Table 5. Serious and/or Common Adverse Reactions Associated With Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

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This table should not be considered a comprehensive list of all possible adverse reactions to each medication. For additional information, clinicians should consult other appropriate resources, such as the U.S. Food and Drug Administration prescribing information. The most serious or common adverse reactions for each drug in the table are generally listed first. For information regarding the effects of these medications on a pregnant woman and the fetus, please refer to the Special Considerations During Pregnancy section of the individual chapter in the guidelines (e.g., see Special Considerations During Pregnancy in the Herpes Simplex Virus chapter for information on the use of acyclovir during pregnancy).

Drug(s)	Adverse Reactions
Acyclovir	• Crystalluria and nephrotoxicity secondary to obstructive urolithiasis, particularly after rapid high-dose IV infusion. Risk is increased with dehydration or pre-existing renal impairment. o Administer IV fluid hydration to reduce the risk of nephrotoxicity. • Neurotoxicity with high doses (agitation, confusion, hallucination, seizure, coma), especially in people with renal impairment and/or older adults • Thrombophlebitis at peripheral IV infusion site • Nausea, vomiting, and headache
Adefovir	• Nephrotoxicity, especially in people with underlying renal insufficiency, predisposing comorbidities, or taking concomitant nephrotoxic drugs • Nausea and asthenia
Albendazole	• Rash, pruritus, and fever • Elevated transaminases • Alopecia • Nausea, vomiting, abdominal pain, headache, and dizziness • Bone marrow suppression (i.e., pancytopenia, aplastic anemia, agranulocytosis, and leukopenia) (rare) o Individuals with liver disease, including hepatic echinococcosis, appear to be at higher risk.
Amikacin	• Nephrotoxicity o Administer IV fluid hydration to reduce the risk of nephrotoxicity. • Ototoxicity, both hearing loss and vestibular toxicity, is possible. • Neuromuscular blockade, especially with myasthenia or Parkinson's disease and rapid infusion of large doses (rare)

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Drug(s)	Adverse Reactions
Amphotericin B Deoxycholate and Lipid Formulations	• Nephrotoxicity (lower incidence with liposomal formulations); irreversible nephrotoxicity is related to cumulative dose. o Administer IV fluid hydration to reduce the risk of nephrotoxicity. • Hypokalemia, hypomagnesemia, and hypocalcemia • Infusion-related reactions, including fever, chills, rigors, flank or back pain, and hypotension (lower incidence with liposomal formulations and slower infusion rates) • Thrombophlebitis • Elevated transaminases and bilirubin • Headache, nausea, vomiting, and diarrhea • Heart failure (rarely reported) • Anemia (rare)
Anidulafungin	• Refer to Echinocandins below.
Artemether/Lumefantrine	• QTc prolongation • Anemia, including delayed hemolytic anemia (rare) • Fever, chills, fatigue, arthralgia, and myalgia • Headache, dizziness, asthenia, and insomnia • Nausea, vomiting, diarrhea, abdominal pain, and anorexia • Rash and pruritus
Artesunate	• Acute renal failure requiring dialysis • Hemoglobinuria and jaundice, anemia, thrombocytopenia, neutropenia • Delayed hemolysis and immune hemolytic anemia • QTc prolongation and bradycardia • Hypersensitivity reactions (anaphylaxis) • Dizziness, nausea, and vomiting
Atovaquone	• Elevated transaminases • Rash, nausea, vomiting, abdominal pain, and diarrhea • Fever, headache, and insomnia
Atovaquone/Proguanil	• Abdominal pain, nausea, vomiting, anorexia, diarrhea, headache, asthenia, dizziness, and rash • Elevated transaminases
Azithromycin	• Ototoxicity with prolonged use or high concentrations • Elevated transaminases • Hypersensitivity reactions

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Drug(s)	Adverse Reactions
	• Nausea, vomiting, metallic taste, diarrhea, and abdominal pain • QTc prolongation
Benznidazole	• Photosensitivity and hypersensitivity reactions (including maculopapular rash, allergic dermatitis, TEN, and DRESS) • Paresthesia and peripheral neuropathy, headache, and insomnia • Bone marrow suppression • Nausea, vomiting, abdominal pain, anorexia, and weight loss
Bedaquiline	• QTc prolongation • Elevated transaminases • Nausea, vomiting, anorexia, diarrhea, elevated amylase, arthralgia, headache, and skin rash Note: Due to long medication half-life, adverse effects may persist even after discontinuation.
Bezlotoxumab	• Exacerbation of congestive heart failure • Nausea, fever, and headache • Infusion-related reactions
Brincidofovir	• Elevated transaminases and bilirubin • Nausea, vomiting, and diarrhea • Male infertility
Caspofungin	• Refer to Echinocandins below.
Chloroquine and Hydroxychloroquine	• Auditory and visual disturbances, including blurry vision. Retinal toxicity may occur with long-term use. • QTc prolongation and cardiac arrhythmias • Cardiomyopathy • Bone marrow suppression and hemolysis • Neuropsychiatric changes, including extrapyramidal reactions, suicidal behavior, and convulsive seizures • Hypersensitivity reactions (including TEN, SJS, and EM) • Severe hypoglycemia which may require adjustment of antidiabetic medications • Photosensitivity, pruritus, skin pigmentation, and exacerbation of psoriasis • Dizziness, headache, nausea, vomiting, diarrhea, anorexia, abdominal pain, and hepatitis • Neuromyopathy (may occur with long-term use) (rare)
Cidofovir	• Nephrotoxicity, proteinuria, azotemia, proximal tubular dysfunction (normoglycemic glycosuria, hypophosphatemia), and metabolic acidosis (including Fanconi's syndrome) o Administer IV fluid hydration and oral probenecid to reduce the risk for nephrotoxicity.

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Drug(s)	Adverse Reactions
	• Neutropenia and anemia • Ocular hypotony and anterior uveitis/iritis • Nausea, vomiting, abdominal pain, anorexia, and diarrhea • Asthenia, fever, headache, and alopecia • Side effects most likely related to coadministration with probenecid: rash, nausea, vomiting, anorexia, and gout exacerbation.
Ciprofloxacin	• Refer to Fluoroquinolones below.
Clarithromycin	• Elevated transaminases and hepatotoxicity (rare) • Ototoxicity, including hearing loss and tinnitus, with high doses or prolonged use • QTc prolongation • Increased risk of cardiac complications or death in people with heart disease • Diarrhea • Headache, nausea, vomiting, diarrhea, abdominal cramps, and dysgeusia
Clindamycin	• Diarrhea, including *C. difficile*–associated diarrhea and pseudomembranous colitis • Metallic taste (with IV infusion), thrombophlebitis, and arrhythmia with rapid IV infusion • Hypersensitivity reactions (including SJS and TEN) • Nausea, vomiting, and abdominal pain • Elevated transaminases
Clotrimazole (Troche)	• Nausea, vomiting, anorexia, and metallic taste
Cycloserine	• Neuropsychiatric toxicities, including convulsions, psychosis, somnolence, confusion, inability to concentrate, hyperreflexia, headache, tremor, vertigo, paresis, dysarthria, depression (with suicidal ideation), peripheral neuropathy, and seizures (particularly with higher doses and in people with history of chronic alcoholism) o Administer with pyridoxine. • Hypersensitivity reactions (including SJS), allergic dermatitis, and rash
Dapsone	• Methemoglobinemia, hemolytic anemia, neutropenia, and agranulocytosis o Do not use in people with G6PD deficiency. o Risk may be increased with concomitant use of folic acid antagonists (e.g., pyrimethamine). • Rash, fever • Sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, and hemolysis) • Phototoxicity and severe cutaneous reactions (including SJS and TEN) • Drug-induced lupus erythematosus

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Drug(s)	Adverse Reactions
	• Hepatotoxicity and nephrotic syndrome • Peripheral neuropathy • Nausea and anorexia
Doxycycline	• Pill-induced esophagitis/esophageal ulceration • Intracranial hypertension • Photosensitivity and skin hyperpigmentation • Thrombophlebitis (with IV infusion) • Nausea and vomiting
Echinocandins (anidulafungin, caspofungin, micafungin)	• Histamine-related infusion reactions (flushing, rash, pruritus, hypotension, and dyspnea) and thrombophlebitis • Elevated transaminases and hepatotoxicity • Diarrhea, nausea, vomiting, fever, and headache • Hemolysis (micafungin) (rare)
Emtricitabine	• Headache, nausea, and diarrhea • Skin hyperpigmentation and rash (palms and soles)
Entecavir	• Headache, fatigue, dizziness, and nausea • Lactic acidosis
Ethambutol	• Optic neuritis (dose- and duration-dependent) and peripheral neuropathy • Headache, nausea, vomiting, anorexia, abdominal pain, and hyperuricemia/gout flare • Hypersensitivity reactions
Ethionamide	• Dose-dependent GI side effects, including nausea, vomiting, anorexia, diarrhea, abdominal pain, and metallic taste (dose titration may alleviate some symptoms) • Hepatotoxicity • Dizziness, drowsiness, confusion, clumsiness, visual disturbances, depression, peripheral neuropathy, and postural hypotension o Administer with pyridoxine. • Photosensitivity and severe cutaneous reactions (including SJS, TEN, and DRESS) • Endocrine side effects, including hypothyroidism (with or without goiter), gynecomastia, acne, alopecia, menstrual irregularities, impotence, and hypoglycemia
Famciclovir	• Nephrotoxicity (in people with underlying renal disease) • Headache, nausea, vomiting, and diarrhea
Fidaxomicin	• Nausea, vomiting, and abdominal pain

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Drug(s)	Adverse Reactions
Flucytosine	• Concentration-dependent (>100 mcg/mL) bone marrow suppression (anemia, neutropenia, agranulocytosis, and thrombocytopenia) • Elevated transaminases • Diarrhea, nausea, vomiting, and headache • Rash, pruritus, and photosensitivity
Fluconazole	• Hepatotoxicity • QTc prolongation • Alopecia (with doses ≥400 mg/day for ≥2 months) and dry skin • Nausea, vomiting, diarrhea, and abdominal pain
Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin)	• Restlessness, insomnia, nightmares, confusion, anxiety, paranoia, tremors, seizures, hallucinations, depression, suicidal thoughts, and attempted and completed suicide • Tendonitis and tendon rupture (associated with age over 60, concurrent corticosteroids, diabetes, and kidney, heart, and lung transplant) • Diarrhea, including *C. difficile*–associated diarrhea and colitis • QTc prolongation • Photosensitivity/phototoxicity • Anemia, thrombocytopenia, and leukopenia • Arthralgia and myalgia • Peripheral neuropathy and retinal detachment • Hyper- and hypoglycemia, including hypoglycemic coma • Nausea, diarrhea, bloating, headache, dizziness, and malaise • Vasculitis • Aortic dissection (rare) • Elevated transaminases • Interstitial nephritis (rare) • Severe cutaneous reactions (including SJS and TEN) (rare)
Foscarnet	• Nephrotoxicity and electrolyte imbalances (e.g., hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia) o Administer IV fluid hydration to reduce the risk of nephrotoxicity. • Paresthesia and seizure (associated with electrolyte imbalances) • Anemia • Nausea, vomiting, anorexia, and headache • Genital ulceration • Thrombophlebitis

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Drug(s)	Adverse Reactions
Fumagillin (Investigational)	• Nausea, vomiting, diarrhea, anorexia, and abdominal cramps • Thrombocytopenia, anemia, and neutropenia • Vertigo
Ganciclovir	• Neutropenia, thrombocytopenia, anemia, and pancytopenia • Nephrotoxicity • Thrombophlebitis • Nausea, vomiting, fever, asthenia, and hyperhidrosis
Glecaprevir/Pibrentasvir	• Risk of hepatitis B virus reactivation • Hepatic decompensation/failure in people with advanced liver disease • Mild headache, fatigue, nausea, and diarrhea • Altered glucose tolerance in diabetic patients
Ibrexafungerp	• Diarrhea, nausea, abdominal pain, vomiting, and headache
Isavuconazonium Sulfate (Isavuconazole)	• Hepatotoxicity and cholelithiasis • Infusion-related reactions (hypotension, dyspnea, chills, dizziness, paresthesia, and hypoesthesia) • Hypersensitivity reactions (including SJS) • Shortening of QT interval • Nausea, vomiting, diarrhea, headache, dyspnea, and cough • Hypokalemia
Isoniazid	• Hepatotoxicity or asymptomatic elevation in aminotransferase enzymes • Peripheral neuropathy, paresthesia, seizures, psychosis (rare), and optic neuritis o Administering with pyridoxine may prevent or reduce these adverse effects. • Nausea, diarrhea, and flushing • Arthralgia and lupus-like syndrome • Hypersensitivity reactions (including TEN and DRESS) (rare)
Itraconazole	• New-onset or worsening heart failure, edema, adrenal insufficiency, and hypokalemia • QTc prolongation • Elevated transaminases and hepatotoxicity
Lamivudine	• Nausea and vomiting
Levofloxacin	• Refer to Fluoroquinolones above.

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Drug(s)	Adverse Reactions
Linezolid	• Anemia, neutropenia, and thrombocytopenia (especially with treatment lasting longer than 2–4 weeks, renal insufficiency, or elevated trough concentrations) • Peripheral neuropathy and optic neuritis with long-term therapy • Nausea, vomiting, diarrhea, and headache • Serotonin syndrome (rare) • Seizure (in people with a history of seizure or with risk factors for seizure) (rare) • Lactic acidosis, hypoglycemia, and hyponatremia (rare) • Rhabdomyolysis
Mefloquine	• Depression, psychosis, anxiety, agitation, dizziness, headache, insomnia, and abnormal dreams • QTc prolongation and arrhythmias (extrasystole and sinus bradycardia) • Agranulocytosis and aplastic anemia • Nausea, vomiting, diarrhea, and epigastric pain Note: Due to long medication half-life, side effects may persist even after discontinuation.
Micafungin	• Refer to Echinocandins above.
Miconazole Buccal Tablets	• Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, and headache • Local reactions (e.g., oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, swelling, and dry mouth) • Hypersensitivity reactions (may occur in people with known hypersensitivity reaction to milk product concentrate)
Miltefosine	• Nephrotoxicity and elevated transaminases and bilirubin • Retinal degeneration • Leukocytosis and thrombocytopenia • Impaired fertility, scrotal pain, and impaired ejaculation • Nausea, vomiting, diarrhea, anorexia, headache, and motion sickness • Severe cutaneous reactions (including SJS)
Moxifloxacin	• Refer to Fluoroquinolones above.
Nifurtimox	• People with a history of brain injury, seizures, psychiatric disease, and serious behavioral alterations may experience worsening of their conditions. • Vomiting, nausea, decreased appetite, weight loss, abdominal pain, headache, fever, polyneuropathy, insomnia, restlessness, tremors, dizziness, and vertigo • Carcinogenic and teratogenic potential and impaired fertility • Hypersensitivity reactions with hypotension, angioedema, dyspnea, pruritus, rash, or other severe skin reactions

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Drug(s)	Adverse Reactions
Nitazoxanide	• Nausea, vomiting, diarrhea, abdominal pain, headache, and chromaturia
Nystatin (Oral Preparations)	• Unpleasant taste, nausea, vomiting, anorexia, and diarrhea
Omadacycline	• Nausea, vomiting, and diarrhea • Elevated transaminases • Infusion site reactions
Oteseconazole	• Nausea, diarrhea, and headache
Paromomycin	• Nausea, vomiting, abdominal cramps, anorexia, rash, and headache • Nephrotoxicity (rare) o Inflammatory bowel disease and renal insufficiency may increase risk.
Penicillin G	All Penicillin G Preparations • Hypersensitivity (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, and drug fever • Jarisch-Herxheimer reaction when used for syphilis (occurs most frequently in persons with early syphilis, high non-treponemal antibody titers, and prior penicillin treatment) Benzathine Penicillin G • IM injection-site reactions (pain and erythema), procaine neuropsychiatric reactions (with high dose), and neurovascular damage (due to inadvertent intravascular instead of IM injection) Aqueous Crystalline Penicillin G (IV) • Thrombophlebitis • Neurotoxicity at high doses—especially in people with renal dysfunction—and hyperkalemia or hypernatremia at high doses (depending on formulation)
Pentamidine	IV Administration • Nephrotoxicity, azotemia • Infusion-related hypotension and thrombophlebitis • QTc prolongation, arrhythmias (including Torsades de pointes), and electrolyte abnormalities • Hypoglycemia, hyperglycemia, and diabetes mellitus • Hepatotoxicity and GI intolerance • Leukopenia and thrombocytopenia • Rash • Pancreatitis (rare) Aerosolized Therapy • Bronchospasm, cough, dyspnea, tachypnea, and metallic taste

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Drug(s)	Adverse Reactions
Posaconazole	IV or PO Administration • Hepatotoxicity • QTc prolongation and hypokalemia • Pseudohyperaldosteronism (hypokalemia and hypertension) • Nausea, vomiting, diarrhea, abdominal pain, and headache IV Infusion • Thrombophlebitis, SBECD accumulation, and worsening renal function with IV formulation (especially in people with eGFR <50 mL/min per package labeling, but observational studies with IV voriconazole suggest that this may not be a concern)
Pretomanid	Adverse Events Reported When Used in Combination With Other Antituberculosis Medications • Nausea, vomiting, headache, and diarrhea • Elevated transaminases • Peripheral and optic neuropathy, myelosuppression, and lactic acidosis (with linezolid) • QTc prolongation (with bedaquiline) Other • Dose-related increase in serum creatinine without change in GFR
Primaquine	• Methemoglobinemia, hemolytic anemia (use with caution in people with mild-moderate G6PD deficiency; do not use if severe G6PD deficiency), leukopenia, and neutropenia • QTc prolongation • Abdominal cramps, nausea, vomiting, and dizziness
Pyrazinamide	• Hepatotoxicity • Polyarthralgia and myalgia • Hyperuricemia/gout flare • Thrombocytopenia and sideroblastic anemia • Nausea, vomiting, flushing, rash, and photosensitivity
Pyrimethamine	• Neutropenia, anemia, thrombocytopenia, and megaloblastic anemia o Administer with leucovorin to reduce the risk of bone marrow suppression. • Anorexia, nausea, vomiting, and rash
Quinine	• QTc prolongation and cardiac arrhythmias • Cinchonism (tinnitus, vertigo, and blurred vision) • Hemolytic anemia (especially in patients with G6PD deficiency), thrombocytopenia, and agranulocytosis • Vision abnormalities (e.g., photophobia, altered color perception, and blindness)

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Drug(s)	Adverse Reactions
	• Hypersensitivity reactions (including SJS and TEN) • Hypoglycemia • Headache, nausea, vomiting, and diarrhea
Rifabutin	• Concentration-dependent uveitis, neutropenia, and thrombocytopenia • Arthralgia • Hepatotoxicity • Rash • Nausea, vomiting, abdominal pain, diarrhea, and anorexia • Red-orange discoloration of body fluids (e.g., urine, sweat, saliva)
Rifampin	• Hepatotoxicity (cholestatic hepatitis) • Thrombocytopenia and hemolytic anemia • Renal failure • Hypersensitivity reactions with flu-like syndrome • Interstitial pulmonary disease • Nausea, vomiting, anorexia, abdominal pain, flatulence, diarrhea, headache, confusion, flushing, and rash • Red-orange discoloration of body fluids
Rifapentine	• Hepatotoxicity • Anemia, neutropenia, and lymphopenia • Hypersensitivity reactions, including flu-like symptoms • Arthralgia • Rash and pruritis • Nausea, vomiting, diarrhea, and anorexia • Red-orange discoloration of body fluids
Sofosbuvir/Velpatasvir	• Risk of hepatitis B virus reactivation • Headache, fatigue, and anemia (associated with ribavirin coadministration) • Altered glucose tolerance in diabetic persons
Streptomycin	• Neurotoxicity, including irreversible ototoxicity (both hearing loss and vestibular toxicity) • Nephrotoxicity • Neuromuscular blockade and respiratory paralysis (associated with rapid infusion of large aminoglycoside doses)
Sulfadiazine	• Severe cutaneous reactions (including SJS, EM, and TEN) and photosensitivity • Anemia, neutropenia, agranulocytosis, and thrombocytopenia

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Drug(s)	Adverse Reactions
	• Crystalluria (nephrolithiasis, urolithiasis) and nephrotoxicity o Administer oral or IV fluid hydration to reduce the risk of nephrotoxicity. • Hepatotoxicity • Drug fever • Peripheral neuritis, tinnitus, hallucinations, seizures (rare), vertigo, and insomnia • Nausea, vomiting, diarrhea, and headache
Tafenoquine	• Decreased hemoglobin as a result of methemoglobinemia and hemolytic anemia o Do not use in people with G6PD deficiency; may cause harm to fetuses and breastfeeding infants who are G6PD-deficient. • Psychiatric adverse reactions (in people with history of psychiatric illness) • Hypersensitivity reactions (angioedema and urticaria) • Visual disturbances • Dizziness, nausea, vomiting, and headache
Tecovirimat	IV or PO Administration • Headache, nausea, abdominal pain, and vomiting IV Infusion • Infusion site pain, swelling, erythema, and extravasation • Contains hydroxypropyl-β-cyclodextrin, which may accumulate in people with renal impairment and has the potential to cause renal toxicity
Tedizolid	• Nausea, vomiting, and diarrhea • Headache and dizziness • Infusion- or injection-related reactions • Thrombocytopenia
Tenofovir Disoproxil Fumarate	• Renal insufficiency and Fanconi syndrome (proximal renal tubulopathy with hypophosphatemia, hypouricemia, proteinuria, and normoglycemic glycosuria) • Decreased bone mineral density • Nausea and vomiting
Tenofovir Alafenamide	• Lower incidence of renal or bone toxicities than with tenofovir disoproxil fumarate
Trimethoprim-Sulfamethoxazole	• Cutaneous reactions (in some cases SJS, EM, and TEN) and photosensitivity • Anemia, neutropenia, agranulocytosis, and thrombocytopenia • Hepatotoxicity • Dose-dependent increase in serum creatinine (without change in eGFR), interstitial nephritis, crystalluria (in people with inadequate hydration), and hyperkalemia (with high-dose TMP) o Encourage oral hydration when using oral TMP-SMX.

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Drug(s)	Adverse Reactions
	• Hypoglycemia and hyponatremia • Drug fever • Nausea and vomiting • Aseptic meningitis and pancreatitis (rare)
Valacyclovir	• Neurotoxicity (e.g., agitation, confusion, hallucination, seizure, coma) with high doses, especially in people with renal impairment • Nephrotoxicity o Encourage oral fluid hydration to reduce the risk of nephrotoxicity. • Nausea, vomiting, abdominal pain, and headache
Valganciclovir	• Bone marrow suppression • Confusion, fever, and tremor • Nephrotoxicity o Encourage oral fluid hydration to reduce the risk of nephrotoxicity. • Carcinogenic and teratogenic potential and impaired fertility • Nausea, vomiting, and diarrhea
Voriconazole	• Visual disturbances (e.g., abnormal vision, color vision change, and/or photophobia) • Optic neuritis (associated with >28 days treatment) • Headache, delirium, hallucination, peripheral neuropathy (rare), and encephalopathy (associated with trough >5.5 mcg/mL) • Hepatotoxicity • QTc prolongation • Photosensitivity • Voriconazole-associated cutaneous squamous cell carcinoma (with long-term use) • Fluorosis and periostitis with high dose and/or prolonged use • Fever, nausea, vomiting, chills, tachycardia, and peripheral edema • Nail changes and alopecia (with long-term use) • SBECD accumulation with IV formulation and worsening renal function (especially in people with eGFR <50 mL/min per package labeling, but observational studies suggest that this may not be a concern)

Key: DRESS = drug reaction with eosinophilia and systemic symptoms; eGFR = estimated glomerular filtration rate; EM = erythema multiforme; G6PD = glucose-6-phosphate dehydrogenase; GFR = glomerular filtration rate; GI = gastrointestinal; IM = intramuscular; IV = intravenous; PO = oral; QTc = QT corrected for heart rate; SBECD = sulfobutylether cyclodextrin; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; TMP = trimethoprim; TMP-SMX = trimethoprim-sulfamethoxazole