic bronchitis exacerbation, community-acquired pneumonia, uncomplicated skin and skin structure infections, gonorrhea, urethritis and cervicitis, mixed infections of the urethra and cervix, pelvic inflammatory disease, uncomplicated cystitis, complicated urinary tract infections, and prostatitis<br><br>Ophthalmic: conjunctivitis and corneal ulcer<br><br>Otic: otitis media, chronic otitis media, and otitis externa | **Usual oral dose:** 200 to 400 mg every 12 to 24 hours<br><br>**Usual ophthalmic dose:**<br>1 to 2 drops every 2 to 6 hours<br>**Usual otic dose:** 10 drops 1 to 2 times per day | • May cause serious hypoglycemia: greater risk in patients with diabetes and elderly patients<br>• Rarely can cause peripheral neuropathy: discontinue if symptoms occur<br>• Use with caution in patients with hepatic impairment<br>• Use with caution in patients with rheumatoid arthritis or seizure disorder<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Do not administer 2 hours before or after food, antacids, zinc, magnesium, and aluminum supplements<br>• Can delay or mask symptoms of syphilis: assess for this infection before initiating treatment for gonorrhea<br>• Warm the otic solution to room temperature before administering it<br>• Monitor: CBC, renal and hepatic function with extended use |

## Sulfonamides

Universal prescribing alerts

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Sulfadiazine<br>▲ PD | Treatment of susceptible bacteria that cause chancroid, trachoma, inclusion conjunctivitis, nocardiosis, UTI, toxoplasmosis encephalitis, malaria, meningococcal meningitis, otitis medias, and meningitis<br><br>Prophylaxis against rheumatic fever | **Usual oral dose for UTI:**<br>2 to 4 g per day divided into 3 to 6 doses | • May cause blood dyscrasias, including fatal agranulocytosis<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Can cause SJS or TEN: discontinue if rash develops<br>• May cause hepatic necrosis: monitor and discontinue if adverse event becomes severe<br>• Use with caution in patients with asthma, hepatic impairment, or renal impairment<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Administer with 8 ounces of water<br>• Avoid concomitant intake of vitamins or acidic foods due to increased risk of crystalluria<br>• May give leucovorin to prevent adverse effects from folate deficiency<br>• Monitor: CBC, urinalysis, CD4+ count if treating for toxoplasmosis in HIV patients, sulfonamide blood levels if severe infection |
| **Generic Name**<br>Co-trixomazole | | | |
| **Generic Name**<br>Sulfamthoxazole/ Trimethoprim<br>**Brand Name**<br>Bactrim<br>Septra<br>Sulfatrim<br>▲ PD | Oral formulations treat susceptible bacteria that cause urinary tract infections, otitis media, chronic bronchitis exacerbations, prophylaxis and treatment of *Pneumocystis* pneumonia (PCP), traveler's diarrhea, and enteritis *(for example: E. coli, Klebsiella, Enterobacter, M. morganii, P. mirabilis, P. vulgaris, H. influenzae, S. pneumoniae, S. flexneri, S. sonnei)*<br><br>IV treats susceptible bacteria that cause PCP, enteritis, and complicated or severe urinary tract infections | **Usual oral dose:** 1 to 2 double-strength (DS) every 12 to 24 hours<br><br>**Usual parenteral dose:**<br>IV: 8 to 20 mg/kg per day divided into doses every 6 to 12 hours | • May cause blood dyscrasias, including fatal agranulocytosis and thrombocytopenia<br>• Can cause SJS or TEN: discontinue if rash develops<br>• May cause hepatic necrosis, hyperkalemia, hypoglycemia, hyponatremia: monitor and discontinue if adverse event becomes severe<br>• Use with caution in patients with asthma, thyroid dysfunction, folate deficiency, porphyria, and slow acetylators<br>• Do not use with leucovorin when treating PCP in HIV patients: increases risk of failure and death<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Dosing is based on the trimethoprim component<br>• Double-strength: sulfamethoxazole 800 mg and trimethoprim 160 mg<br>• Administer oral formulations with 8 ounces of water<br>• Some dosage forms contain propylene glycol; large amounts are toxic<br>• Monitor: CBC, potassium blood level, SCr, BUN<br>• May cause sun sensitivity<br>Contraindications:<br>• Megaloblastic anemia caused by folate deficiency<br>• Severe hepatic or renal impairment |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Sulfasalazine<br><br>**Brand Name**<br>Azulfidine<br>Sulfazine<br><br>PD | Treatment of susceptible bacteria that cause juvenile rheumatoid arthritis (EC), rheumatoid arthritis (EC), and ulcerative colitis (IR and EC) | **Usual oral dose for ulcerative colitis:**<br>uncoated tablets: 1 g every 6 to 8 hours<br><br>enteric coated tablets:<br>3 to 4 g per day divided doses and given every 8 hours. | • May cause blood dyscrasias, including fatal agranulocytosis<br>• Rarely can cause death from irreversible neuromuscular and central nervous system changes or from fibrosing alveolitis<br>• Can cause SJS or TEN: discontinue if rash develops<br>• May decrease folate absorption<br>• May cause hepatic necrosis: monitor and discontinue if adverse event becomes severe<br>• Reports of serious infections have occurred, including sepsis and pneumonia: monitor CBC with differential and watch for signs and symptoms of infection during and after treatment<br>• Use with caution in patients with asthma, hepatic impairment, or renal impairment, and slow acetylators<br>• Hemolytic anemia is more likely to occur in patients with G6PD deficiency<br>• Administer in evenly divided doses after meals<br>• Keep patients well hydrated to prevent crystalluria<br>• To prevent common gastrointestinal adverse effects, use EC or titrate dose to goal<br>• If EC tablets are found in stool, discontinue and use IR formulation<br>• Monitor: CBC with differential and LFTs at baseline and throughout therapy, urinalysis, renal function tests, stool frequency<br>Contraindications:<br>• Intestinal or urinary obstruction<br>• Porphyria |

## Tetracyclines

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use
- Can cause permanently discolored teeth; refer to pediatric medication management guidelines
- May cause photosensitivity; protect skin from direct sunlight
- Some agents require administration 2 hours before or 4 hours after antacids, aluminum, and magnesium supplements to maintain absorption; refer to PI

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Demeclocycline<br><br>**Brand Name**<br>Declomycin<br><br>PD | Treatment of susceptible bacteria that cause acne, urinary tract infections, and respiratory infections<br><br>Covers gram-negative and gram-positive organisms | **Usual oral dose:**<br>150 mg 4 times per day<br>300 mg twice daily | • Can cause nephrogenic diabetes insipidus: dose dependent<br>• May increase BUN: use with caution in patients with renal impairment<br>• Rarely causes pseudotumor cerebri: resolves when discontinued<br>• Use with caution in patients with hepatic and renal impairment: specific recommendations are not stated, but dose decrease or less frequent dosing interval is advised |

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|---|---|---|---|
| | | | • Administer 1 hour before or 2 hours after food or milk intake<br>• Administer with fluids to prevent esophageal irritation<br>• Monitor: CBC, renal and hepatic function |
| **Generic Name**<br>Doxycycline<br><br>**Brand Name**<br>Adoxa<br>Vibramycin<br>Acticlate<br>Avidoxy<br>Doryx<br>Monodox<br>Morgidox<br>TargaDOX<br>Oracea<br>Targadox<br>PD | Treatment of susceptible bacteria that cause syphilis, gonorrhea, community-acquired pneumonia, anthrax, plague, tularemia, Q fever, intestinal amebiasis, severe acne, and the following organisms:<br>*Rickettsia, Chlamydia, Chlamydophila, Mycoplasma, Listeria, A. israelii, Clostridium, B. recurrentis, U. urealyticum, H. decreyi, V. cholera, C. fetus, Brucella, B. bacilliformis, K. granulomatis*<br><br>Prophylaxis against malaria<br><br>Oracea: inflammatory lesions due to rosacea<br><br>Excels at treating uncommon gram-negative and gram-positive bacteria | **Usual oral dose for lower respiratory tract infections:**<br>100 to 200 mg per day in 1 to 2 divided doses<br><br>IV dose is the same | • Rarely can cause hepatotoxicity: discontinue if signs and symptoms occur<br>• May cause hypersensitivity syndromes such as DRESS, angioneurotic edema, and systemic lupus erythematosus exacerbation<br>• May increase BUN: use with caution in patients with renal impairment<br>• Rarely causes pseudotumor cerebri: do not use with isotretinoin; will resolve when discontinued<br>• Can cause hyperpigmentation in various body tissues, including nails and skin<br>• IV and oral formulations are bioequivalent except for Oracea<br>• Oral formulation is preferred; needs to be infused slowly, but prolonged administration can cause thrombophlebitis<br>• Administer oral formulations with 8 ounces of water while sitting up for 30 minutes to decrease esophageal irritation<br>• Administer Oracea on an empty stomach<br>• Can take with food to lessen stomach upset<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations.<br>• IV formulations with ascorbic acid may cause a false-negative urine glucose when using glucose oxidase tests (Clinistix, Diastix, Tes-Tape)<br>• Monitor: CBC; hepatic and renal function with extended use; test of cure 7 days after treatment for gonorrhea |
| **Generic Name**<br>Minocycline<br><br>**Brand Name**<br>Minocin<br>Solodyn<br>PD | Treatment of susceptible bacteria that cause intestinal amebiasis, acne, actinomycosis, anthrax, cholera, listeriosis, meningitis, ophthalmic infections, relapsing fever, respiratory tract infections, Rocky Mountain spotted fever, typhus fever, Q fever, rickettsialpox, tick fevers, sexually transmitted infections, skin and skin structure infections, urinary tract infections, Vincent infection, yaws, psittacosis, plague, tularemia, brucellosis, and bartonellosis *(for example:* | **Usual dose for lower respiratory tract infections:**<br>IV or oral : 200 mg, then 100 mg every 12 hours | • Can cause autoimmune syndromes such as lupus-like, hepatitis, and vasculitis autoimmune syndromes: discontinue and monitor LFT, antinuclear antibodies (ANA), and CBC<br>• Rarely can cause hepatotoxicity when using for acne: discontinue if signs and symptoms occur<br>• May cause severe skin reactions such as SJS and DRESS: discontinue if rash or other signs and symptoms appear<br>• May increase BUN: use with caution in patients with renal impairment<br>• Rarely causes pseudotumor cerebri: do not use with isotretinoin; will resolve when discontinued<br>• Can cause hyperpigmentation in various body tissues, including nails and skin<br>• Oral formulation is preferred; needs to be infused slowly, but prolonged administration can cause thrombophlebitis<br>• Administer oral formulations with 8 ounces of water while sitting up for 30 minutes to decrease esophageal irritation |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| | *Campylobacter fetus, Clostridium, Acinetobacter, E. coli, E. aerogenes, Shigella, N. meningitides, C. trachomatis, H. influenzae, Klebsiella, M. pneumoniae, S. pneumoniae, U. urealyticum, K. granulomatis, Treponema pallidum, S. aureus, Klebsiella)*<br><br>Treatment of asymptomatic carriers of *N. meningitides* | | • Can take with food to lessen stomach upset<br>• Caution patients about operating machinery and driving until effects of the medication are known: may cause dizziness<br>• IV formulation contains magnesium: use with caution in patients with renal impairment<br>• Monitor: liver and renal function tests and BUN with extended use; magnesium in patients with renal impairment; if symptoms of an autoimmune disorder occur, ANA and CBC; visual exams, if visual disturbances occur; if treating for syphilis, follow up with a serologic test 3 months after treatment |
| **Generic Name**<br>Tetracycline<br><br>**Brand Name**<br>Sumycin<br><br>▲ PD | Treats susceptible bacteria that cause acne, chronic bronchitis exacerbations, gonorrhea syphilis, tularemia<br><br>Gram-positive organisms, gram-negative organisms, *Mycoplasma, Chlamydia, Rickettsia*<br><br>Treats *H. pylori* when used with additional medications to reduce duodenal ulcer recurrence | **Usual oral dose for upper respiratory tract infections:**<br>250 to 500 mg 2 to 4 times per day | • Rarely can cause hepatotoxicity: use with caution in patients with renal and hepatic impairment<br>• May increase BUN: use with caution in patients with renal impairment<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Expired medications can cause nephropathy<br>• Rarely causes pseudotumor cerebri: do not use with isotretinoin; will resolve when discontinued<br>• Administer on an empty stomach to increase absorption<br>• Monitor: renal, hepatic, and hematologic function; temperature; WBC |
| **Glycylcyclines** | | | |
| Universal prescribing alerts<br>• Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Tigecycline<br><br>**Brand Name**<br>Tygacil<br><br>■ ■ | Treatment of susceptible bacteria that cause community-acquired pneumonia, complicated skin and skin structure infections, and complicated intra-abdominal infections *(for example: S. pneumoniae,* | **Usual parenteral dose for skin and skin structure infections:** 100 mg one-time dose, then 50 mg every 12 hours for 7 to 14 days | • Can cause antianabolic effects (increase in BUN, azotemia, acidosis, hyperphosphatemia)<br>• Hepatotoxic<br>• Can cause pancreatitis<br>• Can cause pseudotumor cerebri<br>• Suitable solutions for administration are yellow-orange in color<br>• Can cause significant nausea/vomiting; may need to premedicate patients with antiemetics |

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| | *H. influenzae, L. pneumophila, Citrobacter, Enterobacter, E. coli, Klebsiella, E. faecalis, S. aureus* (MSSA/MRSA), *S. anginosus, Bacteroides, Clostridium, Peptostreptococcus S. agalactiae, S. pyogenes, E. cloacae)* | | • Can cause photosensitivity<br>• Monitor: CBC, allergic reactions<br>• Associated with an increase in all-cause mortality (0.6%) compared to other antibiotics<br>• Switch to appropriate oral therapy as soon as medically appropriate. |

## Miscellaneous Antibacterials

### *Bacitracins*

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Bacitracin<br><br>**Brand Name**<br>Baciim<br>Ocu-Tracin<br>AK-Tracin<br>Baciguent<br><br>PD | Treatment of susceptible bacteria that cause superficial ocular infections<br><br>Topical ointment prgevents infection in minor cuts, scrapes, and burns: not recommended to use for longer than 1 week | **Usual ophthalmic dose:** apply 1 to 3 times daily on the lower eyelid<br><br>**Topical:** apply 1 to 3 times daily on affected area | • Extended use may lead to overgrowth of nonsusceptible bacteria, such as fungi: treat if new infection develops<br>• Systemic formulation use is indicated only in specific age populations; refer to PI<br>• Ointment: 1 unit = 0.026 mg |

### *Cyclic Lipopeptides*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Daptomycin<br><br>**Brand Name**<br>Cubicin<br><br>▲ | Treatment of susceptible bacteria that cause complicated skin and skin structure infections and bloodstream infections *(for example: S. aureus including MRSA, S. pyogenes, S. agalactiae, S. dysgalactiae subspecies equismilis, E. faecalis)* | **Usual parenteral dose for skin and skin structure infections:** IV: 4 mg/kg once daily for 7 to 14 days<br><br>Duration of treatment depends on severity of infection. Longer treatment may be warranted in certain cases | • May cause eosinophilic pneumonia, usually 2 to 4 weeks after initiating therapy<br>• May cause myopathy: discontinue if creatine phosphokinase (CPK) 10 times upper normal limit (UNL) or higher or CPK more than 5 times ULN with signs and symptoms<br>• May cause peripheral neuropathy<br>• Do not use with ReadyMED elastomeric infusion pumps due to leaching of an impurity into the solution<br>• May falsely increase both PT and INR<br>• Monitor: CPK weekly or more often if using a statin, compromised renal function, or unexpected rise in CPK levels<br>• Specific recommendations for patients undergoing dialysis |

| *Glycopeptides* | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Dalbavancin<br><br>**Brand Name**<br>Dalvance | Treatment of susceptible bacteria that cause acute skin and skin structure infections *(for example: S. aureus* including MRSA, *S. pyogenes, S. agalactiae, S. dysgalactiae, S. anginosus* group, *E. faecalis)* | **Usual parenteral dose:**<br>IV: 1500 mg single dose<br>1000 mg on day 1, then 500 mg 1 week later | • May cause reversible increase in transaminase levels<br>• May cause an infusion reaction resembling red man syndrome (hypotension, flushing, and/or maculopapular rash): slowing the infusion may alleviate symptoms<br>• Suitable solutions for administration range in color from colorless to yellow<br>• Monitor: BUN, renal and liver function, infusion-related reaction symptoms |
| **Generic Name**<br>Oritavancin<br><br>**Brand Name**<br>Orbactiv | Treatment of susceptible bacteria that cause acute skin and skin structure infections *(for example: S. aureus* including MRSA, *S. pyogenes, S. agalactiae, S. dysgalactiae, S. anginosus* group, *E. faecalis)* | **Usual parenteral dose:**<br>IV: 1200 mg single dose | • May cause infusion reactions, which are resolved by slowing or discontinuing the infusion<br>• May cause osteomyelitis<br>• Infuse over 3 hours<br>• Suitable solutions for administration range in color from colorless to pale yellow<br>• Monitor: serum urea nitrogen, renal and liver function<br>Contraindication:<br>• If heparin is used 120 hours after oritavancin dose due to false elevation of activated partial thromboplastin time (aPTT) |
| **Generic Name**<br>Telavancin<br><br>**Brand Name**<br>Vibativ | Treatment of susceptible bacteria that cause complicated skin and skin structure infections, hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP)<br><br>*S. aureus* (including MRSA), *E. faecalis, S. pyogenes, S. agalactiae, S. anginosus* | **Usual parenteral dose for HAP:**<br>IV: 10 mg/kg every 24 hours for 1 to 3 weeks | • May cause red man syndrome indicated by hypotension, flushing, and/or maculopapular rash: slow or discontinue infusion<br>• May cause QTc prolongation: use with caution in patients with preexisting prolongation or heart conditions<br>• Handle as a hazardous agent<br>• May interfere with coagulation tests: perform levels as close to the next dose as possible (at least 18 hours after previous dose)<br>• Monitor: renal function at baseline, during therapy, and 48 to 72 hours after last dose<br>• Infuse over 60 minutes<br>Associated with nephrotoxicity:<br>• Use with caution in patients with risk factors and monitor renal function throughout therapy and 48 to 72 hours after last dose<br>• Increased all-cause mortality compared to vancomycin when CrCl 50mL/min or less when treating for HAP/VAP |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Vancomycin<br><br>**Brand Name**<br>Vancocin<br><br>▲ (PD) | IV treats infection caused by staphylococci or streptococci, including meningitis, pneumonia, and prophylaxis against endocarditis<br><br>Oral dosing: *C. difficile*–associated diarrhea and enterocolitis from *S. aureus* (including MRSA) | **Usual parenteral dose for lower respiratory infections:**<br>IV: 15 to 20 mg/kg per dose every 8 to 12 hours<br>Alternatively may give 500 mg every 6 hours<br><br>Dose should be based on actual body weight<br><br>**Usual oral dose:**<br>500 mg daily in divided doses every 6 hours | • May cause nephrotoxicity: use with caution if patient has risk factors<br>• May cause neurotoxicity<br>• May cause neutropenia: higher risk if use is greater than 1 week and total dose exceeds 25 g<br>• May cause ototoxicity<br>• May cause red man syndrome indicated by hypotension, flushing, and/or maculopapular rash: slow infusion, dilute further, and treat with antihistamines and steroids<br>• Oral vancomycin use in inflammatory bowel disease may cause systemic absorption (IV product may be used orally)<br>• Vancomycin is an irritant: avoid extravasation; if extravasation does occur, stop the infusion as soon as possible and aspirate the solution<br>• Monitor: IV: renal function tests, urinalysis, WBC, troughs if therapy extends for more than 3 days with high-intensity dosing |

*Lincomycins*

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Clindamycin<br><br>**Brand Name**<br>Cleocin<br>Clindacin<br>Clindagel<br>ClindaMax<br>Clindesse<br>Evoclin<br><br>■ (PD) | Treatment of susceptible bacteria that cause bone and joint infections, gynecologic infections, intra-abdominal infections, lower respiratory tract infections, septicemia, and skin and skin structure infections<br>*S. aureus* (including community-acquired MRSA), anaerobes, *S. pneumoniae*, streptococci (not *E. faecalis*), *S. pyogenes*<br><br>Treatment of serious infections caused by streptococci, pneumococci, and staphylococci<br><br>Topical agents: acne<br><br>Vaginal agents: bacterial vaginosis | **Usual oral dose for skin and skin structure infections:**<br>150 to 450 mg every 6 hours<br>**Usual parenteral dose:**<br>IM, IV: 600 to 2700 mg in 2 to 4 divided doses daily<br>(IV max 4800 mg per day)<br><br>**Topical:** apply 1 to 2 times daily<br><br>**Vaginal cream:** insert 1 applicatorful once daily for 1 to 7 days (product specific durations) | • Use with caution in patients with severe allergy to tartrazine; reaction is more likely to occur if patients have allergy to aspirin<br>• May cause severe skin reactions such as TEN: discontinue if severe rash occurs<br>• Use with caution in patients with hepatic impairment: less accumulation occurs if dose is given every 8 hours<br>• Use with caution in patients with atopy<br>• Do not administer undiluted solution as a bolus<br>• Do not administer more than 600 mg in a single IM dose<br>• Administer oral dosage forms with plenty of water to decrease the risk of esophageal ulceration<br>• Do not refrigerate oral solution: will thicken<br>• Not for meningitis: does not penetrate cerebrospinal fluid (CSF) adequately<br>• If bacteria are erythromycin resistant, perform D-zone test to ensure the pathogen is not clindamycin-resistance inducible<br>• Monitor: LFTs in patients with severe hepatic impairment; CBC, renal tests, and LFTs with extended use; signs and symptoms of colitis<br>• Associated with severe colitis that can be fatal: use only if necessary, and use with caution in patients with preexisting gastrointestinal disease<br>• Vaginal creams are generally recommended for installation just prior to bedtime (Clindesse brand is only 1 single dose at any time of the day) |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Lincomycin<br><br>**Brand Name**<br>Lincocin<br><br>▲ ■ (PD) | Treatment of severe bacterial infections caused by susceptible strains of streptococci, pneumococci, and staphylococci<br>For patients who have severe allergy to penicillins | **Usual parenteral dose:**<br>IM: 600 mg every 12 to 24 hours<br><br>IV: 600 to 1000 mg every 8 to 12 hours<br><br>(max 8 g IV per day) | • Extended use can cause overgrowth of bacteria or fungi<br>• Use with caution in patients with asthma, gastrointestinal diseases (especially colitis), or poor hepatic or renal function<br>• Do not give IV bolus of undiluted solution<br>• Infuse over 1 hour per gram to avoid cardiopulmonary arrest and hypotension<br>• Not for meningitis: does not penetrate CSF adequately<br>• Monitor: baseline SCr and LFTs; renal tests, LFTs, and CBC with differential with extended use; bowel changes throughout therapy |

## *Oxazolidinones*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Linezolid<br><br>**Brand Name**<br>Zyvox<br><br>(PD) | Enterococcal vancomycin-resistant infections<br><br>Pneumonia:<br>Community-acquired (CAP): *S. pneumoniae*, *S. aureus*<br><br>Hospital-acquired: *S. aureus* (MSSA/MRSA), *S. pneumoniae*<br><br>Skin and skin structure infections<br>Complicated: *S. aureus* (MSSA/MRSA), *S. pyogenes*, *S. agalactiae*<br><br>Uncomplicated: *S. aureus*, *S. pyogenes* | **Usual dose for CAP:**<br>Oral, IV: 600 mg every 12 hours for 10 to 14 days<br>Longer treatment durations may be warranted based on severity and extent of infection. | • Can cause lactic acidosis<br>• Myelosuppression may be dependent on length of use<br>• Peripheral and optic neuropathy with extended use<br>• Rarely can cause serotonin syndrome<br>• Monitor for hypoglycemia in patients with diabetes<br>• Use with caution in patients with history of seizures<br>• Do not mix or infuse with other medications; flush line before and after use<br>• Yellow color of the solution can intensify over time<br>• Avoid consumption of large amounts of tyramine-containing foods<br>• Protect tablets, suspensions, and infusions from light<br>• Do not shake the suspension<br>• Monitor: CBC weekly; visual function; hematopoietic/neuropathic adverse events in patients with poor renal function<br>• Specific recommendations for patients undergoing dialysis |
| **Generic Name**<br>Tedizolid<br><br>**Brand Name**<br>Sivextro | Treatment of susceptible bacteria that cause acute skin and skin structure infections (for example: *S. aureus* [including MRSA], *S. pyogenes*, *S. agalactiae*, *S. anginosus* group, *E. faecalis*) | **Usual dose:**<br>Oral, IV: 200 mg once daily for 6 days | • Do not use if neutrophil count is less than 1000 cells/$mm^3$<br>• Suitable solutions for administration range in color from colorless to pale yellow<br>• Inhibits monoamine oxidase, which can cause drug interactions<br>• Monitor: CBC with differential |

## *Polymyxins*

Universal prescribing alerts:
- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Colistimethate/colistin<br>**Brand Name**<br>Coly-Mycin<br>▲ | Sensitive to certain gram-negative bacilli that are typically resistant to other antibiotics<br>*P. aeruginosa*<br>Used in meningitis if bacteria are resistant and/or patient is allergic to first-line agents | **Usual dose expressed as colistin base:** IM, IV: 2.5 to 5 mg/kg per day in 2 to 4 divided doses (max 5 mg/kg per day) | • Can cause transient CNS adverse effects such as dizziness, numbness, slurred speech, and tingling: reducing dose may alleviate symptoms<br>• Dose-dependent renal toxicity may develop: interrupt therapy if signs and symptoms of renal impairment occur<br>• Reports of respiratory arrest have occurred: use with caution in patients with poor renal function<br>• Colistimethate is the prodrug of colistin (equivalence data are available in the package insert)<br>• In obese patients, use ideal body weight to calculate the dose<br>• Caution patients about operating machinery and driving until tolerance of the medication is established<br>• Monitor: renal function test at baseline; for nephrotoxicity, neurotoxicity, and pulmonary toxicity throughout therapy |
| **Generic Name**<br>Polymyxin B<br>▲ ■ PD | Treatment of susceptible strains of *P. aeruginosa* | **Usual otic dose:** 1 to 2 drops 3 to 4 times daily<br>**Usual ophthalmic dose:** 1 to 3 drops every 1 to 6 hours daily<br>**Usual parenteral dose:** IM: 25,000 to 30,000 units/kg per day divided every 4 to 6 hours<br>IV: 15,000 to 25,000 units/kg per day divided every 12 hours<br>**Intrathecal:** 50,000 units daily or every other day<br>**Topical irrigation:** 0.1 to 0.25% solution as part of wet dressings or as a wound irrigation | • IM formulation is not recommended due to the severe pain it causes<br>• IV formulation is reserved for patients in whom other antibiotics fail<br>• Monitor: renal function tests, neurotoxicity signs/symptoms<br>Associated with:<br>• Nephrotoxicity: avoid use with other nephrotoxic agents<br>• Neurotoxicity that can cause respiratory paralysis: use with caution in patients with renal impairment and high polymyxin serum levels<br>• Need for giving only IM/intrathecal formulations in the hospital |

## *Rifamycins*

Universal prescribing alerts:
- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Rifaximin<br>**Brand Name**<br>Xifaxan | Hepatic encephalopathy<br>Irritable bowel syndrome with diarrhea<br>Traveler's diarrhea caused by *E. coli* | **Usual oral dose for irritable bowel syndrome:** 550 mg 3 times daily for 14 days | • Use with caution in patients with severe hepatic impairment: efficacy may be diminished in preventing encephalopathy<br>• Do not use for diarrhea if blood appears in the stool or the patient has a fever<br>• Some dosage forms contain propylene glycol: large amounts are toxic<br>• Not for systemic infections: not adequately absorbed<br>• Monitor: body temperature and for presence of blood in the patient's stool |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Rifabutin | Refer to the Antimycobacterials section. | | |
| **Generic Name**<br>Rifampin | Refer to the Antimycobacterials section. | | |
| **Generic Name**<br>Rifapentine | Refer to the Antimycobacterials section. | | |

*Streptogramins*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Quinupristin and dalfopristin<br><br>**Brand Name**<br>Synercid | Treatment of susceptible bacteria that cause complicated skin and skin structure infections *(for example: S. aureus, S. pyogenes)* | **Usual parenteral dose for skin and skin structure infections:** IV: 7.5 mg/kg every 12 hours for at least 7 days. | • Can cause arthralgia or myalgia: decrease dosing frequency in such cases<br>• May cause hyperbilirubinemia<br>• May cause phlebitis if used peripherally: hydrocortisone and diphenhydramine do not relieve symptoms<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Infuse over 60 minutes to decrease toxicity: if venous irritation occurs, dilute further<br>• Monitor: culture and sensitivity, periodically check infusion site |

*Miscellaneous Urinary Anti-infectives*

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Fosfomycin<br><br>**Brand Name**<br>Monurol | Treatment of susceptible bacteria that cause uncomplicated urinary tract infections in women *(for example: E. coli, E. faecalis)* | **Usual oral dose:**<br>3 g single dose in 3 to 4 ounces of water | • Always mix powder with water before administering<br>• High concentrations persist for up to 48 hours in the urine<br>• Monitor: urine culture with sensitivity |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Methenamine<br><br>**Brand Name**<br>Hiprex<br>Urex<br>Mandelamine<br><br>PD | Treatment of susceptible bacteria that cause recurrent urinary tract infections<br><br>Prophylaxis against urinary tract infections<br><br>Decreases urinary tract discomfort secondary to hypermotility | **Usual oral dose:**<br>Hippurate: 1 g twice daily<br><br>Mandelate: 1 g 4 times/day after meals and at bedtime | • Use with caution in patients with gout<br>• Use with caution in elderly patients<br>• Foods or dinks that may alkalinize the urine can decrease the activity of methenamine<br>• Monitor: urinalysis, hepatic function periodically<br>Contraindications:<br>• Severe renal or hepatic impairment<br>• Severe dehydration |
| **Generic Name**<br>Nitrofurantoin<br><br>**Brand Name**<br>Furadantin<br>Macrobid<br>Macrodantin<br><br>BL PD | Treatment of susceptible bacteria that cause urinary tract infections *(for example: E. coli,* enterococci, *S. aureus, Klebsiella, Enterobacter)*<br><br>Macrobid: indicated only for acute uncomplicated urinary tract infections *(for example: E. coli, S. saprophyticus)* | **Usual oral dose for UTI:**<br>50 to 100 mg every 6 hours<br>Alternatively may give<br>**Macrobid products:**<br>100 mg twice daily<br>Treatment usually for 7 days or 3 days after obtaining sterile urine<br><br>**Prophylaxis (all products except Macrobid):**<br>50 to 100 mg at bedtime | • Macrobid formulation and oral suspension are not interchangeable with other nitrofurantoin products<br>• May cause optic neuritis<br>• May cause peripheral neuropathy: use with caution if patient has risk factors<br>• Pulmonary toxicity has occurred: discontinue immediately if signs and symptoms occur<br>• Administer with meals to increase absorption<br>• Suspension may be mixed with water, milk, or fruit juice<br>• Protect suspension from light to prevent darkening of nitrofurantoin<br>• Patients with G6PD deficiency are at higher risk of hemolytic anemia<br>• Monitor: signs of pulmonary toxicity, signs of numbness or tingling of the extremities, CBC, hepatic function periodically, renal function with extended use<br>Contraindications:<br>• In patients with CrCl less than 60 mL/min<br>• Previous hepatic dysfunction associated with nitrofurantoin |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Trimethoprim<br><br>**Brand Name**<br>Primsol<br><br>▲ QT PD | Treatment of susceptible bacteria that cause UTI, (for example: *E. coli, P. mirabilis, K. pneumoniae, Enterobacter*, coagulase-negative *Staphylococcus, S. saprophyticus*)<br><br>Treatment of otitis media<br>*S. pneumoniae*, *H. influenzae* | **Usual oral dose for UTI:**<br>100 mg every 12 hours<br>Alternatively may give<br>200 mg every 24 hours<br>Treatment is generally recommended for 10 to 14 day duration | • May cause hyperkalemia: use with caution if administering high doses or in patients with renal impairment<br>• Use with caution in patients with hepatic or renal impairment<br>• Administer with milk or food<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• May need to supplement with folic acid<br>• Monitor: CBC and potassium with extended use<br>Contraindications:<br>• Megaloblastic anemia due to folate deficiency |

## Antifungal Agents

### Allylamines

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Terbinafine<br><br>**Brand Name**<br>Lamisil<br>Terbinex<br><br>PD | Onychomycosis (tablets) caused by dermatophytes<br><br>Tinea capitis (granules)<br><br>Topical formulations: tinea pedis, tinea cruris, and tinea corporis | **Usual oral dose:**<br>250 mg once daily for at least 6 weeks<br><br>**Topical:**<br>Cream: apply 2 times daily for 1 to 2 weeks<br><br>Gel or solution: apply once daily for at least 1 week | • Not recommended for use in chronic or active hepatic disease or if CrCl 50 mL/minute or less<br>• May cause depression<br>• May cause taste and smell disturbances: discontinue if symptoms occur<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Can cause transient hematologic effects: monitor CBC in immunosuppressed patients if therapy lasts longer than 6 weeks<br>• Rare cases of hepatic failure have occurred: assess the patient for this condition if signs and symptoms occur; discontinue if LFTs are significantly elevated<br>• Serious skin reactions have been reported, such as SJS and DRESS: discontinue if rash progresses<br>• Rarely can cause ocular changes in the lens and retina<br>• Can exacerbate or precipitate lupus: discontinue if signs and symptoms develop<br>• Administer granules with food: sprinkle on soft food that is not acidic, such as pudding or mashed potatoes, and swallow without chewing<br>• When administering topical solution, hold 4 to 6 inches away from skin<br>• Monitor: LFTs at baseline and again if duration of therapy exceeds 6 weeks; changes in taste or smell |

| Azoles | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Efinaconazole<br><br>**Brand Name**<br>Jublia | Treatment of onychomycosis caused by *T. rubrum* or *T. mentagrophytes* | **Usual topical dose:** apply to affected toenails once daily for 48 weeks | • May cause local irritation<br>• Toenails should be dry and clean before administration<br>• Avoid nail products, such as nail polish, while using medication |
| **Generic Name**<br>Fluconazole<br><br>**Brand Name**<br>Diflucan<br><br>▲ QT PD | Treatment of candidiasis infections: esophageal, oropharyngeal, peritoneal, urinary tract, vaginal, candidemia, pneumonia, and disseminated candidiasis<br><br>Treatment of cryptococcal meningitis<br><br>Prophylaxis against candidiasis in allogenic bone marrow transplant recipients | **Usual dose for oropharyngeal candidiasis:**<br>Oral, IV: 200 mg once, then 100 daily for 2 weeks after the resolution of symptoms | • Can cause arrhythmias and QTc prolongation: use with caution in patients with preexisting arrhythmias and with concurrent use of agents that have a similar effect<br>• Drug interactions may require dose adjustments<br>• May cause hepatotoxicity that can be fatal: discontinue if signs and symptoms occur<br>• Rarely causes exfoliative skin disorders: discontinue if rash develops<br>• Do not use IV solution if cloudy or precipitated<br>• Hazardous agent: use caution in preparing and disposing of medication<br>• Caution patients about operating machinery and driving until tolerance of the medication is established due to the potential for dizziness or seizures<br>• Monitor: liver and renal function tests periodically, potassium |
| **Generic Name**<br>Isavuconazonium sulfate<br><br>**Brand Name**<br>Cresemba<br>QT | Invasive aspergillosis<br><br>Invasive mucormycosis | **Usual dose for treatment:**<br>Oral, IV: 372 mg every 8 hours for 6 doses then once daily | • Drug interactions may require dose adjustments<br>• May cause hepatotoxicity that can be fatal: discontinue if signs and symptoms occur<br>• Infusion-related reactions may occur such as hypotension, chills, and paresthesia: discontinue if they occur<br>• IV solution may contain clear to white particulates of isavuconazole: use 0.2- to 1.2-micron in-line filter<br>• Monitor: LFTs at baseline and during therapy, infusion-related reactions during infusion<br>Contraindications:<br>• Familial short QT syndrome |
| **Generic Name**<br>Itraconazole<br><br>**Brand Name**<br>Sporanox<br>Onmel<br>■ QT | Treatment of aspergillosis, blastomycosis, and histoplasmosis in immunocompromised and non-immunocompromised patients (capsule) | **Usual oral dose for allergic bronchopulmonary aspergillosis:**<br>600 mg in divided doses for 3 days, then 400 mg daily in divided doses | • Can cause transient or permanent hearing loss: usually resolves upon discontinuation<br>• May cause hepatotoxicity that can be fatal: discontinue if signs and symptoms occur<br>• May cause neuropathy<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| | Onychomycosis caused by dermatophytes (capsule), *Trichophyton rubrum* (tablet), or *Trichophyton mentagrophytes* (tablet)<br><br>Oral solution: oropharyngeal/esophageal candidiasis | | • Use with caution in patients with cystic fibrosis: displays erratic pharmacokinetics; use alternative therapy if infection does not improve<br>• Do not give more than 200 mg at one time<br>• Do not administer with antacids: capsules and tablets need gastric acidity for proper absorption<br>• Capsules and oral solutions are not bioequivalent<br>• Administer capsules and tablets with food; administer oral suspension on an empty stomach<br>• Swish and swallow oral solution if treating for oropharyngeal and esophageal candidiasis<br>• Caution patients about operating machinery and driving until tolerance of the medication is established due to the potential for CNS depression<br>• Monitor: LFTs if preexisting impairment and duration is greater than 1 month; itraconazole blood levels, especially for oral therapy; renal function tests; signs and symptoms of heart failure<br>Associated with:<br>• Heart failure: discontinue if signs and symptoms develop<br>• Ventricular dysfunction if treating patients for onychomycosis |
| **Generic Name**<br>Ketoconazole<br><br>**Brand Name**<br>Nizoral<br>Extina<br>Ketodan<br>Nizoral A-D<br>Xolegel<br>■ QT PD | Treatment of systemic fungal infections including blastomycosis, histoplasmosis, paracoccidoidomycosis, coccidoidomycosis, and chromomycosis when other therapies have failed<br><br>Cream: tinea corporis, tinea cruris, tinea versicolor, cutaneous candidiasis, and seborrheic dermatitis<br><br>Foam/gel: seborrheic dermatitis<br><br>Shampoo: dandruff, seborrheic dermatitis, and tinea versicolor | **Usual oral dose:**<br>200 to 400 mg once daily<br><br>**Usual topical dose:**<br>Cream: apply 1 to 2 times daily (dose varies on affected area targeted for treatment)<br><br>OTC 1% shampoo: apply and rinse once or twice weekly<br><br>Foam: apply twice daily<br><br>Gel: apply once daily | • Drug interactions may require dose adjustments<br>• May cause adrenocortical dysfunction that resolves upon discontinuation<br>• Can cause increased long bone fragility<br>• Administer 2 hours before antacid use to maintain gastric acidity for absorption<br>• In patients with achlorhydria, administer with acidic liquids<br>• Poorly penetrates the brain and should not be used for fungal meningitis<br>• Gel and foam preparations are flammable<br>• Shampoo may remove curls, discolor hair, and change hair texture<br>• Monitor: LFTs at baseline and throughout therapy, calcium and phosphorus with extended use, adrenal function as needed<br>Contraindications:<br>• Acute or chronic liver disease<br>Associated with:<br>• QTc prolongation: do not use with other medications that can cause QTc prolongation<br>• Hepatotoxicity that can be fatal: discontinue if signs and symptoms occur<br>• Use only if other therapies have failed and the benefit outweighs the risk |

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|---|---|---|---|
| **Generic Name**<br>Luliconazole<br><br>**Brand Name**<br>Luzu | Treatment of susceptible fungi that cause tinea pedis, tinea cruris, and tinea corporis<br><br>*T. rubrum, E. floccosum* | **Usual topical dose:** apply to affected area and 1 inch of surrounding area once daily for 1 to 2 weeks | • Topical use only |
| **Generic Name**<br>Posaconazole<br><br>**Brand Name**<br>Noxafil<br><br>QT | Prophylaxis against invasive *Aspergillus* and *Candida* infections in severely immunocompromised patients<br><br>Suspension: oropharyngeal candidiasis | **Usual dose for oral candidiasis:**<br>Oral suspension: 100 to 400 mg 1 to 3 times daily<br><br>**Usual dose for candiasis prophylaxis:**<br>IV/Oral (DR tablets): 300 mg 2 times per day on the first day, then once daily. Duration of therapy is based on clinical progress and recovery | • Can cause QTc prolongation and arrhythmias: use with caution in patients at high risk for arrhythmias<br>• Drug interactions may require dose adjustments<br>• Can cause hepatotoxicity that can be fatal: discontinue if signs and symptoms occur; effects are usually reversible upon discontinuation<br>• DR tablets and oral suspensions are not interchangeable on a mg per mg basis<br>• If glomerular filtration rate (GFR) less than 50 mL/min, do not use IV due to accumulation of cyclodextrin<br>• Limit peripheral IV infusion to one 30-minute infusion due to increased chance of infusion-site reactions<br>• Administer suspension and DR tablets with food<br>• Suitable IV solution color is clear to yellow<br>• Monitor for breakthrough fungal infections in patients weighing more than 120 kg due to lower blood levels<br>• Monitor: LFTs at baseline ad throughout therapy, renal function tests, electrolytes, CBC, breakthrough fungal infections |
| **Generic Name**<br>Voriconazole<br><br>**Brand Name**<br>Vfend<br><br>QT | Treatment of invasive aspergillosis; esophageal candidiasis; candidemia (if non-neutropenic); disseminated *Candida* infections of the skin and abdomen, kidney, bladder wall, and wounds<br><br>Used in serious infections caused by *Scedosporium apiospermum* and *Fusarium* if other treatments failed | **Usual parenteral dose:**<br>IV: 3 to 6 mg/kg every 12 hours<br><br>**Usual oral dose:**<br>Adjusted body weight ABW 40 kg or greater: 200 mg every 12 hours | • Can cause QTc prolongation and arrhythmias: caution in patients at high risk for arrhythmias, correct electrolytes prior to use<br>• Drug interactions may require dose adjustments<br>• Can cause severe dermatologic reactions including melanoma and SJS: avoid exposure to direct sunlight, perform skin examinations for lesions periodically, and discontinue if signs and symptoms appear<br>• Oral dosing based on adjusted body weight<br>• Can cause hepatotoxicity that can be fatal: discontinue if signs and symptoms occur; effects are usually reversible upon discontinuation<br>• Can cause ocular adverse effects such as change in visual acuity, blurred vision, and photophobia: reversible if duration of therapy is 28 days or less; long-term effects have not been studied<br>• May cause renal toxicity in severely ill patients: use with caution if administering concurrently with other nephrotoxic agents |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| | | | • Can cause fluorosis or periostitis with extended use: discontinue if bone pain develops and is supported by radiologic findings<br>• Can cause pancreatitis (rare)<br>• Infusion reactions presenting as anaphylactoid may occur: discontinue if reaction occurs<br>• If CrCl is less than 50 mL/min, recommend using oral formulations due to accumulation of cyclodextrin in the IV formulation<br>• Do not infuse IV in same line with other medications; do not infuse at the same time (even when using separate lines) as concentrated electrolytes and blood products<br>• Administer oral formulations 1 hour before or after meals to increase absorption<br>• Caution patients about operating machinery and driving until tolerance of the medication is established due to the potential for visual changes<br>• A small increase in dose can cause toxicity leading to neurologic and dermatologic effects<br>• Monitor: hepatic and renal function and electrolytes at baseline and throughout therapy; eye exams if duration is greater than 28 days; voriconazole blood levels on day 5, then weekly if treating severe infections, and otherwise as needed; full-body skin examination yearly; phototoxic adverse events |
| **Echinocandins** | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Anidulafungin<br><br>**Brand Name**<br>Eraxis | Treatment of *Candida* infections including intra-abdominal, peritoneal, esophageal, and candidemia | **Usual parenteral dose for invasive candidiasis:**<br>IV: 200 mg dose for day 1, then 100mg once daily | • May cause hepatic impairment: discontinue if impairment progresses<br>• Infusion reactions such as bronchospasm, hypotension, and rash may occur if the rate of infusion is too high<br>• Monitor: LFTs |
| **Generic Name**<br>Caspofungin<br><br>**Brand Name**<br>Cancidas<br><br>PD | Treatment of invasive *Aspergillus* infections when other agents fail<br><br>Treatment of candidemia and *Candida* infections, including intra-abdominal abscesses, peritonitis, and pleural space infections | **Usual parenteral dose for invasive candidiasis:**<br>IV: 70 mg dose for day 1, then 50mg once daily | • May cause hepatic impairment: discontinue if impairment progresses<br>• Dose interactions may require dose adjustment or avoidance of certain drug combinations<br>• Histamine-related reactions may occur, such as rash, flushing, and facial edema<br>• Monitor: hepatic function, hypersensitivity reactions |

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| | Treatment of esophageal candidiasis<br><br>Empiric treatment in patients with febrile neutropenia | | |
| **Generic Name**<br>Micafungin<br><br>**Brand Name**<br>Mycamine<br><br>PD | Treatment of candidemia, disseminated candidiasis, *Candida* peritonitis and abscesses, and esophageal candidiasis<br><br>Prophylaxis against *Candida* infections during hematopoietic stem cell transplant | **Usual parenteral dose for invasive candidiasis:**<br>IV: 100 mg once daily<br>Treatment duration depends on severity of infection and patient's clinical progress | • Hemolytic anemia and hemoglobinuria have been reported<br>• May cause hepatic and renal impairment: discontinue if impairment progresses<br>• Monitor: hepatic function |

| Oxaboroles | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Tavaborole<br><br>**Brand Name**<br>Kerydin | Treatment of onychomycosis due to *T. rubrum* or *T. mentagrophytes* | **Usual topical dose:** apply to affected toenails once daily for 48 weeks | • May cause local irritation<br>• Before applying, make sure toenails are dry and clean<br>• Discard 3 months after opening bottle |

| Polyenes | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Amphotericin B<br><br>**Brand Name**<br>Amphocin<br>*Conventional*<br><br>Amphotec<br>*Cholesteryl sulfate complex* | Conventional: Treats life-threatening fungal infections including aspergillosis, cryptococcosis, North American blastomycosis, systemic candidiasis, coccidioidomycosis, histoplasmosis, zygomycosis, *Conidiobolus, Basidiobolus,* and sporotrichosis | **Usual parenteral dose:**<br><br>**Conventional:**<br>IV: 0.3 to 1.5 mg/kg/day (max 1.5 mg/kg/day)<br><br>**Amphotec:**<br>IV: 3 to 4 mg/kg/day (max 6 mg/kg/day) | • Use extra care when selecting amphotericin products. Liposomal product doses are generally HIGHER than conventional doses. Use extra care to check if conventional product ordered exceeds 1.5 mg/kg (this may have been intended for liposomal administration).<br>• Amphotericin B conventional is Amphocin<br>• Amphotericin B cholesterol sulfate complex (ABCD) is Amphotec<br>• Amphotericin B lipid complex (ABLC) is Abelcet<br>• Amphotericin B liposomal injection (LAmB) is AmBisome<br>• Administer the first dose with careful observation for respiratory distress<br>• Can cause severe infusion reactions (fever, chills, shaking, hypotension, nausea, vomiting, headache, tachypnea) 1 to 3 hours after initiating the infusion: pretreat with medication or decrease the rate; with subsequent doses, the reactions become more tolerable |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| Abelcet<br>*Lipid complex*<br><br>AmBisome<br>*Liposomal*<br><br>■ PD | Can be used in leishmaniasis, but is not first choice<br><br>Abelcet: invasive aspergillosis after failure to respond to amphotericin B deoxycholate<br><br>Amphotec: invasive aspergillosis after failure to respond to amphotericin B deoxycholate and in patients with poor renal function<br><br>AmBisome: invasive aspergillosis after failure to respond to amphotericin B deoxycholate and in patients with poor renal function<br><br>Treatment of *Aspergillus*, *Candida*, and *Cryptococcus* infections that are refractory to amphotericin B deoxycholate; cryptococcal meningitis in HIV patients; visceral leishmaniasis<br><br>Empiric therapy in febrile, neutropenic patients | **Abelcet:**<br>IV: 5 mg/kg once daily<br><br>**AmBisome:**<br>IV: 3 to 6 mg/kg/day | • Can cause nephrotoxicity: interrupt therapy, decrease the dose, or decrease the frequency of dosing to help improve renal function; use with caution in high-risk patients<br>• If renal impairment is due to use of the conventional infusion, decrease the dose by 50%<br>• Separate dosing from leukocyte transfusions to prevent pulmonary reactions in neutropenic patients (conventional, lipid complex)<br>• Rarely causes leukoencephalopathy (conventional)<br>• Conventional formulation is thought to have the highest rate of infusion-related reactions and nephrotoxicity<br>• If infusion-related reactions such as chills, fever, hypotension, and nausea occur, pretreat the patient 30 to 60 minutes before infusion with a nonsteroidal anti-inflammatory drug (NSAID) with or without diphenhydramine or acetaminophen (APAP) with or without diphenhydramine or hydrocortisone 50 to 100 mg with or without NSAID and diphenhydramine<br>• If the patient experiences rigors during the fusion, meperidine may be administered<br>• To reduce nephrotoxicity, give a bolus of normal saline before the infusion or before and after the infusion; doses greater than 1 mg/kg/day (conventional) have a higher risk of nephrotoxicity<br>• If therapy is interrupted for more than 7 days, restart at the lowest dose and titrate up gradually<br>• Monitor: LFTs, electrolytes, renal function, BUN, SCr, CBC, PTT, temperature, I/O, signs and symptoms of hypokalemia<br>Associated with:<br>• Check product name and dose if conventional dose exceeds 1.5 mg/kg<br>• Use in progressive, life-threatening infections only |
| **Generic Name**<br>Nystatin<br><br>**Brand Name**<br>Bio-Statin<br>Nyamyc<br>Nystop<br>Pediaderm AF Complete<br><br>PD | Treatment of susceptible fungus that cause cutaneous, mucocutaneous, and oral cavity infections<br><br>*Candida* | **Usual oral dose:** 400,000 to 600,000 units 3 to 4 times per day<br><br>**Usual topical dose:**<br>Cream/ointment: apply twice daily<br><br>**Powder:** apply 2 to 3 times/day | • Swish the suspension in the mouth as long as possible before swallowing (a few minutes)<br>• Refrigerate suspension<br>• Apply powder in the shoes when treating tinea pedis |

| Pyrimidines | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Flucytosine<br><br>**Brand Name**<br>Ancobon<br>  | An adjunctive to treat systemic fungal infections (septicemia, endocarditis, urinary tract infections, meningitis, pulmonary infections)<br><br>*Candida*, *Cryptococcus* | **Usual oral dose:**<br>50 to 150 mg/kg/day in divided doses every 6 hours | • Use with caution in patients with preexisting bone marrow depression or hematologic disease: can cause irreversible bone toxicity<br>• Can cause hepatotoxicity: use with caution in patients with preexisting hepatic dysfunction<br>• To diminish nausea and vomiting, administer a couple of capsules at once over 15 minutes<br>• Interferes with SCr measurements when using the Ektachem analyzer<br>• Monitor: perform baseline tests on electrolytes, CBC with differential, BUN, renal function, and blood culture; during treatment, monitor CBC with differential and LFTs frequently, flucytosine blood levels, renal function<br>Associated with:<br>• Renal dysfunction<br>• Need to monitor renal, hepatic, and hematologic function |
| **Miscellaneous Antifungals** | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Griseofulvin<br><br>**Brand Name**<br>Grifulvin V (microsize)<br>Gris-PEG (ultramicrosize)<br>PD | Treatment of susceptible fungi that cause tinea infections of the skin, hair, and nails<br><br>*Microsporum, Epidermophyton, Trichophyton* | **Usual oral dose for tinea corporis:**<br>Microsize: 500 mg once daily (or in divided doses) for 2 to 4 weeks<br><br>Ultramicrosize: 300 to 375 mg once daily (or to or in divided doses) for 2 to 4 weeks | • May cause granulocytopenia: discontinue if reaction occurs<br>• May cause hepatic dysfunction<br>• Rarely causes SJS or TEN: discontinue if reaction occurs<br>• Administer with a fatty meal to increase absorption<br>• Causes increased photosensitivity: wear sunscreen and avoid direct sunlight<br>• Avoid ethanol use: will cause a disulfiram-like reaction<br>• Monitor: renal, hepatic, and hematopoietic function periodically<br>Contraindications:<br>• Liver failure<br>• Porphyria |
| Potassium iodide | Refer to the Hormones and Synthetic Substitutes chapter. | | |

## Antimycobacterial

### Antituberculosis Agents

Universal prescribing alerts:

- Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Aminosalicylic acid<br><br>**Brand Name**<br>Paser<br><br>PD | Treatment of tuberculosis in combination with other agents | **Usual oral dose:**<br>8 to 12 g per day in 2 to 3 divided doses | • Use with caution in patients with gastric ulcer or hepatic impairment<br>• Do not use granules if color is brown or purple or if packet is swollen<br>• When dispensed, store in refrigerator or freezer<br>• Monitor: hepatic function at baseline, thyroid function at baseline and every 3 months with extended use<br>Contraindications:<br>• Severe renal impairment |
| **Generic Name**<br>Bedaquiline<br><br>**Brand Name**<br>Sirturo<br><br>■ QT | Treatment of susceptible strains of multidrug-resistant pulmonary tuberculosis when other agents cannot be used<br><br>Use with 3 or more agents active against the patient's tuberculosis strand | **Usual oral dose:** 400 mg once daily for 2 weeks then 200 mg 3 times per week for weeks 3 to 24<br><br>Directly observe therapy | • May cause hepatic dysfunction and increase in hepatic enzymes<br>• Use with caution in patients with poor renal function<br>• Administer with food to increase absorption<br>• For weeks 3 to 24 of regimen, doses should be administered at least 48 hours apart from each other<br>• Store in original container or discard within 3 months<br>• Monitor: ECG at baseline and weeks 2, 12, and 24 or weekly if patient has risk factors; baseline potassium, calcium, and magnesium; hepatic function tests at baseline and monthly; weekly for arthralgia, chest pain, headache, hemoptysis, nausea, and rash<br>• Drug interactions may require dose adjustments<br>Associated with:<br>• Arrhythmias and QTc prolongation; discontinue if interval is greater than 500 ms<br>• Increased risk of death: use as last-line therapy |
| **Generic Name**<br>Capreomycin<br><br>**Brand Name**<br>Capastat Sulfate<br><br>▲ ■ GD | Treatment of pulmonary tuberculosis with concurrent use of other agents when primary agents are ineffective | **Usual parenteral dose:**<br>IM, IV: 1 g once daily for 5 to 7 days a week, reduced to 2 to 3 times a week after the first 2 to 4 months<br>Total duration of treatment often requires culture conversion | • Can cause electrolyte imbalances: monitor calcium, potassium, and magnesium<br>• May cause nephrotoxicity: if BUN greater than 30 mg/dL or renal function is falling, adjust dosing or discontinue<br>• Can cause permanent hearing impairment: monitor using audiometric assessment<br>• Dosing per weight is based on ideal body weight<br>• Specific doses for those 60 years and older<br>• Monitor: audiometric assessment and vestibular function at baseline and throughout therapy, renal function at baseline and weekly during treatment, electrolytes at baseline and throughout therapy, hepatic function tests<br>Associated with:<br>• Hearing impairment and/or renal impairment<br>• Increased risk with concurrent use of other ototoxic or nephrotoxic agents<br>• Increased risk with concurrent use with other IV antituberculous agents due to high risk of toxic effects |

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| **Generic Name**<br>Cycloserine<br><br>**Brand Name**<br>Seromycin | Treatment of pulmonary or extrapulmonary tuberculosis with concurrent use of other agents when primary agents are inadequate<br><br>Treatment-susceptible bacteria causing urinary tract infections when organism is resistant<br><br>*Enterobacter, E. coli* | **Usual oral dose:** 250 mg every 12 hours for 14 days, then 500 to 1000 mg/day in 2 divided doses | • Dose-related CNS effects, such as seizures, psychosis, depression, and confusion have occurred: pyridoxine can help prevent/treat CNS adverse effects<br>• Can cause allergic dermatitis: decrease dose or discontinue if rash develops<br>• May need to supplement with folic acid and vitamin $B_{12}$<br>• Monitor: hepatic, renal, and hematologic function; cycloserine blood levels; neuropsychiatric status at least every month<br>Contraindications:<br>• Severe renal function<br>• Epilepsy<br>• Depression<br>• Severe anxiety<br>• Psychosis<br>• Excessive use of alcohol |
| **Generic Name**<br>Ethambutol<br><br>**Brand Name**<br>Myambutol<br>  | Treatment of pulmonary tuberculosis with concurrent use of other agents | **Usual oral dose:**<br>15 to 25 mg/kg once daily | • May cause hepatotoxicity: monitor LFTs<br>• Dosing strategy is based on whether patient is treatment naïve or if they have already received therapy<br>• Can cause optic neuritis: discontinue immediately if changes in vision occur; usually reversible over a period of time<br>• Use with caution in patients with ocular disease: determine if visual changes are due to ocular disease or ethambutol use<br>• Can administer with food to decrease stomach irritation<br>• Monitor: visual examination at baseline and monthly if receiving more than 15 mg/kg/day (test in both eyes separately and together); hepatic, renal, and hematopoietic function at baseline and throughout therapy<br>Contraindications:<br>• Optic neuritis<br>• Unconscious patients<br>• Patients who cannot communicate visual changes due to ethambutol |
| **Generic Name**<br>Ethionamide<br><br>**Brand Name**<br>Trecator<br>  | Treatment of tuberculosis along with other mycobacterial diseases with concurrent use of other agents when primary agents fail | **Usual oral dose:**<br>15 to 30 mg/kg/day (max 1 g per day in divided doses) | • Can cause hypoglycemia: use with caution in patients with diabetes<br>• Can cause porphyria and hypothyroidism<br>• Use with cycloserine has resulted in seizures<br>• Can increase isoniazid blood levels if used concurrently and cross-resistance may develop if *inhA* mutation is present<br>• Administering with food, at bedtime, or with an antiemetic may alleviate gastrointestinal adverse events |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| | | | • Concurrent use of pyridoxine can prevent or treat the neurotoxic effects<br>• Do not drink alcohol: can cause psychotic adverse events<br>• Monitor: LFTs at baseline and throughout therapy, blood glucose, thyroid-stimulating hormone (TSH) every 6 months, ophthalmic exams at baseline and throughout therapy<br>Contraindications:<br>• Severe hepatic impairment due to risk of hepatotoxicity |
| **Generic Name**<br>Isoniazid<br><br>**Brand Name**<br>Nydrazid<br>■ PD | Treatment of tuberculosis and latent tuberculosis with concurrent use of other agents | **Usual dose:**<br>PO, IM: 5 mg/kg per dose once daily or 5 times per week<br>(maximum 300 mg per day)<br><br>Dosing recommendations by the CDC may change with changes in resistance patterns<br><br>Oral is preferred route of administration | • If ALT or AST is more than 3 times the UNL, then temporarily hold isoniazid<br>• Use with caution in patients with severe renal impairment<br>• Drug interactions may require dose adjustments<br>• May need to supplement folic acid, niacin, and magnesium<br>• If IV vials crystalize, warm the vial to room temperature to dissolve the precipitates<br>• Pyridoxine use can help prevent peripheral neuropathies in high-risk groups such as patients with HIV, malnourished patients, and patients with diabetes<br>• Isoniazid is a weak monoamine oxidase (MAO) inhibitor and may cause adverse effects with tyramine-containing food<br>• Avoid histamine-containing foods (tuna, tropical fish) due to potential adverse effects of headache, sweating, palpitations, flushing, diarrhea, wheezing, itching, dyspnea, and hypotension: treat with corticosteroids and antihistamines<br>• May cause a false-positive urinary glucose result with Clinitest<br>• Monitor: LFTs at baseline and throughout therapy, sputum cultures monthly until 2 consecutive cultures are negative, signs and symptoms of hepatitis, regular ophthalmic exams<br>• Specific recommendations for patients undergoing dialysis<br>Contraindications:<br>• Acute liver disease<br>• History of drug-induced hepatitis<br>• History of hepatic injury due to isoniazid<br>• Previous severe reaction to isoniazid<br>Associated with:<br>• Hepatitis, which can be fatal: monitor for signs and symptoms and liver function regularly |
| **Generic Name**<br>Pyrazinamide<br>▲ PD | Treatment of tuberculosis with concurrent use of other agents | **Usual oral dose:**<br>15 to 30 mg/kg per dose once daily (max 3g per day) or 50 to 70 mg/kg per dose 2 times per week | • Hepatotoxicity is dose dependent and rarely can cause liver atrophy<br>• Use with caution in patients with history of alcoholism, concurrent use of hepatotoxic medications, porphyria, and renal impairment<br>• May inhibit secretion of uric acid, leading to gout attacks |

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| | | | • Can cause a pink-brown color when used with Acetest and Ketostix<br>• Monitor: LFTs, uric acid blood levels, sputum culture, chest x-ray 2 to 3 months after first dose and upon completion of therapy<br>• Specific recommendations for patients undergoing dialysis<br>Contraindications:<br>• Severe hepatic impairment<br>• Active gout flare |
| **Generic Name**<br>Rifabutin<br><br>**Brand Name**<br>Mycobutin<br>  | Prevents *Mycobacterium avium* complex (MAC) in patients with HIV | **Usual oral dose:**<br>300 mg once daily<br>150 mg twice daily | • Can cause hematologic toxicity: discontinue if signs of thrombocytopenia occur<br>• May cause uveitis: increased risk with concurrent macrolide or azole use; refer the patient to an ophthalmologist if signs and symptoms of uveitis occur<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Use with caution in patients with hepatic impairment: discontinue if significant elevation in LFTs occurs<br>• Do not administer if patient has active TB: may cause resistance to rifampin<br>• Can be administered with meals to reduce nausea<br>• A brown/orange discoloration of bodily fluids and the skin may occur: remove contact lenses to prevent staining<br>• Monitor: LFTs, CBC with differential, platelet count |
| **Generic Name**<br>Rifampin<br><br>**Brand Name**<br>Rifadin | Treatment of active tuberculosis in combination with other agents<br><br>Eradicates meningococci from asymptomatic carriers | **Usual dose:** Oral, IV: 10 mg/kg per dose given once daily or 2, 3 or 5 times per week<br>(max 600 mg per day) | • May cause flu-like symptoms: more likely if patient takes more than 600 mg 1 to 2 times/week<br>• Can cause hematologic adverse events including thrombocytopenia: more likely if patient takes more than 600 mg 1 to 2 times/week<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• May cause hyperbilirubinemia: discontinue if signs and symptoms develop<br>• Use with caution in patients with hepatic impairment and alcoholism: dose adjustments may be necessary<br>• Use with caution in patients with porphyria: exacerbations can occur<br>• Administer oral formulations on an empty stomach with 8 ounces of water to increase absorption<br>• Separate administration time of oral formulations from antacids<br>• A brown/orange discoloration of bodily fluids may occur: remove contact lenses to prevent staining<br>• Can cause false-positive detection of opioids in the urine<br>• Interferes with standard microbiological assays for measuring folate and vitamin B12 blood levels<br>Monitor: LFTs at baseline and every 2 to 4 weeks during therapy; CBC; CNS effects; sputum culture; chest x-ray 2 to 3 months after first dose |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Rifapentine<br><br>**Brand Name**<br>Priftin<br><br>PD | Treatment of active tuberculosis in combination with other agents<br><br>Not recommended in HIV patients during the continuation phase due to increased failure rate<br><br>Treatment of latent tuberculosis in combination with other agents | **Usual oral dose for treatment of TB:**<br>600 mg 2 times per week for 2 months with interval of no less than 3 days (72 hours) between doses<br>Must be administered with at least one other antituberculosis agent | • Use with caution in patients with hepatic impairment: use only when necessary and monitor LFTs<br>• Use with caution in patients with porphyria: exacerbations can occur; use in this population is not recommended<br>• Administer with food to increase absorption<br>• Ensure compliance before starting therapy or resistance may develop<br>• A brown/orange discoloration of bodily fluids, skin, and teeth may occur: remove contact lenses to prevent staining<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Interferes with standard microbiological assays for measuring folate and vitamin B12 blood levels<br>• Monitor: LFTs at baseline and every 2 to 4 weeks if preexisting hepatic impairment exists; LFTs at baseline and as needed if treating latent disease in HIV patients, patients with hepatic impairment, and patients with constant alcohol consumption |
| Amikacin<br>Ciprofloxacin<br>Clarithromycin<br>Levofloxacin<br>Moxifloxacin<br>Streptomycin | Refer to the Antibacterials section. | | |

| Miscellaneous Antimycobacterials | | | |
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| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Dapsone<br><br>**Brand Name**<br>Avlosulfon<br>Aczone<br><br>PD | Leprosy<br><br>Dermatitis herpetiformis<br><br>Acne vulgaris | **Usual oral dose for dermatitis herpetiformis:**<br>50 once daily. Maintenance doses may range 25 to 300 mg daily<br><br>**Usual topical dose:** apply once daily | • May cause severe blood dyscrasias: monitor<br>• Rarely serious skin reactions can occur, such as TEN<br>• May cause peripheral neuropathy<br>• Use with caution in patients with G6PD deficiency: higher risk for anemia<br>• Use lowest effective dose possible<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations<br>• Use with caution in patients with hemoglobin M or methemoglobin reductase deficiency: higher risk of methemoglobinemia<br>• Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use<br>• Separate the time it is given from intake of antacids, alkaline foods, or alkaline medications<br>• If using with benzoyl peroxide, may cause reversible yellow/orange color to the skin<br>• Monitor: G6PD levels baseline; CBC weekly for first month, monthly for 6 months, then semiannually; reticulocyte counts; LFTs |

## Antiviral Agents

### Adamantanes

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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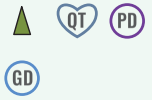
| **Generic Name**<br>Amantadine<br><br>**Brand Name**<br>Symmetrel<br><br>  | Prophylaxis and treatment of influenza A<br><br>Drug-induced extrapyramidal symptoms<br><br>Parkinson's disease | **Usual oral dose for treatment of influenza A virus infection:**<br>200 mg daily<br>100 mg 2 times per day | • May cause compulsive behavior such as gambling, hypersexuality, and binge eating if used for Parkinson's disease: reduce dose or discontinue<br>• Increased risk of developing melanoma in patients with Parkinson's disease: monitor for new/changed skin lesions<br>• May cause neuroleptic malignant syndrome if dose is decreased or discontinued<br>• May worsen psychiatric illness: monitor for suicidal ideation<br>• Use with caution in patients with the following conditions: cardiovascular disease, eczema, glaucoma, poor hepatic or renal function, seizure history<br>• Influenza A is highly resistant to therapy, and resistance can develop during therapy<br>• Administer within 48 hours of flu symptoms' appearance<br>• Caution patients about operating machinery and driving until tolerance of the medication is established<br>• May cause withdrawal syndrome: taper slowly, especially in patients with Parkinson's disease<br>• Tolerance can develop over time<br>• Elderly patients are at an increased risk of experiencing CNS adverse effects such as dizziness and weakness<br>• May lead to false-positive results for amphetamines<br>• Monitor: renal function, mental status, blood pressure, and symptoms of Parkinson's disease or influenza<br>• Special recommendations for patients undergoing dialysis<br>• Additional reference to drug use in Central Nervous System |
| **Generic Name**<br>Rimantadine<br><br>**Brand Name**<br>Flumadine<br><br>  | Prophylaxis and treatment of influenza A | **Usual oral dose:** 100 mg 2 times per day | • Use with caution in patients with hepatic and/or renal impairment<br>• Avoid use in patients with psychosis<br>• Use with caution in patients with history of seizures: increased risk of seizures<br>• Influenza A is highly resistant to therapy, and resistance can develop during therapy<br>• Administer within 48 hours of flu symptoms' appearance<br>• Elderly patients are at an increased risk of experiencing CNS adverse effects such as dizziness and weakness<br>• Monitor for CNS and gastrointestinal symptoms in elderly patients, patients with impaired renal function, and patients with impaired hepatic function |

| Antiretrovirals | | | |
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| *HIV Entry and Fusion Inhibitors* | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Enfuvirtide<br><br>**Brand Name**<br>Fuzeon<br><br>PD | Treatment of HIV-1 infection when used with other antiretroviral agents in treatment-experienced patients | **Usual parenteral dose:**<br>SubQ: 90 mg 2 times a day | • May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Commonly causes injection-site reactions<br>• Patients are more likely to develop pneumonia: use with caution in patients with a high viral load<br>• Increased risk of bleeding in patients with preexisting coagulation disorders<br>• Rotate injection sites<br>• Powder for injection may take up to 45 minutes to completely dissolve<br>• Do not inject near a nerve to avoid nerve pain<br>• Monitor: viral load, CD4 count |
| **Generic Name**<br>Maraviroc<br><br>**Brand Name**<br>Selzentry<br><br>▲ ■ | Treatment of CCR5-tropic HIV-1 infection when used with other antiretroviral agents | **Usual oral dose:** 300 mg twice daily | • May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Can cause postural hypotension: use with caution in patients with poor renal function and cardiovascular disease<br>• Hypersensitivity reactions such as SJS and DRESS have occurred: discontinue use<br>• Caution patients about operating machinery and driving until tolerance of the medication is established due to the potential for dizziness<br>• Monitor: viral load, CD4 count, LFTs, and bilirubin before treatment and during therapy; tropism testing before initiation<br>• Contraindicated in patients with CrCl less than 30 mL/min with other factors that add risk, such as drug interactions that may require dose adjustments<br>• Dose recommendations are specific for CYP inhibitors and inducers; refer to PI<br>Associated with:<br>• Drug-induced hepatotoxicity with allergic-type features: use with caution in patients with hepatic impairment; discontinue if signs and symptoms occur |
| *HIV Protease Inhibitors* | | | |
| Universal prescribing alerts:<br>• Can cause fat redistribution, elevated bilirubin, prolonged PR interval, diabetes, hepatic impairment, nephrolithiasis, hemolytic anemia, elevated triglycerides, and elevated cholesterol<br>• Contraindicated in patients who experience specific drug-induced hypersensitivity reactions (including SJS and DRESS) and drug interactions that may require dose adjustments | | | |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Atazanavir<br><br>**Brand Name**<br>Reyataz<br><br>■ QT PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>300 mg once daily with ritonavir 100 mg or cobicistat 150 mg<br><br>Additional adjustments when used with $H_2$ antagonist or proton pump inhibitor (i.e., increase to 400 mg once daily) | • May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Not recommended for use in antiretroviral-experienced patients with end-stage renal disease (ESRD)<br>• Administer with food, and separate administration from that of antacids and buffered medications<br>• Limit dose of $H_2$ blocker (see PI) AND when using $H_2$ blockers, administer at the same time as atazanavir or at least 10 hours after the atazanavir dose.<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Specific recommendations for patients undergoing dialysis<br>• Confirm that baseline/pretreatment HIV RNA greater than 100,000 copies/mL<br>• Monitor: viral load, CD4 count, blood glucose, LFTs, bilirubin, atazanavir levels if used with interacting medications, ECG in patients with preexisting prolonged PR interval or concurrent use of atrioventricular (AV) nodal-blocking medications |
| **Generic Name**<br>Darunavir<br><br>**Brand Name**<br>Prezista<br><br>PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>800 mg once daily with ritonavir 100 mg or cobicistat 150 mg<br><br>**Suspected resistance:**<br>600 mg twice daily<br>Treatment experienced patients may require higher doses | • Can cause fat redistribution, diabetes, hepatic impairment, pancreatitis, and elevated cholesterol<br>• Drug interactions may require dose adjustments<br>• May cause hypersensitivity reactions such as SJS or DRESS: discontinue if rash appears<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Not recommended in patients with severe hepatic impairment: discontinue if hepatic function worsens during therapy<br>• Administer with food<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Do not use darunavir/ritonavir if CD4 count is less than 200 cells/mm3 and/or HIV RNA greater than 100,000 copies/mL<br>• Monitor: viral load, CD4 count, baseline genotyping in treatment-experienced patients, blood glucose, LFTs at baseline and throughout therapy, cholesterol, triglycerides |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Fosamprenavir<br><br>**Brand Name**<br>Lexiva<br><br>PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>1400 mg with ritonavir 100 to 200 mg once daily<br>Alternatively may give:<br>700 mg with ritonavir 100 mg twice daily | • May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Drug interactions may require dose adjustments<br>• Administer suspension without food in adults; if vomiting occurs within 30 minutes, readminister<br>• Administer tablet with food if taken with ritonavir<br>• Twice-daily dosing is recommended in protease inhibitor–experienced adults<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, LFTs in patients with hepatitis B or C, cholesterol, triglycerides<br>• Regimens without ritonavir are available, but not recommended by guidelines |
| **Generic Name**<br>Indinavir<br><br>**Brand Name**<br>Crixivan | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>800 mg with ritonavir 100 to 200 mg 2 times per daily<br><br>Alternative dose schedules using other antiretrovirals are available, refer to PI | • May cause tubulointerstitial nephritis: monitor for leukocytopenia (rare)<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Use with caution in patients with preexisting hepatic disease: can exacerbate symptoms<br>• Drug interactions may require dose adjustments<br>• Administer with water on an empty stomach when unboosted<br>• Keep patients well hydrated: drink 48 ounces of water daily to help prevent nephrolithiasis<br>• Dispense in original container<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, LFTs, cholesterol, triglycerides, CBC, urinalysis (especially monitor for leukocyturia)<br>• Regimens without ritonavir are available, but not recommended by guidelines |
| **Generic Name**<br>Lopinavir and ritonavir<br><br>**Brand Name**<br>Kaletra<br><br>QT PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>lopinavir 400 mg with ritonavir 100 mg twice daily<br>Alternatively may give:<br>Lopinavir 800 mg with ritonavir 200 mg once daily | • May cause QTc prolongation and other conduction abnormalities, and patients may have a higher risk of myocardial infarction (MI): use with caution in patients with preexisting cardiac disease<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer solution with food<br>• Drug interactions may require dose adjustments<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Use with caution in patients with poor renal function to ensure accumulation and toxicity do not occur |

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| | | | • Monitor: viral load, CD4 count, baseline genotyping or phenotypic testing before starting therapy, blood glucose, LFTs, electrolytes, cholesterol, triglycerides<br>• Specific recommendations for patients undergoing dialysis |
| **Generic Name**<br>Nelfinavir<br><br>**Brand Name**<br>Viracept<br><br>QT PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>750 mg 3 times per day<br><br>1250 mg 2 times per day | • May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Not recommended in patients with moderate to severe hepatic impairment: discontinue if hepatic function worsens during therapy<br>• Administer with food; mixing a crushed tablet with acidic foods or juices will cause a bitter taste<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, LFTs, cholesterol, triglycerides, CBC with differential |
| **Generic Name**<br>Ritonavir<br><br>**Brand Name**<br>Norvir<br><br>■ QT PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>600 mg 2 times per day (titrate up from 300 mg 2 times per day and increase by 100 mg 2 times per day every 2 to 3 days) | • Use dose escalation strategy to reduce nausea<br>• Can cause fat redistribution, QT interval prolongation, diabetes, hepatic impairment, pancreatitis, and elevated cholesterol<br>• Drug interactions may require dose adjustments<br>• Use with caution in patients with preexisting cardiovascular disease<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Not recommended in patients with severe hepatic impairment: discontinue if hepatic function worsens during therapy<br>• Tablets are not bioequivalent to capsules<br>• Administer with food and advise patients to stay well hydrated<br>• Mix solution with chocolate to mask bad taste<br>• Contains 43% ethanol and 26.57% propylene glycol: monitor for toxicity<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, LFTs, cholesterol, triglycerides, CBC, CPK, uric acid, amylase and lipase serum levels<br>• Lower doses of ritonavir are used to enhance or "boost" the serum concentrations of other antiretroviral agents (purposeful drug interaction) |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Saquinavir<br><br>**Brand Name**<br>Invirase<br><br>QT | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>1000 mg with ritonavir 100 mg 2 times per day | • Can cause QTc prolongation, fat redistribution, photosensitivity, diabetes, hepatic impairment, electrolyte imbalances, and elevated cholesterol<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer within 2 hours after a meal; do not take with grapefruit juice<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, cholesterol and triglycerides at baseline and throughout treatment; ECG at baseline and 3-4 days after starting therapy; potassium and magnesium blood levels<br>• Contraindicated for use in patients with severe hepatic impairment |
| **Generic Name**<br>Tipranavir<br><br>**Brand Name**<br>Aptivus<br><br>■ PD | Treatment of HIV infection when used with other antiretroviral agents in treatment-experienced or multiple protease inhibitor–resistant patients | **Usual oral dose:**<br>500 mg with ritonavir 200 mg 2 times per day for 7 days, then may increase to standard dose of 1000 mg with ritonavir 100 mg 2 times per day | • Can cause fat redistribution, skin reactions such as rash and photosensitivity, impaired platelet aggregation, diabetes, hepatic impairment, and elevated cholesterol<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Not recommended in patients with severe hepatic impairment: discontinue if hepatic function worsens during therapy<br>• Administer with food when administering with ritonavir tablets<br>• Solution contains vitamin E; capsules contain dehydrated ethanol<br>• Patients with hemophilia A or B are at an increased risk of bleeding<br>• Monitor: viral load, CD4 count, blood glucose, LFTs (including bilirubin) at baseline and frequently throughout therapy, cholesterol and triglycerides at baseline and throughout treatment; monitor patients coinfected with hepatitis B or C carefully<br>Associated with:<br>• Hepatotoxicity when used with certain other drugs, which can be fatal<br>• Use with caution in patients with preexisting hepatic impairment<br>• Rare cases of intracranial hemorrhage when used with certain other drugs |
| *HIV Integrase Inhibitors* | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Dolutegravir<br><br>**Brand Name**<br>Tivicay | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>50 mg once a day, may increase to 50 mg 2 times daily when coadministered with specific antiretrovirals; refer to PI | • Risk of lactic acidosis when used in combination with higher doses of metformin<br>• Avoid co-administration with multivitamins or supplements containing calcium, magnesium, or iron |

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| **Generic Name**<br>Elvitegravir and cobicistat<br><br>**Brand Name**<br>Vitekta | Treatment of HIV infection when used with other antiretroviral agents in adults who are antiretroviral experienced | **Usual oral dose:**<br>85 mg (with ritonavir 100 mg and atazanavir 300 mg) once a day | • Higher dose options are available in combination with other agents<br>• May cause elevations in serum creatinine<br>• Avoid in renal dysfunction |
| **Generic Name**<br>Raltegravir<br><br>**Brand Name**<br>Isentress<br>PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>400 mg twice daily | • Can cause myopathy: use with caution in patients who are at risk for elevated CK<br>• Severe skin and hypersensitivity reactions have occurred, including SJS and TEN: discontinue if rash occurs<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Store chewable tablets and oral suspensions in their original containers<br>• Chewable tablets, oral suspensions, and film-coated tablets are not bioequivalent<br>• Do not use darunavir/ritonavir and raltegravir if the patient's pre-antiretroviral therapy (ART) CD4 count less than 200 cells/$mm^3$ and/or HIV RNA greater than 100,000 copies/mL<br>• Monitor: viral load, CD4 count, complete lipid profile<br>• Drug interactions may require dose adjustment or avoidance of certain drug combinations |
| *HIV Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)* | | | |
| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
| **Generic Name**<br>Delavirdine<br><br>**Brand Name**<br>Rescriptor | Treatment of HIV-1 infection when used with other antiretroviral agents | **Usual oral dose:**<br>400 mg 3 times per day | • May cause fat redistribution or a rash that requires interruption of therapy<br>• Use with caution in patients with hepatic and renal impairment<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Do not administer with antacids to ensure gastric acidity for absorption<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Monitor: viral load, CD4 count, LFTs if used with saquinavir |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Efavirenz<br><br>**Brand Name**<br>Sustiva<br><br>PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>600 mg once per day | • Not recommended in patients with moderate to severe hepatic impairment; avoid use in patients with HIV-associated dementia<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer on an empty stomach; recommended to take at bedtime due to increased tolerability of CNS effects<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Oral solution is available only through an expanded access program<br>• Do not use efavirenz with abacavir and lamivudine if the patient's pre-ART HIV RNA greater than 100,000 copies/mL<br>• Can cause false-positive tests for cannabinoids if using the CEDIA DAU Multilevel THC assay<br>• Can cause false-positive tests for benzodiazepines<br>• Monitor: LFTs, cholesterol and triglycerides, psychiatric adverse effects |
| **Generic Name**<br>Etravirine<br><br>**Brand Name**<br>Intelence<br><br>PD | Treatment of HIV infection when used with other antiretroviral agents in treatment-experienced patients with NNRTI resistance | **Usual oral dose:**<br>200 mg 2 times per day | • May cause fat redistribution or a rash (SJS, TEN, DRESS): discontinue if rash becomes severe<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer after meals<br>• Can disperse in water; do not use grapefruit juice, carbonated drinks, or warm water when taking etravirine<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Monitor: cholesterol and triglycerides, blood glucose, LFTs if signs and symptoms of hypersensitivity occur |
| **Generic Name**<br>Nevirapine<br><br>**Brand Name**<br>Viramune<br>Viramune XR<br><br>■ PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>IR: 200 mg once daily for 14 days, then increase to twice daily<br><br>XR: 400 mg once daily for maintenance (must have received 200 mg IR formulation before XR; refer to PI for details) | • May cause fat redistribution or rhabdomyolysis<br>• Not recommended in combination with nevirapine due to increased adverse effects<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Do not administer in antiretroviral-naïve patients if CD4+ cell counts greater than 250 cells/mm3 in females or CD4+ cell counts greater than 400 cells/mm3 in males<br>• If rash appears during first 14 days of use, do not increase dose until it disappears; use alternative therapy if rash duration exceeds 28 days |

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| | | | • Monitor: viral load; CD4 count; CBC; baseline LFTs, then every 2 weeks for the first 4 weeks and monthly for the first 18 weeks, then every 3 to 4 months; signs of rash<br>Contraindications:<br>• Moderate to severe hepatic impairment<br>• Use in postexposure prophylaxis<br>Associated with:<br>• Severe hepatotoxicity: risk is greatest in the first 6 weeks; monitor intensely for the first 18 weeks<br>• Life-threatening skin reactions such as SJS and TEN: risk is greatest in the first 6 weeks; monitor intensely for the first 18 weeks |
| **Generic Name**<br>Rilpivirine<br><br>**Brand Name**<br>Edurant<br>QT | Treatment of HIV infection when used with other antiretroviral agents in treatment-naïve patients if HIV RNA 100,000 copies/ml or less and/or pre-ART CD4 count greater than 200 cells/mm3 | **Usual oral dose:**<br>25 mg once daily | • May cause depressive disorders, fat redistribution, hepatotoxicity, or hypersensitivity reaction such as DRESS: discontinue if severe or rash develops<br>• Drug interactions may require dose adjustments<br>• Use with caution in patients with severe renal impairment<br>• Doses greater than 25 mg/day can cause QTc prolongation<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer with a meal—not just a protein shake<br>• Keep in original container<br>• Monitor: viral load, CD4, cholesterol and triglycerides, LFTs |

*Nucleoside and Nucleotide Reverse Transcriptase Inhibitors*

Universal prescribing alerts:

Associated with

- Lactic acidosis and severe hepatomegaly with steatosis: use with caution in patients at risk for liver disease
- Pancreatitis: discontinue upon diagnosis

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Abacavir<br><br>**Brand Name**<br>Ziagen<br>■ ■ PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>300 mg twice daily<br><br>600 mg once daily | • Use with caution in patients with coronary heart disease<br>• May cause fat redistribution<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Ethanol can increase the risk of toxicity; avoid use<br>• Monitor: CBC with differential, CK, CD4 count, HIV RNA levels, LFTs, triglycerides, amylase, HLA-B*5701 genotype testing before starting therapy, signs and symptoms of hypersensitivity reactions |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| | | | Associated with:<br>• Serious hypersensitivity reactions; testing for HLA-B*5701 allele is recommended before treatment as these patients are at an increased risk<br>• Severe hepatotoxicity and/or lactic acidosis |
| **Generic Name**<br>Didanosine<br><br>**Brand Name**<br>Videx<br>Videx EC<br>▲ ■ PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>For patients weighing 60 kg or more:<br>Oral solution: 200 mg twice daily (preferred) or 400 mg once daily<br><br>Capsule: 400 mg once daily | • May cause noncirrhotic portal hypertension: discontinue if signs and symptoms occur<br>• May cause retinal changes and optic neuritis, peripheral neuropathy, and fat redistribution<br>• Use with caution in patients with hepatic and renal impairment<br>• Specific recommendations for patients undergoing dialysis<br>• Drug interactions may require dose adjustments or avoidance of certain drug combinations<br>• Dosing for patients weighing less than 60 kg is available; refer to PI<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Administer on an empty stomach<br>• Oral suspension needs to be mixed with antacid solution before dispensing<br>• Monitor: viral load, CD4 count, potassium, uric acid, SCr, hemoglobin, CBC with neutrophil and platelet count, LFTs, bilirubin, albumin, INR, amylase, retinal exam every 6 months, ultrasonography if portal hypertension is suspected<br>Associated with:<br>• Hepatotoxicity and/or lactic acidosis<br>• Pancreatitis |
| **Generic Name**<br>Emtricitabine<br><br>**Brand Name**<br>Emtriva<br>▲ ■ PD | Treatment of HIV infection when used with other antiretroviral agents<br><br>Recommended as initial therapy with other agents | **Usual oral dose:**<br>Capsule:<br>200 mg once daily<br><br>Solution:<br>240 mg once daily | • May cause fat redistribution<br>• Use with caution in patients with renal impairment<br>• Avoid use with lamivudine due to potential for cross-resistance<br>• Capsules and solution are not interchangeable on a mg per mg basis<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Monitor: viral load, CD4 count, LFTs, hepatitis B screening before initiating therapy<br>• Specific recommendations for patients undergoing dialysis<br>Associated with:<br>• Coinfection with hepatitis B: severe exacerbations of HBV have occurred when discontinuing HIV therapy<br>• Hepatotoxicity and/or lactic acidosis |

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| **Generic Name**<br>Lamivudine<br><br>**Brand Name**<br>Epivir<br>Epivir HBV<br>  | Treatment of HIV-1 infection when used with other antiretroviral agents<br><br>Recommended for initial therapy (including in patients coinfected with HBV) when used with other agents<br><br>Treatment of chronic hepatitis B (has not been studied in coinfected patients with HIV and is not recommended as first-line therapy) | **Usual oral dose:**<br>150 mg twice per day or 300 mg once per day | • May cause fat redistribution and pancreatitis<br>• Use with caution in patients with renal impairment, not recommended in patients with impaired renal function.<br>• Use caution when lamivudine is used in patients on interferon alfa (i.e., HIV/HBV-coinfected patients) due to increased risk of hepatotoxicity. Not recommended for use in patients with impaired hepatic function<br>• Avoid use with emtricitabine due to potential for cross-resistance<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Monitor: viral load; CD4 count; amylase; bilirubin; LFTs every 3 months; hematologic parameters; HBV DNA if treating for HBV; HBeAg and anti-HBe 1 year after starting HBV therapy, then every 3 to 6 months; signs/symptoms of relapse after stopping HBV treatment for several months<br>Associated with:<br>• Need to monitor patients after discontinuing therapy for hepatitis B: exacerbations may develop that require retreatment<br>• HIV-1 resistance development if treating for chronic hepatitis B: if patients are unaware they have HIV-1, resistance can develop<br>• Need to use Epivir HBV tablets or solution only for hepatitis B and not HIV infection<br>• Hepatotoxicity and/or lactic acidosis |
| **Generic Name**<br>Stavudine<br><br>**Brand Name**<br>Zerit<br>  | Treatment of HIV infection when used with other antiretroviral agents | **Usual oral dose:**<br>For patients weighing 60 kg or more:<br>40 mg every 12 hours | • May cause fat redistribution and peripheral neuropathy<br>• May cause motor weakness: discontinue if it develops<br>• Use with caution in patients with renal and hepatic impairment or preexisting bone marrow suppression<br>• Avoid use with didanosine, hydroxyurea, and zidovudine due to increased risk of adverse events; use with caution when patients are also receiving interferon alfa<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Doses for those weighing less than 60 kg are available; refer to PI<br>Associated with:<br>• Pancreatitis when used with certain other drugs upon diagnosis<br>• Hepatotoxicity and/or lactic acidosis |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Tenofovir<br><br>**Brand Name**<br>Viread<br><br>▲ ■ PD | Treatment of HIV infection when used with other antiretroviral agents<br><br>Recommended in initial regimen when used with other agents<br><br>Treatment of chronic hepatitis B infection | **Usual oral dose:**<br>300 mg once daily | • May cause fat redistribution, decrease in bone mineral density, osteomalacia, pancreatitis, or renal toxicity: avoid use in high-risk patients<br>• Use with caution in patients with hepatic and renal impairment<br>• If treating the patient for HBV, screen for HIV to ensure resistance will not develop to HIV<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• Mix powder with 2 to 4 ounces of soft food to avoid bitter taste<br>• May need to supplement with calcium and vitamin D due to decrease in bone mineral density<br>• Monitor:<br>  • HIV: viral load, CD4 count, CBC with differential, reticulocyte count, CK, HIV RNA levels, phosphorus, SCr at baseline and throughout therapy, urine glucose and protein if at risk for renal impairment, LFTs, bone density if at risk, screen for HBV before use<br>  • HBV: phosphorus, SCr, urine glucose and protein, bone density, HBV DNA every 3 to 6 months, HBeAg and anti-HBe, LFTs every 3 months and several months after therapy<br>Associated with:<br>• Severe exacerbations of HBV upon discontinuation<br>• Monitor for relapse for several months<br>• Hepatotoxicity and/or lactic acidosis |
| **Generic Name**<br>Zidovudine<br><br>**Brand Name**<br>Retrovir<br><br>▲ ■ PD | Treatment of HIV infection when used with other antiretroviral agents | **Usual parenteral dose:**<br>1 mg/kg per dose every 4 hours around the clock<br><br>**Usual oral dose:**<br>300 mg twice per day<br><br>Oral therapy is preferred | • May cause fat redistribution<br>• Use with caution in patients with hepatic and renal impairment<br>• Specific recommendations for patients undergoing dialysis<br>• May cause immune reconstitution syndrome, in which an inflammatory reaction develops due to a residual opportunistic infection or activation of an autoimmune disorder<br>• If assay is negative for HIV in an infant who received preventive therapy, retest in 2 to 4 weeks to confirm diagnosis<br>• The injection vial's stopper contains latex<br>• Monitor: viral load, CD4 count, CBC with differential every 3 to 6 months, LFTs every 6 to 12 months, lipid profile, blood glucose levels<br>Associated with:<br>• Hematologic toxicity, including neutropenia and anemia; may need to interrupt therapy<br>• Myopathy over prolonged use<br>• Hepatotoxicity and/or lactic acidosis |

| Interferons | | | |
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| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
| **Generic Name**<br>Interferon alfa<br><br>**Brand Name**<br>Intron<br>Alferon N<br>  | Alfa-2b: AIDS-related Kaposi sarcoma, chronic hepatitis B, chronic hepatitis C with other agents, condylomata acuminata, follicular lymphoma with other agents, and hairy cell leukemia; adjunct therapy for malignant melanoma<br><br>Alferon N: condylomata acuminata | **Usual parenteral dose for AID's related Kaposi's sarcoma:**<br>IM, SubQ: 30 million units/$m^2$ 3 times/week until disease progression is confirmed or achievement of maximum response after 16 weeks of treatment | • Causes bone marrow suppression, which can lead to anemia, neutropenia, and thrombocytopenia<br>• In combination with ribavirin can cause dental and periodontal disorders, including dry mouth<br>• Can cause hypertriglyceridemia, changes in vision and other eye disorders, pulmonary infections and other disorders, arrhythmias, thyroid disorders, strokes, and diabetes<br>• Use with caution in patients with coagulation and pulmonary disorders<br>• Recommended to administer acetaminophen before injection to reduce adverse effects<br>• If dose is 10 million units/$m^2$ or greater, recommend using an antiemetic concurrently<br>• Administration in the evening results in increased tolerability<br>• Inject IM into the anterior thigh, deltoid, and superlateral buttock<br>• IM injection is preferred; use SubQ administration if concerned about bleeding or thrombocytopenia<br>• Continue to use the same brand for in the patient due to differences in dosages<br>• Monitor:<br>  • Baseline and as needed: chest x-ray, SCr, albumin, PTT<br>  • Baseline and during therapy: CBC with differential; platelets (PLT); hemoglobin; LFTs; electrolytes; TSH; ophthalmic exams; ECG if preexisting cardiac conditions or advanced cancer; bilirubin; lactate dehydrogenase (LDH) at 2, 8, and 12 weeks, then every 6 months<br>  • During therapy: weight, neuropsychiatric changes<br>Contraindications:<br>• Autoimmune hepatitis<br>• Severe liver disease<br>Associated with:<br>• Causing or exacerbating neuropsychiatric disorders, including depression, psychosis, mania, suicidal ideation, and homicidal ideation: discontinue if symptoms worsen; usually is reversible upon discontinuation<br>• Causing or exacerbating autoimmune diseases infectious disorders, and ischemic disorders: discontinue if symptoms worsen<br>• Fever and flu-like symptoms associated with interferon administration requires extra caution in patients with cardiac disease<br>• Hepatotoxicity, which can be fatal: discontinue if severe injury develops |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Peginterferon alfa<br><br>**Brand Name**<br>Pegasys (2a)<br>Peg-Intron (2b)<br>Sylatron (2b)<br>  <br>PD | Alfa-2a: chronic hepatitis B and chronic hepatitis C<br><br>Hepatitis C should also be treated concurrently with antiviral medications<br><br>Alfa-2b: chronic hepatitis C; adjunct therapy for melanoma | **Usual parenteral dose:**<br>**Alfa-2a (Pegasys):**<br>SubQ: 180 mg once weekly<br><br>**Alfa-2b PegIntron:**<br>max doses SubQ 1 mcg/kg/week for monotherapy or 1.5 mcg/kg/week for combination therapy<br><br>**Alfa-2b Sylatron:**<br>max doses: SubQ 6 mcg/kg/week | • Causes bone marrow suppression, which can lead to anemia, neutropenia, and thrombocytopenia<br>• Can cause hepatotoxicity, which can be fatal: discontinue if severe injury develops<br>• In patients with hepatitis B, flares may occur for ALT levels: reduce the dose and discontinue if ALT does not drop<br>• Can cause serious skin reactions such as SJS and exfoliative dermatitis, flu-like symptoms, gastrointestinal ulcerative colitis and other serious disorders, hypertriglyceridemia, changes in vision and other eye disorders, pancreatitis, pulmonary infections and other disorders, arrhythmias, thyroid disorders, dental/periodontal disorders in combination therapy, and diabetes<br>• Do not drink alcohol<br>• Do not shake vial, syringe, or autoinjector<br>• Warm by rolling between the palms of the hands for a vial and syringe; let the autoinjector warm by setting it outside the refrigerator<br>• Caution patients about operating machinery and driving due to the potential for CNS depression<br>• Continue to use the same brand for the patient due to differences in dosages<br>• Monitor: CBC, hemoglobin, PLT, LFTs, and uric acid at weeks 1, 2, 4, 6, and 8, and every 4 to 6 weeks after; TSH every 12 weeks; ECG if preexisting cardiac disease; neuropsychiatric symptoms<br>Contraindications:<br>• Autoimmune hepatitis<br>• Severe liver disease<br>Associated with:<br>• Causing or exacerbating neuropsychiatric disorders, including depression, psychosis, mania, suicidal ideation, and homicidal ideation: discontinue if symptoms worsen; usually is reversible upon discontinuation<br>• Causing or exacerbating autoimmune diseases infectious disorders, and ischemic disorders: discontinue if symptoms worsen<br>• Drug interactions that require dose adjustments or avoidance of certain drug combinations<br>• Myocardial infarction and stroke |

| Neuraminidase Inhibitors | | | |
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| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Oseltamivir<br><br>**Brand Name**<br>Tamiflu<br>  | Prophylaxis against and treatment of influenza A and B<br><br>Recommended to be used in patients at a higher risk for complications from influenza | **Usual oral dose:**<br>75 mg 1 to 2 times daily for 5 to 10 days<br><br>Start within 48 hours of symptoms or contact with an infected individual | • Rarely causes neuropsychiatric adverse events, including confusion and hallucinations<br>• Use with caution in patients with cardiovascular disease, severe hepatic impairment, renal impairment, and respiratory disease<br>• Safety and efficacy have not been proved in immunocompromised patients<br>• Monitor: signs and symptoms of neuropsychiatric changes |
| **Generic Name**<br>Peramivir<br><br>**Brand Name**<br>Rapivab<br>  | Treatment of acute influenza when patient has been symptomatic for 2 or fewer days | **Usual parenteral dose:**<br>IV: 600 mg single dose | • May cause severe skin reactions, such as SJS<br>• Infuse over 15 to 30 minutes<br>• Administer within 48 hours of onset of flu symptoms<br>• May cause neuropsychiatric events, such as delirium and hallucination: usually symptoms appear soon after use and in pediatric patients<br>• Hypersensitivity reactions have been reported when peramivir is used with other neuraminidase inhibitors: caution is advised<br>• Monitor: BUN and SCr, rash after administration |
| **Generic Name**<br>Zanamivir<br><br>**Brand Name**<br>Relenza Diskhaler | Prophylaxis against and treatment of influenza A and B<br><br>Recommended to be used in patients at a higher risk for complications from influenza | **Usual oral inhaled dose:**<br>2 inhalations 1 to 2 times daily for 5 days<br><br>Treatment: begin within 2 days of symptoms<br><br>Prophylaxis: begin within 36 hours to 5 days after contact with an infected person | • May cause neuropsychiatric adverse events, including confusion, seizures, and hallucinations<br>• May cause bronchospasm: not recommended for use in patients with respiratory disease; discontinue if lung function decreases<br>• Efficacy has not been established for use as prophylaxis in nursing homes<br>• If patient needs a bronchodilator, use it before administering zanamivir<br>• Monitor: signs and symptoms of neuropsychiatric changes and bronchospasm |
| **Nucleosides and Nucleotides** | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Acyclovir | Oral therapy: herpes zoster (shingles), genital herpes simplex virus, varicella (chickenpox) | **Usual oral dose for herpes zoster in immunocompetent patients:**<br>800 mg every 4 hours (5 times per day) for 7 to 10 days | • Can cause renal impairment: use with caution in patients at high risk<br>• May cause thrombocytopenic purpura/hemolytic uremic syndrome in immunocompromised patients<br>• Treatment for chickenpox should start within 24 hours of rash appearance if patient is at an increased risk of complications<br>• Treatment for shingles should start within 72 hours of rash appearance |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Brand Name**<br>Zovirax<br>Sitavig<br>▲ PD | Parenteral (IV) therapy: herpes simplex virus in immunocompromised patients, severe genital herpes simplex virus, herpes simplex encephalitis, herpes zoster (shingles) in immunocompromised patients<br><br>Buccal tablet/cream: recurrent herpes labialis (cold sores)<br><br>Ointment: genital herpes simplex virus and mild mucocutaneous herpes simplex virus infections in immunocompromised patients | **Usual parenteral dose for immunocompromised patients:**<br>IV: 10 mg/kg per dose every 8 hours for 7 days<br><br>**Topical:**<br>Ointment: apply ½-inch ribbon per 4-inch square surface every 3 hours for 7 days<br><br>Cream/ointment:<br>apply 5 times/day for 4 days to lesions | • Use IV acyclovir with caution in patients with neurologic abnormalities, severe hepatic dysfunction, serious electrolyte imbalances, or significant hypoxia<br>• If patient is obese, dose based on ideal body weight (IBW)<br>• Keep well hydrated to help protect the kidneys<br>• Infuse IV formulation over 1 hour to avoid kidney damage<br>• Available also as a buccal tablet<br>• If buccal tablet falls out within 6 hours of placement, replace the tablet or apply a new tablet: for maximum effect, apply 1 hour after prodromal symptoms are noted<br>• Apply ointment while wearing a glove to prevent transmission of virus to other parts of the body<br>• Monitor: urinalysis, BUN, SCr, LFTs, CBC |
| **Generic Name**<br>Adefovir<br><br>**Brand Name**<br>Hepsera<br>▲ ■ | Treatment of chronic hepatitis B if there is evidence of active viral replication | **Usual oral dose:**<br>10 mg once daily | • Do not use with tenofovir, as it decreases the efficacy of tenofovir<br>• Not a first-line treatment<br>• Monitor: HIV status before starting therapy, SCr at baseline and throughout therapy, LFTs for several months after stopping therapy, HBV DNA every 3 to 6 months while using adefovir, HBeAg and anti-HBe<br>Associated with:<br>• Severe lactic acidosis and hepatomegaly with steatosis when using nucleoside analogues: use with caution in patients with risk factors for liver dysfunction; interrupt therapy if signs and symptoms occur<br>• Severe exacerbation of hepatitis B upon discontinuation: usually occurs within the first 12 weeks and may dissipate or resolve with initiating treatment<br>• Risk of developing HIV resistance in patients who do not realize they are HIV infected: determine status before treatment<br>• Nephrotoxicity: use with caution in patients at high risk for toxicity or with preexisting renal impairment |

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| **Generic Name**<br>Cidofovir<br><br>**Brand Name**<br>Vistide<br>  | Treatment of cytomegalovirus (CMV) retinitis in patients infected with AIDS | **Usual parenteral dose:**<br>IV: 5 mg/kg per dose every other week while receiving maintenance therapy | • Reports of metabolic acidosis have been reported: monitor for signs and symptoms including low bicarbonate and renal wasting syndrome<br>• Ensure proper hydration throughout<br>• Can cause ocular dysfunction: monitor intraocular pressure; treat the patient with a topical steroid if uveitis or iritis occurs<br>• Monitor: SCr and urine protein at baseline and within 48 hours prior to administering a dose, WBC with differential before each dose, intraocular pressure and visual acuity, signs and symptoms of uveitis/iritis and metabolic acidosis<br>Contraindications:<br>• Use of nephrotoxic agents with the last 7 days<br>• Direct intraocular injection<br>• SCr greater than 1.5 mg/dL, CrCl 55 mL/min or less, or 2+ proteinuria<br>Associated with:<br>• Categorized as a possible carcinogen and teratogen based on animal data; can cause hypospermia<br>• Renal failure and death when administering 1 to 2 doses: monitor renal function within 48 hours before administering a dose; must administer with probenecid and saline<br>• Neutropenia |
| **Generic Name**<br>Entecavir<br><br>**Brand Name**<br>Baraclude<br>  | Treatment of chronic hepatitis B with evidence of active viral replication in patients with elevated transaminase or histologically active disease | **Usual oral dose:**<br>0.5 to 1 mg once daily | • Use with caution in patients with hepatic impairment<br>• Administer on an empty stomach: food delays absorption<br>• Available as tablet and solution<br>• Cross-resistance may develop in patients who have failed lamivudine therapy: resistance can develop quickly<br>• Monitor: HIV status before starting therapy; hepatic and renal function tests; if coinfected with HIV, monitor HIV viral load and CD4 count; HBV DNA every 3 months; HBeAg<br>Associated with:<br>• Severe lactic acidosis and hepatomegaly with steatosis when using nucleoside analogues: use with caution in patients with risk factors for liver dysfunction; interrupt therapy if signs and symptoms occur<br>• Severe exacerbation of hepatitis B upon discontinuation: may dissipate or resolve with initiating treatment<br>• Risk of developing HIV resistance in patients who do not realize they are HIV infected: determine status before treatment |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Famciclovir<br><br>**Brand Name**<br>Famvir<br>  | Treatment of herpes zoster (shingles), herpes labialis (cold sores), and recurrent orolabial/genital herpes simplex in HIV-infected patients<br><br>Treatment and suppression of recurrent genital herpes | **Usual oral dose for treatment of herpes zoster:**<br>500 mg every 8 hours for 7 days<br><br>Cold sores: 1500 mg once as single dose | • Use with caution in patients with renal impairment: dose appropriately<br>• Treatment for shingles should start within 72 hours of rash's appearance<br>• Monitor: CBC with extended use |
| **Generic Name**<br>Ganciclovir<br><br>**Brand Name**<br>Cytovene<br>Zirgan<br>  | Treatment of susceptible viruses that cause CMV retinitis in immunocompromised patients<br><br>Prophylaxis against CMV infection in transplant patients | **Usual parenteral dose for CMV retinitis:**<br>IV: 5 mg/kg per dose every 12 hours for a minimum of 14 days | • When handling, use hazardous precautions due to its extreme basic nature<br>• Administer via slow IV infusion over 1 hour<br>• Monitor: CBC with differential, platelet count, SCr<br>Associated with:<br>• Blood dyscrasias: may need to adjust or interrupt therapy until white blood cell levels increase<br>• Carcinogenic and potential teratogenic effects |
| **Generic Name**<br>Ribavirin<br><br>**Brand Name**<br>Copegus<br>Moderiba<br>Rebetol<br>Ribasphere<br>Virazole<br>  | Chronic hepatitis C infection: | **Usual oral dose (tablets) for chronic hepatitis C with concurrent use of other recommended medications:**<br>1000 to 1200 mg per day in 2 divided doses daily<br><br>Treatment duration and formulation selected is individualized based on patient's clinical status and dose is based on weight (patients weighing less than 75 kg are recommended to get lower dose) | • Use with caution in patients with hepatic and renal impairment<br>• Risk of autoimmune/infectious disorders, bone marrow suppression, dental and periodontal disorders, dermatologic reactions such as SJS, diabetes, serious ophthalmic disorders, pancreatitis, psychiatric disorders, and pulmonary adverse events<br>• Administer with food to increase absorption<br>• Inhalation monitoring: respiratory function, hemoglobin, reticulocyte count, CBC with differential, ins and outs (I&O)<br>• Oral monitoring: hematologic and biochemical tests before administration and during therapy, dental exam, ECG if preexisting cardiac disease exists, ophthalmic exam, TSH at week 12, pregnancy screening and tests monthly, HCV RNA before administration and at 12, 24, and 24 weeks after completion<br>• Formulations have different indications for use; refer to PI prior to prescribing.<br>Contraindications:<br>• Hemoglobinopathy and concurrent use of didanosine<br>• CrCl less than 50 mL/min<br>• Hepatic decompensation in cirrhosis (when used with other specific agents)<br>• Autoimmune hepatitis |

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| | | | Associated with:<br>• Hemolytic anemia: can worsen cardiac diseases; use with caution in patients at risk for anemia<br>• Should not be used as monotherapy in patients with chronic hepatitis C<br>• Sudden respiratory deterioration when initiating via inhalation in infants<br>• Interference with effective ventilation; use of inhalation formulation in patients with assisted ventilation may increase risk |
| **Generic Name**<br>Telbivudine<br><br>**Brand Name**<br>Tyzeka<br> | Treatment of chronic hepatitis B with evidence of active viral replication in patients with elevated transaminase or histologically active disease | **Usual oral dose:**<br>600 mg once daily | • May cause myopathy and peripheral neuropathy: discontinue if either condition is diagnosed<br>• Safety and efficacy have not been studied in African American and Hispanic subpopulations; in patients coinfected with HIV, hepatitis C, or hepatitis D; or in liver transplant patients<br>• Cross-resistance may develop in patients who failed to respond to lamivudine<br>• Not considered first-line therapy due to the high rate of resistance<br>• Monitor: LFTs during therapy and post therapy, renal function tests before initiating and during use, CK, HBV DNA every 3 to 6 months, HBeAg and anti-Hbe<br>• Specific recommendations for patients undergoing dialysis.<br>Associated with:<br>• Severe lactic acidosis and hepatomegaly with steatosis when using nucleoside analogues: use with caution in patients with risk factors for liver dysfunction; interrupt therapy if signs and symptoms occur<br>• Severe exacerbation of hepatitis B upon discontinuation: may dissipate or resolve with initiating treatment |
| **Generic Name**<br>Valacyclovir<br><br>**Brand Name**<br>Valtrex<br>  | Treatment of susceptible viruses that cause shingles, genital herpes, suppression of genital herpes in immunocompetent and HIV-infected patients, cold sores, and chickenpox | **Usual oral dose:** 1 to 2 g 2 times per day for 1 to 7 days<br>Dose and duration are individualized based on type of episode and severity of infection | • May cause CNS effects such as hallucinations, delirium, seizures, and encephalopathy<br>• Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome has occurred in immunocompromised patients: use caution with doses of 8 g per day<br>• Has not been studied in severely immunocompromised patients: use with caution when CD4 < 100 cells/mm3<br>• Start treatment as soon as symptoms arise: treatment for shingles and genital herpes should begin within 72 hours (24 hours if recurrent genital herpes)<br>• Monitor: urinalysis, BUN, SCr, LFTs, CBC |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| **Generic Name**<br>Valganciclovir<br><br>**Brand Name**<br>Valcyte<br>  | Treatment of cytomegalovirus (CMV) retinitis in patients with AIDS<br><br>Prevention of CMV disease in high-risk patients who are getting a kidney, heart, or pancreas transplant | **Usual oral dose:**<br>900 mg once or twice per day depending on indication for use and severity of infection | • Can cause renal failure: keep patient well hydrated and use with caution with other nephrotoxic agents<br>• Manufacturer recommends tablets over solution in adults<br>• Administer with meals to increase absorption<br>• Use gloves to avoid contact with crushed tablets, powder from solution, and oral solution due to their carcinogenic and mutagenic potential<br>• Monitor: ophthalmic exam every 4 to 6 weeks when treating CMV retinitis, CBC, platelet count, SCr at baseline and throughout therapy<br>Associated with:<br>• Blood dyscrasias: may need to adjust or interrupt therapy until white blood cell levels increase<br>• Carcinogenic and potential teratogenic effects |
| *HCV Antiviral Agents NS5B Polymerase Inhibitors* | | | |
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Dasabuvir<br><br>**Brand Name**<br>Viekira Pak<br>(in combination with ombitasvir, paritaprevir, and ritonavir) | Treatment of chronic hepatitis C with or without coinfection of HCV/HIV-1 when used with other medication<br><br>For genotypes 1b and 1a without cirrhosis or with compensated cirrhosis | **Usual oral dose:**<br>250 mg 2 times per day | • May cause hepatic decompensation, and ALT elevation<br>• Drug interactions may require dose adjustments<br>• Viekira Pak and Viekira SR are not interchangeable on a mg per mg basis<br>• Take with food for optimal absorption<br>• Dispense in original container<br>• Monitor: hepatic function tests, serum HCV RNA, hepatic decomposition if patient has cirrhosis |
| **Generic Name**<br>Sofosbuvir<br><br>**Brand Name**<br>Sovaldi | Treatment of chronic hepatitis C with or without infection of HCV/HIV-1 with other medications<br><br>Genotypes 1, 2, 3, and 4 | **Usual oral dose:**<br>400 mg daily with ribavirin and with or without peginterferon alfa for 12 to 24 weeks or until liver transplant for patients with hepatocellular carcinoma | • Can cause bradycardia when used with amiodarone<br>• Dispense in original container<br>• Monitor: bilirubin, LFTs, SCr, inpatient EKG monitoring for 48 hours when on amiodarone and self-monitoring for 2 weeks of heart rate, serum HCV RNA<br>• Can be used for treatment naïve patients and those with prior relapse able to receive interferon products |

| *NS3/4A Protease Inhibitors* | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Grazoprevir<br><br>**Brand Name**<br>Zepatier (in combination with elbasvir) | Treatment of chronic hepatitis C infection with or without cirrhosis and with or without infection of HCV/HIV-1<br><br>Genotypes 1a, 1b, and 4 | **Usual oral dose:**<br>100 mg once per day for 12 to 16 weeks | • Keep in original container until use<br>• Drug interactions may require dose adjustments<br>• May cause elevated ALT: discontinue if ALT remains higher than 10 times the upper limit of normal<br>• Monitor: hepatic function tests at baseline, week 8, and week 12; testing for NS5A resistance for genotype 1a; serum HCV RNA at baseline, weeks 4, 8, and 12, and during follow-up |
| **Generic Name**<br>Paritaprevir<br><br>**Brand Name**<br>Technivie<br>(in combination with ombitasvir and ritonavir)<br><br>Viekira Pak<br>(in combination with ombitasvir, ritonavir, and dasabuvir) | Treatment of chronic hepatitis C with or without coinfection of HCV/HIV-1 when used with other medication<br><br>Genotypes 1b and 1a without cirrhosis or with compensated cirrhosis (Viekira)<br><br>Genotype 4 without cirrhosis (Technivie) | **Usual oral dose:**<br>Technivie: 2 tablets every morning for 12 weeks<br><br>Viekira Pak: 2 tablets every morning for 12 to 24 weeks | • May cause hepatic decompensation, and ALT elevation<br>• Drug interactions may require dose adjustments<br>• Take with food for optimal absorption<br>• Dispense in original container<br>• Monitor: hepatic function tests, serum HCV RNA, hepatic decomposition if patient has cirrhosis<br>• Discontinue Technivie if ALT is continuously greater than 10 times ULN |
| **Generic Name**<br>Simeprevir<br><br>**Brand Name**<br>Olysio | Treatment of chronic hepatitis C for 12 to 24 weeks in combination with other medications<br><br>Genotypes 1 and 4 | **Usual oral dose:**<br>150 mg once daily | • May cause hepatic decomposition; photosensitivity when used with peginterferon alfa and ribavirin, which has led to hospitalization; and rash, which usually appears within 4 weeks of therapy initiation<br>• Drug interactions may require dose adjustments<br>• Administer with food<br>• Dispense in original container<br>• Monitor: bilirubin and liver enzymes; serum HCV RNA at baseline and weeks 4, 12, and 24; screen for NS3 Q80K polymorphism for genotype 1a; inpatient EKG monitoring for 48 hours when on amiodarone and self-monitoring for 2 weeks of heart rate |

| *NS5A Replication Complex Inhibitors* | | | |
|---|---|---|---|
| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Daclatasvir<br><br>**Brand Name**<br>Daklinza | Treatment of chronic hepatitis C with or without compensated cirrhosis<br><br>Genotypes 1 and 3 | **Usual oral dose:** 60 mg once daily with sofosbuvir for 12 to 24 weeks and with or without ribavirin | • May cause bradycardia when used with amiodarone; use with caution in patients with cardiovascular diseases and hepatic disease<br>• Drug interactions may require dose adjustments<br>• Monitor: screen for NS5A polymorphisms for genotype 1a in patients with cirrhosis; LFTs; SCr; inpatient EKG monitoring for 48 hours when on amiodarone and self-monitoring for 2 weeks of heart rate |
| **Generic Name**<br>Elbasvir<br><br>**Brand Name**<br>Zepatier (in combination with grazoprevir) | Treatment of chronic hepatitis C infection with or without cirrhosis and with or without infection of HCV/HIV-1<br><br>Genotypes 1a, 1b, and 4 | **Usual oral dose:** 50 mg once daily for 12 to 16 weeks | • Keep in original container until use<br>• Drug interactions may require dose adjustments<br>• May cause elevated ALT: discontinue if ALT remains higher than 10 times the upper limit of normal (moderate to severe hepatic impairment)<br>• Monitor: hepatic function tests at baseline and weeks 8 and 12; testing for NS5A resistance for genotype 1a; serum HCV RNA at baseline, weeks 4, 8, and 12, and during follow-up |
| **Generic Name**<br>Ledipasvir<br><br>**Brand Name**<br>Harvoni (in combination with sofosbuvir) | Treatment of chronic hepatitis C with or without infection of HCV/HIV with or without ribavirin<br><br>Genotypes 1, 4, 5, and 6 | **Usual oral dose:** 90 mg once daily for 12 to 24 weeks | • Can cause bradycardia when used with amiodarone<br>• Dispense in original container<br>• Monitor: bilirubin, LFTs, SCr, inpatient EKG monitoring for 48 hours when on amiodarone and self-monitoring for 2 weeks of heart rate, serum HCV RNA |
| **Generic Name**<br>Ombitasvir<br><br>**Brand Name**<br>Technivie<br>(in combination with paritaprevir and ritonavir) | Treatment of chronic hepatitis C with or without coinfection of HCV/HIV when used with other medication<br><br>Genotypes 1b and 1a without cirrhosis or with compensated cirrhosis (Viekira) | **Usual oral dose:**<br>Technivie: 2 tablets every morning for 12 weeks<br><br>Viekira Pak: 2 tablets every morning for 12 to 24 weeks | • Contraindicated in patients with moderate to severe hepatic impairment and ribavirin use<br>• May cause QTc prolongation that is concentration dependent (Viekira only), hepatic decompensation, and ALT elevation<br>• Drug interactions may require dose adjustments<br>• Take with food for optimal absorption<br>• Dispense in original container<br>• Monitor: hepatic function tests, serum HCV RNA, hepatic decomposition if patient has cirrhosis |

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| Viekira Pak (in combination with paritaprevir, ritonavir, and dasabuvir)  | Genotype 4 without cirrhosis (Technivie) | | • Discontinue Technivie if ALT is continuously greater than 10 times ULN<br>• Viekira Pak and Viekira XR are not interchangeable on a mg per mg basis |

*Miscellaneous Antivirals*

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Foscarnet<br><br>**Brand Name**<br>Foscavir  | Treatment of acyclovir-resistant mucocutaneous herpes simplex virus infections in immunocompromised patients<br><br>Treatment of CMV retinitis in patients with AIDS | **Usual parenteral dose for herpes simplex indication:** IV: 40 mg/kg per dose every 8 to 12 hours for 2 to 3 weeks or until lesions are healed | • May cause anemia, and granulocytopenia<br>• May cause electrolyte imbalances: correct before initiating treatment<br>• Some products contain sodium: use with caution in patients with heart failure<br>• Foscarnet is a vascular irritant; administer into a vein with adequate blood flow<br>• Monitor: 24-hour CrCl at baseline and throughout therapy; during induction, monitor CBC and electrolytes twice weekly, then weekly during maintenance therapy; hydration status<br>Associated with:<br>• Renal impairment: most patients will experience some degree of renal impairment; reduce dose if needed and monitor carefully<br>• Seizures associated with electrolyte imbalance |

## Antiprotozoals

### Amebicides

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Iodoquinol<br><br>**Brand Name**<br>Yodoxin  | Treatment of intestinal amebiasis<br><br>Trophozoite and cyst forms of *Entamoeba histolytica* | **Usual oral dose:** 650 mg 3 times/day for 20 days (max 1.95 g/day) | • May cause optic atrophy/neuritis: avoid extended use at high doses and use with caution in elderly patients<br>• May cause peripheral neuropathy: avoid extended use at high doses<br>• Use with caution in patients with thyroid abnormalities<br>• Administer after meals<br>• Monitor: ophthalmologic exam with extended use<br>Contraindications:<br>• Hepatic impairment |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Paromomycin<br><br>**Brand Name**<br>Humatin | Intestinal amebiasis<br><br>Hepatic coma adjunct or encephalopathy | **Usual oral dose for hepatic coma:** 4 g daily in divided doses for 5 to 10 days<br><br>**Intestinal amebiasis:** 25 to 35 mg/kg/day in 3 divided doses for 7 to 10 days | • Patients with ulcerative bowel lesions may experience renal toxicity due to increased absorption<br>• Administer with food<br>• Alternative agent; not first-line therapy<br>• Not effective for extra-intestinal amebiasis<br>• Contraindicated in: intestinal obstruction |
| **Generic Name**<br>Metronidazole | Refer to the Miscellaneous Antiprotozoals section. | | |

## Antimalarials

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Generic Name**<br>Artemether and lumefantrine<br><br>**Brand Name**<br>Coartem<br><br>QT PD | Treatment of uncomplicated malaria due to *Plasmodium falciparum*<br><br>Sensitive to regions with chloroquine resistance | **Usual oral dose:**<br>4 tablets per dose (20 mg artemether/120 mg lumefantrine per tablet);<br>treat with a 3-day oral regimen with a total of 6 doses including the initial dose, then a second dose 8 hours later, then 1 dose PO twice daily (morning and evening) for the next 2 days for a total course of 24 tablets. | • May cause QTc prolongation<br>• Drug interactions may require dose adjustment: avoid use of grapefruit juice because it increases the concentration of the medication<br>• Use with caution in patients with hepatic and renal impairment<br>• Administer with a full meal to increase absorption: if vomiting occurs within 2 hours of swallowing tablets, readminister<br>• If malaria returns, treat with a different medication<br>• Monitor: adequate food intake with medication, ECG if patients is concurrently taking other medications that can cause QTc prolongation |
| **Generic Name**<br>Atovaquone and proguanil<br><br>**Brand Name**<br>Malarone<br><br>PD | Treatment of uncomplicated malaria due to *Plasmodium falciparum*<br><br>Sensitive to regions with chloroquine resistance<br><br>Malaria prophylaxis due to *Plasmodium falciparum* | **Usual oral dose:**<br>Prevention: 250 mg/100 mg once daily starting 1 to 2 days before entering malaria region, throughout stay, and 7 days after leaving<br><br>Treatment: 1000 mg/400 mg once daily for 3 days | • Can cause hepatic impairment and rarely hepatic failure: use with caution in patients with preexisting renal function impairment<br>• Diarrhea/vomiting can decrease the absorption of the medication: use an antiemetic or alternative therapy<br>• Administer with food or milk: if patient vomits within 1 hour after taking dose, readminister<br>• In patients who weigh more than 100 kg, treatment failure has been reported: follow up after completion of therapy to ensure cure<br>• Monitor: hepatic and renal function, cure in patients weighing more than 100 kg<br>Contraindications:<br>• Use as prophylaxis if CrCl less than 30 mL/min |

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| **Generic Name**<br>Chloroquine<br><br>**Brand Name**<br>Aralen<br>QT PD | Suppressive treatment and acute treatment of malaria<br><br>*P. vivax*, *P. malariae*, *P. ovale*, *P. falciparum*<br><br>Several regions have highly resistant strands of *P. falciparum*<br><br>Treatment of extraintestinal amebiasis | **Usual oral dose (phosphate):**<br>Chemoprophylaxis: 500 mg weekly 1 to 2 weeks before exposure, during travel, and 4 weeks after<br><br>Treatment: 1 g on day 1, then 500 mg 6 hours, 24 hours, and 48 hours after first dose<br><br>Amebiasis: 1 g daily for 2 days, then 500 mg daily for 2 to 3 weeks | • Can cause ECG changes along with QTc prolongation: use with caution in patients with preexisting QTc prolongation<br>• Can cause extrapyramidal effects that resolve after finishing therapy or treating the symptoms<br>• May can cause hematologic effects, including agranulocytosis: discontinue if severe<br>• May can cause myopathy or neuromyopathy: discontinue if weakness occurs<br>• Can cause severe ophthalmic damage, including macular degeneration: monitor closely and discontinue if signs and symptoms occur<br>• Patients with G6PD deficiency are at higher risk of hemolytic anemia<br>• Use with caution in patients with hepatic impairment, porphyria, psoriasis, and seizures due to exacerbations<br>• Chloroquine phosphate to base equivalence data are available in the package insert<br>• Monitor: ophthalmic exams at baseline and with extended use, CBC with extended use<br>• Drug interactions may require dose adjustments<br>Contraindications:<br>• History of retinal or visual changes due to 4-aminoquinoline compounds or due to other etiology |
| **Generic Name**<br>Hydroxychloroquine<br><br>**Brand Name**<br>Plaquenil<br>■ PD | Suppressive treatment and acute treatment of malaria<br><br>Treatment of systemic lupus erythematosus<br><br>Treatment of rheumatoid arthritis (RA)<br><br>Not effective against chloroquine-resistant *P. falciparum* | **Usual oral dose:**<br>Chemoprophylaxis: 400 mg once weekly starting 2 weeks before and continuing for 8 weeks after exposure<br><br>Treatment: 800 mg, then 400 mg at 6, 24, and 48 hours after first dose | • May cause cardiomyopathy with extended use<br>• May cause hematologic effects, including agranulocytosis: discontinue if severe<br>• May cause myopathy or neuromyopathy: discontinue if weakness occurs<br>• May cause severe ophthalmic damage, including loss of visual acuity: monitor closely and discontinue if signs and symptoms occur<br>• Patients with G6PD deficiency are at higher risk of hemolytic anemia<br>• Use with caution in patients with hepatic impairment, porphyria, and psoriasis, due to exacerbations<br>• Hydroxychloroquine sulfate to base (and chloroquine phosphate) equivalence data are available in the package insert<br>• Chloroquine is preferred to hydroxychloroquine<br>• Refer to CDC guidelines for alternative schedules and dosing based on infection surveillance<br>• Administer with food or milk<br>• Monitor: CBC at baseline and throughout therapy, LFTs, ophthalmic exam at baseline and every 3 months with extended use, muscle strength with extended use |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| | | | Contraindications:<br>• History of retinal or visual changes due to 4-aminoquinoline compounds<br>Associated with:<br>• Should be prescribed only by clinicians familiar with the medication (requires experienced clinician) |
| **Generic Name**<br>Mefloquine<br><br>**Brand Name**<br>Lariam<br>■ PD QT | Treatment of mild to moderate malaria infections due to *P. falciparum* and *P. vivax*<br><br>Sensitive to chloroquine-resistant *P. falciparum*<br><br>Prophylaxis against malaria | **Usual oral dose:**<br>Chemoprophylaxis:<br>250 mg once weekly beginning 1 or 2 weeks prior to exposure, continuing weekly during exposure and 4 weeks after exposure<br><br>Treatment:<br>1250 mg once | • Reports of agranulocytosis and anemia have occurred<br>• Can cause ECG changes and QTc prolongation: use with caution in patients with preexisting QTc prolongation<br>• Drug interactions may require dose adjustments<br>• Use with caution in patients with cardiovascular disease, impaired hepatic function, and seizures<br>• Administer with food and at least 8 ounces of water: if vomiting occurs 30 minutes after dose, readminister; if vomiting occurs 30 to 60 minutes after dose, administer half the dose<br>• If treating for *P. vivax*, also give an 8-aminoquinoline derivative to prevent relapse<br>• Resistance has developed in Southeast Asia: do not use mefloquine in this region<br>• Monitor: LFTs, ophthalmic exams, and for neuropsychiatric adverse events with extended use<br>• Refer to CDC guidelines for alternative schedules and dosing based on infection surveillance<br>Contraindications:<br>• Use as prophylaxis in patients with a history of seizure or major psychiatric disorder<br>Associated with:<br>• Neuropsychiatric adverse events that can outlast therapy (including but not limited to seizures and psychosis): discontinue if they occur during use |
| **Generic Name**<br>Primaquine<br><br>Primaquine phosphate<br>QT | Used to prevent relapse of *P. vivax* malaria | **Usual oral dose:** 15 mg once daily with chloroquine for 14 days | • Can cause ECG changes and QTc prolongation: use with caution in patients with preexisting QTc prolongation<br>• Can cause hematologic effects, including anemia, methemoglobinemia, and leukopenia: discontinue if signs and symptoms occur<br>• Patients with G6PD deficiency are at higher risk of hemolytic anemia<br>• Use with caution in patients with hepatic impairment, porphyria, psoriasis, and seizures due to exacerbations<br>• Primaquine base to phosphate equivalence data are available in the package insert<br>• Administer with meals to lessen gastrointestinal upset: if patient vomits within 30 minutes of taking dose, readminister |

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| | | | • May have cross-resistance with other aminoquinolines<br>• Use with caution in patients with NADH methemoglobin reductase deficiency: methemoglobinemia is more likely to occur<br>• Monitor: screen for G6PD deficiency before initiating therapy, CBC, check urine for darkening color (hematologic symptom), glucose, electrolytes, ECG in patients at high risk for QTc prolongation<br>• If hemolysis is suspected during treatment, monitor CBC, haptoglobin, peripheral smear, and urinalysis dipstick for occult blood<br>Contraindications:<br>• Acutely ill patients who may develop granulocytopenia (systemic lupus erythematosus, rheumatoid arthritis)<br>• Concurrent use of medications that can cause hemolytic anemia or bone marrow suppression<br>• Concurrent or recent use of quinacrine |
| **Generic Name**<br>Pyrimethamine<br><br>**Brand Name**<br>Daraprim<br>PD | Chemoprophylaxis of malaria<br><br>Resistance to pyrimethamine has developed worldwide<br><br>Treatment of malaria and toxoplasmosis in combination with a sulfonamide | **Usual oral dose for toxoplasmosis:**<br>50 to 75 mg once per day, in combination with sulfonamide for 1to 3 weeks | • Can cause hematologic effects, including megaloblastic anemia, thrombocytopenia, and leukopenia: monitor CBC and PLT twice weekly when treating for toxoplasmosis; discontinue if signs and symptoms occur<br>• Patients with G6PD deficiency are at higher risk of hemolytic anemia<br>• Use with caution in patients with folate deficiency, hepatic impairment, renal impairment, and seizures<br>• Administer with meals to decrease gastrointestinal upset<br>• Pyrimethamine can cause folic acid deficiency: supplement with leucovorin<br>• Monitor: CBC; CBC and platelet count twice weekly when treating for toxoplasmosis; liver and renal function tests<br>• Drug interactions may require dose adjustments<br>Contraindications:<br>• Megaloblastic anemia due to folate deficiency |
| **Generic Name**<br>Quinine<br><br>**Brand Name**<br>Qualaquin<br>▲ ■ QT | Treatment of uncomplicated chloroquine-resistant *P. falciparum* malaria with the use of other agents | **Usual oral dose:**<br>648 mg every 8 hours for 7 days; administer with tetracycline, doxycycline, or clindamycin | • Drug interactions may require dose adjustments<br>• Can cause severe hypersensitivity reactions such as SJS: discontinue if signs and symptoms occur<br>• Can cause hypoglycemia<br>• Immune-related thrombocytopenia, including hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, has been reported: usually resolves within 1 week of discontinuation<br>• Can cause QTc prolongation: use with caution in patients with preexisting arrhythmias<br>• Do not use in patients with severe hepatic or renal impairment |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
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| | | | • Do not take with antacids containing aluminum or magnesium due to decreased absorption<br>• Swallow tablet whole to avoid bitter taste<br>• Can cause false-positive results for opioids in the urine<br>• Can cause false-positive results for steroids in the urine when using Zimmerman assay<br>• Monitor: CBC, platelet count, LFTs, blood glucose, ECG, ophthalmic exam<br>• Refer to CDC guidelines for alternative schedules and dosing based on infection surveillance<br>Contraindications:<br>• Prolonged QTc interval<br>• Myasthenia gravis<br>• Optic neuritis<br>• G6PD deficiency<br>Associated with:<br>• Serious and life-threatening hematologic reactions<br>• Benefit does not outweigh risk for the treatment of nocturnal leg cramps |
| Quinidine | Refer to the Cardiovascular Agents chapter. | | |

| Miscellaneous Antiprotozoals | | | |
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| **Drug Name** | **FDA-Approved Indications** | **Adult Dosage Range** | **Precautions and Clinical Pearls** |
| **Generic Name**<br>Atovaquone<br><br>**Brand Name**<br>Mepron | Treatment of mild to moderate *Pneumocystis jirovecii* pneumonia (PCP) in patients who cannot take trimethoprim–sulfamethoxazole (TMP-SMZ)<br><br>Prophylaxis against PCP in patients who cannot use TMP-SMZ | **Usual oral dose:** 1500 mg once daily or 750 mg twice daily | • Use with caution in patients with gastrointestinal disorders: may impair absorption<br>• Use with caution in patients with hepatic impairment<br>• Must be administered with food, preferably high fat<br>• Absorption may be inadequate if patient has diarrhea/vomiting: give with an antiemetic<br>• Monitor: hepatic function tests at baseline and as needed, CD4 count for maintenance treatment in toxoplasmosis, patient's tolerability to ingest atovaquone |

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| **Generic Name**<br>Metronidazole<br><br>**Brand Name**<br>Flagyl<br>Metro<br>MetroCream<br>Metrogel<br>MetroLotion<br>Noritate<br>Nuvessa<br>Rosadan<br>Vandazole<br><br>■ ■ PD | Treatment of susceptible organisms that cause intestinal amebiasis, amebic liver abscess, anaerobic bacterial infections, bacterial septicemia, bone and joint infections, CNS infections, endocarditis, gynecologic infections, intra-abdominal infections, lower respiratory infections, skin and skin structure infections, bacterial vaginosis, and trichomoniasis *(for example: Bacteroides, Clostridium, Peptococcus, Peptostreptococcus, Fusobacterium, Eubacterium, Trichomonas vaginalis)*<br><br>Perioperative colorectal surgery prophylaxis<br><br>Topical: bacterial vaginosis and rosacea | **Usual oral dose for trichomoniasis**<br>500 mg twice daily, or may alternatively use 250 mg 3 times daily for 7 days (max oral or IV 4 g/day)<br><br>**Usual vaginal dose for bacterial vaginosis (product dependent):** One applicatorful 1 to 2 times per day for 5 days day for 1 to 5 days<br><br>**Usual topical dose:** apply 1 to 2 times per day | • May cause CNS effects including aseptic meningitis, encephalopathy, seizures, peripheral neuropathy, and optic neuropathy: avoid chronic therapy with high doses<br>• May cause leukopenia: use with caution in patients with history of blood dyscrasias<br>• Use with caution in patients with ESRD: accumulation may occur<br>• Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use<br>• IV solution should not come in contact with aluminum equipment<br>• Administer ER formulation on an empty stomach<br>• Avoid use of ER tablets in patients with severe hepatic impairment if possible<br>• Injection contains 28 mEq sodium/g: use with caution in patients with sodium-retaining states (e.g., heart failure, edema)<br>• May disrupt AST, ALT, TAG, glucose, and LDH results<br>• Monitor: CBC with differential at baseline and with extended use<br>• IV formulations are available for specific FDA approved indications including surgical prophylaxis<br>Contraindications:<br>• Use of disulfiram in the previous 2 weeks<br>• Ethanol use during therapy and 3 days after the last dose<br>Associated with:<br>• Carcinogenicity in animal data: use only if needed |
| **Generic Name**<br>Nitazoxanide<br><br>**Brand Name**<br>Alinia<br><br>PD | Treatment of diarrhea caused by *Cryptosporidium parvum* or *Giardia lamblia* | **Usual oral dose:** 500 mg every 12 hours for 3 days | • Use with caution in patients with hepatic and renal impairment<br>• Safety and efficacy have not been established in HIV-infected and immunocompromised patients<br>• Administer with food |
| **Generic Name**<br>Pentamidine | Treatment of pneumonia caused by *Pneumocystis jirovecii* (IM, IV) | **Usual parenteral dose:** IM, IV: 4 mg/kg once daily for 14 to 21 days | • May cause hypotension: monitor after infusion<br>• May cause QTc prolongation: use with caution in patients with preexisting cardiovascular disease<br>• May cause anemia, leukopenia, thrombocytopenia, pancreatitis, and SJS<br>• Use with caution in patients with diabetes: can cause abnormal glucose levels<br>• Use with caution in patients with hepatic and renal impairment, |

| Drug Name | FDA-Approved Indications | Adult Dosage Range | Precautions and Clinical Pearls |
|---|---|---|---|
| **Brand Name**<br>Nebupent<br>Pentam<br>QT | Prophylaxis against PCP in high-risk, HIV-infected patients with a history of PCP or with a CD4+ count ≤ 200/mm3 (inhalation) | **Usual inhalation dose:**<br>300 mg nebulized once every 4 weeks | hypocalcemia, and asthma (when using the nebulizer)<br>• Do not dilute with normal saline<br>• Refer to PI for specific nebulizing equipment (Respirgard II nebulizer)<br>• Pentamidine is vesicant-like: avoid extravasation<br>• Drug interactions may require dose adjustments<br>• Monitor: liver and renal function tests, blood glucose, potassium and calcium, CBC and platelets, ECG, blood pressure |
| **Generic Name**<br>Tinidazole<br><br>**Brand Name**<br>Tindamax<br>■ PD | Treatment of trichomoniasis caused by *T. vaginalis*, giardiasis caused by *G. duodenalis*, intestinal amebiasis and amebic liver abscess caused by *E. histolytica*, bacterial vaginosis caused by Bacteroides, Gardnerella vaginalis, and Prevotella in nonpregnant women | **Usual oral dose:**<br>2 g per day for 1 to 5 days<br>Duration is dependent on type and severity of infection | • May cause seizures or peripheral neuropathy<br>• Use with caution in patients with hepatic impairment or history of blood dyscrasia<br>• Can cause *C. difficile*–associated diarrhea and pseudomembranous colitis with extended use<br>• Administer with food<br>• Avoid ethanol during treatment and 3 days after to prevent a disulfiram-like reaction<br>• May interfere with AST, ALT, triglycerides, glucose, and LDH testing<br>Associated with:<br>• Carcinogenic properties; avoid unnecessary use |
| Co-trimoxazole | Refer to the Antibacterials section. | | |
| Dapsone | Refer to the Antimycobacterials section. | | |