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. For persons of childbearing potential, please refer to Table 7. Summary of Pregnancy for information regarding adverse effect potential of these medications 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.
	 Administer IV fluid hydration to reduce the risk for nephrotoxicity.
	Neurotoxicity with high doses (agitation, confusion, hallucination, seizure, coma), especially in patients with renal impairment and/or older patients
	Thrombophlebitis at peripheral IV infusion site
	Nausea, vomiting, and headache
Adefovir	Nephrotoxicity, especially in patients with underlying renal insufficiency, predisposing comorbidities, or taking concomitant nephrotoxic drugs
	Nausea and asthenia
Albendazole	Hepatotoxicity
	Reversible alopecia
	Nausea, vomiting, headache, and dizziness
	Bone marrow suppression (i.e., pancytopenia, aplastic anemia, agranulocytosis, and leukopenia) (rare)
	o Patients with liver disease, including hepatic echinococcosis, appear to be at higher risk.
Amikacin	Nephrotoxicity
	 Administer IV fluid hydration to reduce the risk for nephrotoxicity.
	Ototoxicity, both hearing loss and vestibular toxicity, are possible.
	Neuromuscular blockade, especially with myasthenia or Parkinson's disease and rapid infusion of large doses (rare)
Amphotericin B Deoxycholate	Nephrotoxicity (lower incidence with liposomal formulations)
and Lipid Formulations	 Administer IV fluid hydration to reduce the risk for nephrotoxicity.
	Hypokalemia, hypomagnesemia, and hypocalcemia
	Infusion-related reactions, including fever, chills, rigors, flank or back pain, and hypotension (lower incidence with liposomal formulations)
	Thrombophlebitis

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Drug(s)	Adverse Reactions
	Transaminase and bilirubin elevations
	Headache, nausea, vomiting, and diarrhea
	Heart failure (rarely reported)
	Anemia (rare)
Anidulafungin	Refer to the row on Echinocandins.
Artemether/Lumefantrine	QTc prolongation
	Fever, chills, fatigue, arthralgia, and myalgia
	Headache, dizziness, asthenia, and insomnia
	Nausea, vomiting, diarrhea, abdominal pain, and anorexia
	Rash and pruritus
	Delayed hemolytic anemia (rare)
Artesunate	Acute renal failure requiring dialysis
	Hemoglobinuria and jaundice
	Post-treatment hemolysis that may require transfusion
	QTc prolongation and bradycardia
	Hypersensitivity reactions (anaphylaxis)
	Dizziness, nausea, and vomiting
Atovaquone	Hepatotoxicity
	Rash, nausea, vomiting, and diarrhea
	Fever, headache, and insomnia
Atovaquone/Proguanil	Abdominal pain, nausea, vomiting, anorexia, diarrhea, headache, asthenia, dizziness, and rash
	Reversible transaminase elevations
Azithromycin	Ototoxicity with prolonged use
	Hepatotoxicity
	Hypersensitivity reactions
	Nausea, vomiting, diarrhea, and abdominal pain
	QTc prolongation
Benznidazole	Photosensitivity and hypersensitivity reactions (including allergic dermatitis, TEN, and DRESS)
	Paresthesia and peripheral neuropathy, headache, and insomnia
	Bone marrow suppression
	Embryo-fetal toxicity
	Nausea, vomiting, abdominal pain, anorexia, and weight loss

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Drug(s)	Adverse Reactions
Bedaquiline	QTc prolongation
	Hepatotoxicity
	Nausea, vomiting, anorexia, diarrhea, elevated amylase, arthralgia, headache, and skin rash
Bezlotoxumab	Exacerbation of congestive heart failure
	Nausea, pyrexia, and headache
Brincidofovir	Elevations in hepatic transaminases and bilirubin
	Nausea, vomiting, and diarrhea
	Embryo-fetal toxicity, male infertility
Caspofungin	Refer to the row on Echinocandins.
Chloroquine and	Auditory and visual disturbances, including blurry vision. Retinal toxicity may occur with long-term use.
Hydroxychloroquine	QTc prolongation
	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
	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)
	Administer IV fluid hydration and oral probenecid to reduce the risk for nephrotoxicity.
	Neutropenia and anemia
	Ocular hypotony and anterior uveitis/iritis
	Possibly carcinogenic and teratogenic; may cause hypospermia
	Gastrointestinal intolerance and diarrhea
	Asthenia, fever, headache, and alopecia
	Side effects most likely related to co-administration with probenecid are rash, nausea, vomiting, anorexia, and gout exacerbation.
Ciprofloxacin	Refer to the row on Fluoroquinolones.
Clarithromycin	Hepatotoxicity
	Ototoxicity, including reversible hearing loss and tinnitus, with high doses or prolonged use

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Drug(s)	Adverse Reactions
	QTc prolongation
	Increased risk of cardiac complications or death in patients with heart disease
	Diarrhea
	Headache, nausea, vomiting, diarrhea, abdominal cramps, and dysgeusia
Clindamycin	Diarrhea, including <i>C. difficile</i> —associated diarrhea and colitis
	Metallic taste (with IV infusion), thrombophlebitis, and arrhythmia with rapid IV infusion
	Hypersensitivity reactions (including SJS and TEN)
	Nausea, vomiting, abdominal pain, and abnormal liver function tests
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 patients with history of chronic alcoholism)
	 Administer with pyridoxine.
	Hypersensitivity reactions (including SJS), allergic dermatitis, and rash
Dapsone	Methemoglobinemia, hemolytic anemia, neutropenia, and agranulocytosis
	 Do not use in patients with moderate to severe G6PD deficiency.
	Sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, and hemolysis)
	Phototoxicity and severe cutaneous reactions (including SJS and TEN)
	Drug-induced lupus erythematosus
	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,	Histamine-related infusion reactions (flushing, rash, pruritus, hypotension, and dyspnea) and thrombophlebitis
Micafungin)	Hypersensitivity reactions (including anaphylaxis and anaphylactoid reaction)
	Abnormal liver enzymes and hepatotoxicity
	Hypokalemia
	Embryo-fetal toxicity

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Drug(s)	Adverse Reactions
	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
Ethambutol	Optic neuritis (dose- and duration-dependent) and peripheral neuropathy
	Headache, nausea, vomiting, anorexia, abdominal pain, and hyperuricemia/gout flare
Ethionamide	Postural hypotension, hepatotoxicity, hypothyroidism (with or without goiter), and hypoglycemia
	Dizziness, drowsiness, confusion, clumsiness, visual disturbances, and depression
	o Administer with pyridoxine.
	Dose-dependent gastrointestinal side effects, including nausea, vomiting, anorexia, diarrhea, abdominal pain, and metallic taste
	Photosensitivity and severe cutaneous reactions (including SJS, TEN, and DRESS)
	Gynecomastia, acne, hair loss, and impotence
Famciclovir	Nephrotoxicity (in patients with underlying renal disease)
	Headache, nausea, vomiting, and diarrhea
Fidaxomicin	Nausea, vomiting, and abdominal pain
Flucytosine	Concentration-dependent (>100 mcg/mL) bone marrow suppression (anemia, neutropenia, agranulocytosis, and thrombocytopenia)
	Hepatotoxicity
	Diarrhea, nausea, vomiting, and headache
	Rash, pruritus, and photosensitivity
Fluconazole	Hepatotoxicity, nausea, vomiting, diarrhea, and abdominal pain
	QTc prolongation
	Reversible alopecia (with doses ≥400 mg/day for >2 months)
Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin)	Restlessness, insomnia, nightmares, confusion, anxiety, paranoia, tremors, seizure, 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 <i>C. difficile</i> —associated diarrhea and colitis
	QTc prolongation
	Photosensitivity/phototoxicity
	Anemia, thrombocytopenia, and leukopenia

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Drug(s)	Adverse Reactions
	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)
	Transaminase elevations and interstitial nephritis (rare)
	Severe cutaneous reactions (including SJS and TEN) (rare)
Foscarnet	Nephrotoxicity and electrolyte imbalances (e.g., hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia)
	 Administer IV fluid hydration to reduce the risk for nephrotoxicity.
	Paresthesia and seizure (associated with electrolyte imbalances)
	Anemia
	Nausea, vomiting, anorexia, and headache
	Genital ulceration
	Thrombophlebitis
Ganciclovir	Neutropenia, thrombocytopenia, anemia, and pancytopenia
	Carcinogenic and teratogenic potential and impaired fertility
	Nephrotoxicity
	Neuropathy
	Thrombophlebitis
Glecaprevir/Pibrentasvir	Risk of hepatitis B virus reactivation
	Hepatic decompensation/failure in patients with advanced liver disease
	Mild headache, fatigue, nausea, and diarrhea
	Altered glucose tolerance in diabetic patients
Interferon-Alfa and	Neuropsychiatric effects (e.g., depression, suicidal ideation)
Peginterferon-Alfa	Neutropenia, anemia, and thrombocytopenia
	Flu-like syndrome (e.g., fever, headache, fatigue, myalgia)
	Hepatitis exacerbations, thyroid dysfunction, and alopecia
	Nausea, anorexia, diarrhea, and weight loss
	 Development or exacerbation of autoimmune diseases and ocular effects (e.g., retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots)
	 Ischemic and hemorrhagic cerebrovascular events, cardiovascular and pulmonary effects, hyper- and hypoglycemia, diabetes, severe infection, and colitis

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Drug(s)	Adverse Reactions
	Hypersensitivity reactions
Isavuconazonium Sulfate	Hepatotoxicity and cholelithiasis
(Isavuconazole)	Infusion-related reactions (hypotension, dyspnea, chills, dizziness, paresthesia, and hypoesthesia)
	Hypersensitivity reactions (including SJS)
	Embryo-fetal toxicity
	Shortening of QT interval
	Nausea, vomiting, diarrhea, headache, hypokalemia, dyspnea, and cough
Isoniazid	Hepatotoxicity and asymptomatic elevation in aminotransferase enzymes
	Peripheral neuropathy, paresthesia, seizures, and optic neuritis
	Administer with pyridoxine
	Nausea, diarrhea, and flushing
	Arthralgia and lupus-like syndrome
	Psychosis (rare)
	Hypersensitivity reactions (including TEN and DRESS) (rare)
Itraconazole	Congestive heart failure, edema, and hypokalemia
	QTc prolongation
	Hepatotoxicity
	Hearing loss
	Neuropathy
	Gynecomastia
	Nausea, vomiting, diarrhea, and abdominal pain
Lamivudine	Nausea and vomiting
Levofloxacin	Refer to the row on Fluoroquinolones.
Linezolid	Anemia, neutropenia, and thrombocytopenia (especially with treatment lasting longer than 2–4 weeks and renal insufficiency)
	Peripheral neuropathy and optic neuritis with long-term therapy
	Nausea, vomiting, diarrhea, and headache
	Serotonin syndrome (rare)
	Seizure (in patients with a history of seizure or with risk factors for seizure) (rare)
	Lactic acidosis, hypoglycemia, and hyponatremia (rare)
Mefloquine	Depression, psychosis, anxiety, agitation, dizziness, headache, insomnia, and abnormal dreams
	QTc prolongation and arrhythmias (extrasystole and sinus bradycardia)

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Drug(s)	Adverse Reactions
	Agranulocytosis and aplastic anemia
	Nausea, vomiting, diarrhea, and epigastric pain
Micafungin	Refer to the row on Echinocandins.
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 reaction (may occur in patients with known hypersensitivity reaction to milk product concentrate)
Miltefosine	Nephrotoxicity and elevated transaminases and bilirubin
	Retinal degeneration
	Leukocytosis and thrombocytopenia
	Embryo-fetal toxicity and impaired fertility, scrotal pain, and impaired ejaculation
	Nausea, vomiting, diarrhea, anorexia, headache, and motion sickness
	Severe cutaneous reactions (including SJS)
Moxifloxacin	Refer to the row on Fluoroquinolones.
Nifurtimox	Patients with a history of brain injury, seizures, psychiatric disease, and serious behavioral alterations may experience worsening of their conditions.
	 Vomiting, abdominal pain, headache, decreased appetite, weight loss, nausea, pyrexia, rash, polyneuropathy, insomnia, dizziness, and vertigo
	Carcinogenic and teratogenic potential and impaired fertility
	Hypersensitivity reactions with hypotension, angioedema, dyspnea, pruritus, rash or other severe skin reactions
Nitazoxanide	Nausea, vomiting, diarrhea, abdominal pain, headache, and chromaturia
Nystatin (Oral Preparations)	Unpleasant taste, nausea, vomiting, anorexia, and diarrhea
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

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Drug(s)	Adverse Reactions
	 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 patients with renal dysfunction—and hyperkalemia or hypernatremia at high doses (depending on formulation)
Pentamidine	Nephrotoxicity, 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
	Embryotoxic
	• Rash
	Pancreatitis (rare)
	Aerosolized Therapy
	Bronchospasm, cough, dyspnea, tachypnea, and metallic taste
Posaconazole	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 patients with eGFR <50 mL/min per package labeling, but observational studies with IV voriconazole suggest that this may not be a concern)
Primaquine	 Methemoglobinemia, hemolytic anemia (use with caution in patients 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, thrombocytopenia, and megaloblastic anemia
	o Administer with leucovorin.

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Drug(s)	Adverse Reactions
	Anorexia, vomiting, and rash
Quinine	QTc prolongation and cardiac arrythmias
	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)
	Hypersensitivity reactions (including SJS and TEN)
	Hypoglycemia
	Headache, nausea, vomiting, and diarrhea
Rifabutin	Uveitis (concentration-dependent)
	Neutropenia and thrombocytopenia
	Arthralgia
	Hepatotoxicity
	• Rash
	Nausea, vomiting, abdominal pain, diarrhea, and anorexia
	Red-orange discoloration of body fluids
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, and flushing, rash
	Red-orange discoloration of body fluids
Rifapentine	Hepatotoxicity
	Anemia, neutropenia, and lymphopenia
	Hypersensitivity reactions
	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 co-administration)
	Altered glucose tolerance in diabetic patients

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Drug(s)	Adverse Reactions
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
	Crystalluria (nephrolithiasis, urolithiasis) and nephrotoxicity
	Hepatotoxicity
	Drug fever
	Peripheral neuritis, tinnitus, vertigo, and insomnia
	Nausea, vomiting, and headache
Tafenoquine	Decreased hemoglobin and methemoglobinemia and hemolytic anemia
	 Do not use in patients with G6PD deficiency; may cause harm to fetuses and breastfeeding infants who are G6PD deficient.
	Psychiatric adverse reactions (in patients with history of psychiatric illness)
	Hypersensitivity reactions (angioedema and urticaria)
	Visual disturbances
	Dizziness, nausea, vomiting, and headache
Tecovirimat	Headache, nausea, abdominal pain, and vomiting
	IV formulation
	Infusion site pain, swelling, erythema, and extravasation
	Contains hydroxypropyl-β-cyclodextrin, which may accumulate in patients with renal impairment and has the potential to cause renal toxicity
Tenofovir disoproxil fumarate	Renal insufficiency and Fanconi syndrome (proximal renal tubulopathy with hypophosphatemia, hypouricemia, proteinuria, and normoglycemic glycosuria)
	Decrease in bone mineral density
	Nausea and vomiting
Tenofovir alafenamide	Headache, abdominal pain, fatigue, and nausea
	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 GFR), interstitial nephritis, crystalluria (in patients with inadequate hydration), and hyperkalemia (with high-dose TMP)

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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 patients with renal impairment
	Nephrotoxicity
	Nausea, vomiting, abdominal pain, and headache
Valganciclovir	Bone marrow suppression
	Confusion, pyrexia, and tremor
	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
	Embryo-fetal toxicity
	Nail changes and alopecia (with long-term use)
	• SBECD accumulation with IV formulation and worsening renal function (especially in patients 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; QTc = QT corrected for heart rate; SBECD = sulfobutylether cyclodextrin; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; TMP = trimethoprim