With Dialysis		STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT											
			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.5–1	6	0.5 q6–8h	0.5 q8–12h	0.25–0.5 q12h[g]	0.25–0.5 q12h		1–10			Minimal	3
		0.5–2	8–12	8–12	0.5–1 q12h	0.5–1 q24h	0.5–1 q24h		12			40	
		4	8	8	2 q8–12h	1 q12h	1 q12h						
		5 mg/kg/day	5 mg/kg/day in 2–4 doses	2.5–3.8 mg/kg/ day in 2 doses	1.5–2.5 mg/kg/ day in 1–2 doses	1.5 mg/kg q36h	1.5 mg/kg q24–48h		50	18		25–30	
		1.25 mg/kg q12h	12	12[m]	12[m]	12[m]	12[m]	Minimal					

TABLE 54.21 Antiinfective Agent Pharmacology: Aminoglycosides

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval Oral	Dose (g)/Interval Parenteral	Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
Amikacin[b]	7.5 mg/kg IM	21	832		15–20 mg/kg/day in 1–3 doses[c]	15–20 mg/kg		15–22.5 mg/kg/day in 2–3 doses[c]	15 mg/kg q24–48h	15–17.5 mg/kg q24h	2–3	30–86
	7.5 mg/kg IV[f]	38										
Gentamicin[g]	1 mg/kg IM	4–7.6	113–423		3–7 mg/kg/day in 1–3 doses[c]	3–7 mg/kg		6–7.5 mg/kg/day in 3 doses[c]	4–5 mg/kg q24–48h[c,h]	4–5 mg/kg/q24–36h[c,h]	2–3	24–60
	1 mg/kg IV[i]	4–7.6										
Kanamycin[b] (1)	7.5 mg/kg IM	22			15 mg/kg/day in 1–3 doses[c]	1.5		15 mg/kg/day in 2–3 doses[c]			2–4	27–80
	7.5 mg/kg IV[f]	22										
Neomycin[j] (3)	4 g PO	2.5–6.1		1 PO q6h		4 PO	100 mg/kg/day in 4 doses				2–3	12–24
Streptomycin[k]	0.5 IM	5–12	400 ≥1000		1–2 g/day in 2–4 doses	2					2–3	Up to 110
	1 IM	25–50										
Tobramycin[g]	1 mg/kg IM	4–6	75–100		3–7 mg/kg/day in 1–3 doses[c]	3–7 mg/kg		6–7.5 mg/kg/day in 2–3 doses[c]	4–5 mg/kg q24–48h[c,h]	4–5 mg/kg/day q24–36h[c,h]	2–3	5–70
	1 mg/kg IV[f]	4–6										

[a]Inflamed meninges.
[b]Desired concentrations of amikacin and kanamycin are peak 15–30 μg/mL and trough <5–10 μg/mL. Peak targets generally occur 2 h after a 30–minute infusion using a high-dose, extended-interval approach (total daily dose administered once daily with therapeutic drug monitoring). Divided daily dosing of aminoglycosides is generally reserved for synergy indications (i.e., endocarditis) and special populations including pediatrics and those with renal impairment.
[c]The dosing strategy for aminoglycosides involves the use of ideal (lean) body weight (IBW) for dosage calculation. In obese patients, this approach would result in serum aminoglycoside concentrations less than expected. Alternative dosing recommendations have been proposed that account for the change in drug distribution volume with obesity: (1) IBW + 40% of excess weight, defined as total body weight (TBW) minus IBW (*J Infect Dis.* 1978;138:499–505); (2) IBW + 58% of excess weight (TBW – IBW) (*Clin Pharmacol Ther.* 1979; 26:508); (3) IBW + 38% of excess weight (TBW – IBW) (*Am J Hosp Pharm.* 1980;37:519–522). Extended-interval dosing, where the total daily dose is administered in a single dose, has become increasingly common in clinical practice as a method to optimize pharmacodynamics and improve safety.
[d]Dosing at CrCl ≤10 mL/min should be assisted with serum concentrations.
[e]Specified dose should be administered after a dialysis session to supplement drug clearance during dialysis.
[f]Infused over 30–60 min.
[g]Desired concentrations of gentamicin and tobramycin are peak 4–10 μg/mL and trough <1–2 μg/mL. Peak targets generally occur 2 h after a 30–minute infusion using a high-dose, extended-interval approach (total daily dose administered once daily with therapeutic drug monitoring). Divided daily dosing of aminoglycosides is generally reserved for synergy indications (i.e., endocarditis) and special populations including pediatrics and those with renal impairment.
[h]Lower end of dosing range if weight <2 kg and higher end if >2 kg.
[i]Infused over 2 h.
[j]Parenteral administration of neomycin is no longer recommended.
[k]Desired concentrations: peak 5–25 μg/mL; trough <5 μg/mL.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HD,* hemodialysis; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/Serum (%)	Aqueous Humor/ Serum (%)
		5–7.5 mg/kg	8	8–12	12–48	48[d]	2.5–3.75 mg/kg[e] after HD	2 mg/kg/day	15–24	20		30	Minimal
		1–1.7 mg/kg	8	8–12	12–48	48[d]	1.0–1.7 mg/kg[e] after HD	0.6 mg/kg/day	10–30	30–40		30–60	Minimal
		7.5 mg/kg	8–12	8–12	12–48	≥48[d]	4–5 mg/kg[e] after HD	3.75 mg/kg/day	43	50	35		Minimal
		1 PO	6	6									Minimal
		0.5–1	12	12	24–72	72–96[d]	0.5[e] after HD		20	10–40	<25	40–300	Minimal
		1–1.7 mg/kg	8	8–12	12–48	48[d]	1 mg/kg[e] after HD	0.6 mg/kg/day	14–23	50		10–20	18

TABLE 54.22 Antiinfective Agent Pharmacology: Tetracyclines, Glycylcyclines, and Folate Antagonists

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)					>80	<10
				Oral	Parenteral		Oral	Parenteral	Up to 1 wk	1–4 wk		
Tetracyclines and Glycylcyclines												
Demeclocycline[b] (60–80)	0.15 PO 0.3 PO	0.9–1.2 1.5–1.7		0.6/day in 2–4 doses		0.6	7–13 mg/kg/day in 2–4 doses[c]		Not recommended[c]	Not recommended[c]	10–17	42–68
Doxycycline[b] (90–100)	0.1 PO 0.1 IV[d]	1.5–2.1 2.5		0.1 q12h	0.1 q12h	0.2	2–4 mg/kg/day in 1–2 doses[c]	2–4 mg/kg/day in 1–2 doses[c]	Not recommended[c]	Not recommended[c]	14–24	18–30
Minocycline[b] (90–100)	0.2 PO 0.2 IV	2–3.5 2.52–6.63		0.1 q12h	0.1 q12h	0.2	4 mg/kg/day in 2 doses[c]	4 mg/kg/day in 2 doses[c]	Not recommended[c]	Not recommended[c]	11–26	12–30
Tetracycline[b] (75–80)	0.25 PO 0.5 PO 0.5 PO[e]	1.5–2.2 3–4.3 2–5		0.25–0.5 q6h		2	25–50 mg/kg/day in 2–4 doses[c]		Not recommended[c]	Not recommended[c]	6–12	57–120
Tigecycline	0.1 IV	1.45			0.1 × 1, then 0.05 q12h	0.1–0.2		1.2 mg/kg q12h[c,f]	Not recommended[c]	Not recommended[c]	27–42	27–42
Folate Antagonists												
Trimethoprim-sulfamethoxazole[g] (85–90)	0.16/0.8 PO[h] 0.16–0.8 IV[h]	1.72/68 8.8/105.6		0.16/0.8 q12h	10–20 mg/kg/day in 2–3 doses[i]	1.2[i]	6–12 mg/kg/day in 2 doses[i]	6–12 mg/kg/day in 2 doses[i]	Not recommended		8–15/7–12	24/22–50
Trimethoprim (80)	0.1 PO 0.2 PO	1 2	30–60	0.1 q12h		0.2	4–10 mg/kg/day in 2 doses[m]				8–15	24
Sulfadiazine[g] (70–90)	3 PO	50		2–4 g/day in 3–6 doses		4	120–150 mg/kg/day in 4–6 doses[n]	Not recommended	Not recommended		17	34
Dapsone	0.2 PO	0.1–7[h]		0.05–0.1 q24h		0.1	1–2 mg/kg/day in 1–2 doses				20–30	

[a]Inflamed meninges.
[b]All tetracyclines should be given 1 h before or 2 h after meals.
[c]The tetracyclines cause a brown discoloration of the teeth and may retard the growth of bone in the human fetus and children. The American Academy of Pediatrics recommends that tetracyclines be used only in children who are 8 years of age or older.
[d]Infused over 60 min.
[e]At steady state.
[f]Not FDA approved for use in pediatric patients. Dose is recommended based on limited pharmacokinetic data for patients 8–12 years of age when no alternative is available.
[g]Decreased rate and/or extent of absorption when given with food.
[h]At steady state.
[i]Based on the trimethoprim component.
[j]Uninflamed meninges.
[k]Amniotic fluid concentrations (μg/mL).
[l]Specified dose should be administered after a dialysis session to supplement drug clearance during dialysis.
[m]Not approved for children <6 months old.
[n]In children 2 mo or older.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HD,* hemodialysis; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.15–0.3	6–12	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended	Minimal		70	200–3200	10–30
18–30		0.1	12	12	12	12	0.1 g q12h	0.1 g q12h	26		30–40	200–3200	10–13
		0.1	12	12	12	12	0.1 g q12h	0.1 g q12h		77	8–26	200–3200	17
		0.25–0.5	6	6	8–12	24			7	60–70	25–150	200–3200	9–11
27–42		0.1 × 1, then 0.05	12	12	12	12	12	12				> 100	
		0.16/0.8	12	12	12–24	Avoid	0.16/0.8 q48h	0.16/0.8 q48h	50/40[j]	80/50[k]	125/10	100–200/ 40–70	10–45/ 20–30
		5 mg/kg IV[i]	6–8	8	8–12	12	5–10 mg/kg after HD[i,l]						
		0.1	12	12	18–24	Avoid			30–50	70–100	100	100	10
		0.5–1	4–6						50–80	≥50			
		0.05–0.1	24								69		

TABLE 54.23 Antiinfective Agent Pharmacology: Macrolides, Azalides, Lincosamides, and Miscellaneous Antibacterial Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)			
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)		With Dialysis	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval Oral	Dose (g)/Interval Parenteral	Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10	HD	PD
Macrolides and Azalides														
Azithromycin[b] (35–40)	0.5 PO 0.5 IV 0.3 PO	0.09–0.44 3.63 0.5	8.64–26.8	0.25–0.5 q24h	0.25–0.5 q24h	0.5	5–12 mg/kg/day	10–12 mg/kg/day[c]	10 mg/kg/day	10 mg/kg/day	68	68	68	68
Clarithromycin (50–55)	0.25 PO[d] 0.5 PO[d] 0.5 PO[d]	1 2–3 1[e]		0.25–0.5 q12h		1	7.5 mg/kg q12h				5–7			
Erythromycin base[f,g]	0.25 PO	0.1–2		0.25–0.5 q6h		2	30–50 mg/kg/day in 3–4 doses				1.5–2	6		
Erythromycin stearate[g]	0.25 PO	0.1–2		0.25–0.5 q6h		2	30–50 mg/kg/day in 3–4 doses				1.5–2	6		
Erythromycin ethyl succinate[g]	0.4 PO	0.1–2		0.4 q6h		4	30–50 mg/kg/day in 3–4 doses				1.5–2	6		
Erythromycin lactobionate[h,i]	0.2 IV	3–4			0.5–1 q6h	4		15–20 mg/kg/day in 4 doses			1.5–2	6		
Fidaxomicin[j]	0.2 PO	0.0052		0.2 q12h		0.4					11	11	11	11
Lincosamides														
Clindamycin[f] (90)	0.15 PO 0.6 IV[m]	1.9–3.9 10		0.15–0.45 q6–8h	0.3–0.9 q6–8h	12.7 PO/IV	10–40 mg/kg/day in 3–4 doses	20–40 mg/kg/day in 3–4 doses	5 mg/kg q8–12h[k,l]	5 mg/kg/day q6–8h[k,l]	2–3	2–3.5		
Lincomycin[f] (20–30)	0.5 PO 0.6 IM 0.6 IV[n]	1.8–5.3 9.3–18.5 15.9–20.9			0.6–1 q8–12h	8		10–20 mg/kg/day in 2–3 doses	Not indicated	Not indicated	4–6.4	10		
Miscellaneous Antibacterial Agents														
Chloramphenicol[o] (75–90)	1 PO 1 PO[d] 1 IV	11 18 4.9–12			0.25–1 q6h	4			25 mg/kg/day in 4 doses[p]	50 mg/kg/day in 4 doses[q]	1.5–4.1	3–7		3–7
Metronidazole[f] (80)	0.25 PO 7.5 mg/kg[d]	4.6–6.5 26		0.25–0.75 q8h	0.5 q6–8h	4	30–50 mg/kg/day in 3 doses	22.5–40 mg/kg/day in 3 doses	7.5 mg/kg/day q8–12h[l]	7.5 mg/kg/day q6–12h[l]	6–14	8–15		8–15
Rifaximin[j]	0.2 PO q8h	0.00081		0.2–0.55 q8–12h		1.65					5.6–6			
Secnidazole	2 PO	45.4		2 × 1		2								

[a]Inflamed meninges.
[b]Decreased extent of absorption of capsule formulation only when given with food.
[c]No studies to support; extrapolated from adult conversion.
[d]At steady state.
[e]Of 14-hydroxyclarithromycin (active metabolite).
[f]Denotes decreased rate and/or extent of absorption when given with food.
[g]Erythromycin and its derivatives have varying degrees of bioavailability (18%–45%).
[h]Oral erythromycin therapy should replace IV therapy as soon as possible.
[i]Because of the local irritative effects, the drug must not be administered rapidly by direct IV injection (IV push).
[j]Negligible oral bioavailability.
[k]When IV clindamycin is given to neonates and infants, organ system functions should be monitored.
[l]Lower end of dosing range if weight <2 kg and higher end if >2 kg.
[m]Over 20 min.
[n]When given over 2 h.
[o]Chloramphenicol dosage should be administered to maintain plasma concentrations of 10–25 mg/L for peak and 5–10 mg/L for trough.
[p]Age <2 wk.
[q]Age >2 wk.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HD,* hemodialysis; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT											
	For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/Serum (%)[a]	Newborn Serum/Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/Serum (%)	Aqueous Humor/ Serum (%)
0.25–0.5	24	24	24	24	24	24			>100		
0.25–0.5	12	12	12–24	24			Minimal		30	7000	
0.25–0.5	6	6	6	6	0.25–0.5 q6h	0.25–0.5 q6h	2–13	5–20	50		
0.25–0.5	6	6	6	6	0.25–0.5 q6h	0.25–0.5 q6h	2–13	5–20	50		
0.4	6	6	6	6	0.4 q6h	0.4 q6h	2–13	5–20	50		
0.5–1	6	6	6	6	0.5–1 q6h	0.5–1 q6h	2–13	5–20	50		
0.2	12	12	12	12	12	12					
0.15–0.45 PO 0.6–0.9 IV	6 8	6 8	6 8	6 8	0.15–0.3 PO q6h 0.6–0.9 IV q8h	0.15–0.3 PO q6h 0.6–0.9 IV q8	Minimal	46	38–50	250–300	
0.6–1 IV	8–12	8–12	8–12	24–36			18	25	13	250–400	8.75
0.25–1 IV	6	6	6	6	0.25–1 IV q6h	0.25–1 IV q6h	45–89	30–80	100	100	33–50
0.25–0.75 PO 0.5 IV	8 6–8	8 6–8	8 6–8	8 6–8	0.25–0.75 PO q8h 0.5 IV q6–8h	0.25–0.75 PO q8h 0.5 IV q6–8h	≥100	97	100		
0.2–0.55	8–12										

TABLE 54.24 Antiinfective Agent Pharmacology: Glycopeptides, Lipopeptides, Lipoglycopeptides, Polypeptides, Oxazolidinones, and Streptogramins

	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
Drug (Oral Absorption, %)	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval Oral	Dose (g)/Interval Parenteral	Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
Dalbavancin[b]	1 IV 1.5 IV	287 423			1.5 × 1	1.5					204	
Daptomycin	4 mg/kg IV 6 mg/kg IV	57.8 93.9			4–6 mg/kg q24h	8–12 mg/kg[c]		5–10 mg/kg q24h[d]			9.4	27.8
Linezolid (100)	0.4 PO 0.6 PO 0.6 IV	8.1 12.7 15.1		0.4–0.6 q12h	0.4–0.6 q12h	1.2	10 mg/kg q8h	10 mg/kg q8h	10 mg/kg q8–12h[e]	10 mg/kg q8h	5.5	7.1
Oritavancin	1.2 IV	138			1.2 × 1	1.2					245	
Quinupristin/dalfopristin	7 mg/kg IV	3/4			7.5 mg/kg q8–12h	22.5 mg/kg/day		7.5 mg/kg q12h[g]			8.6	
Tedizolid (100)	0.2 PO 0.2 IV	2 2.3									12	12
Telavancin	7.5 mg/kg IV 15 mg/kg IV	87.5 186			10 mg/kg q24h	10 mg/kg					6–8	
Vancomycin[i,j]	1 IV	25		0.125–0.5 q6h	15 mg/kg q8–12h	1 PO, 2 IV	40 mg/kg/day in 4 doses[k]	40–60 mg/kg/day in 3–4 doses	7.5–30 mg/kg/day in 1–2 doses[l]	7.5–30 mg/kg/day in 1–2 doses[l]	4–6	44.1–406.4

[a]Inflamed meninges.
[b]Doses are approved either as a single dose or as a two-dose regimen divided on days 1 and 8. The divided regimens are as follows: 1500 mg = 1000 mg on day 1, 500 mg day 8; 1125 mg = 750 mg on day 1, 375 mg on day 8.
[c]Some experts recommend the use of daptomycin 8–12 mg/kg in patients with infective endocarditis, persistent MRSA bacteremia, vancomycin-resistant enterococcal infections, or vancomycin treatment failures in adults. Alternatively, an empirical fixed daily dose of 750 mg may be optimal in critically ill patients, whereas doses >1000 mg/day are likely to increase the probability of skeletal muscle toxicity without significantly increasing the probability of effect.
[d]Doses are recommended for ages 1–17 years for the treatment of cSSSI. Higher doses per unit body weight are recommend for younger patients.
[e]Lower end of dosing range if weight <2 kg and higher end if >2 kg.
[f]Oritavancin has not been studied in severe renal impairment (CrCl < 30 mL/min).
[g]Children >12 years of age.
[h]Use is not recommended in patients with CrCl <50 mL/min unless benefit outweighs risk owing to increased mortality in this subpopulation in a trial of telavancin for nosocomial pneumonia.
[i]Negligible oral bioavailability.
[j]Vancomycin dosing should ideally occur with therapeutic drug monitoring to achieve a target AUC/MIC of 400. Although monitoring of trough levels (target 10–20 μg/mL) as a surrogate for AUC is currently the most common strategy in the clinical setting, this practice likely leads to overexposure in an important proportion of patients. The most rigorous monitoring strategy to optimize safety and efficacy involves obtaining two levels (peak and trough) and calculating the AUC to target values of 400–600.
[k]Not to exceed 2 g/day.
[l]Dosing recommended by the American Academy of Pediatrics is based on neonatal serum creatinine as follows: <0.7 mg/dL = 15 mg/kg q12h; 0.7–0.9 mg/dL = 20 mg/kg q24h; 1–1.2 mg/dL = 15 mg/kg q24h; 1.3–1.6 mg/dL. = 10 mg/kg q24h; >1.6 mg/dL = 15 mg/kg q48h.
[m]Refer to the Matzke nomogram (*Antimicrobial Agents Chemother*. 1984;25:433–437) for more precise recommendations for empirical renal dosing of vancomycin. Therapeutic drug monitoring should occur for safety and efficacy in most patients, but is essential in patients with renal impairment.
[n]Initial doses of 20–25 mg/kg are recommended, with further dosing based on therapeutic drug monitoring. Vancomycin doses in hemodialysis are frequently administered thrice weekly with the last hour or after the dialysis run.
[o]Specified dose should be administered after a dialysis session to supplement drug clearance during dialysis.
AUC, Area under the concentration-time curve; *CrCl,* creatinine clearance; *CSF,* cerebrospinal fluid; *MIC,* minimal inhibitory concentration; *cSSSI,* complicated skin and skin structure infection; *HD,* hemodialysis; MRSA, methicillin-resistant *Staphylococcus aureus*; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/Serum (%)	Aqueous Humor/ Serum (%)
		1.5 × 1	1.5 × 1	1.5 × 1	1.125–1.5 × 1	1.125 × 1	1.125 × 1						
29.8		4–6 mg/kg	24	24	24–48	48	4–6 mg/kg q48h	4–6 mg/kg q48h					
		0.4–0.6	12	12	12	12	0.4–0.6 q12h	0.4–0.6 q12h	20				
		1.2 × 1	1.2 × 1	1.2 × 1	1.2 × 1[f]								
		7.5 mg/kg	8–12	8–12	8–12	8–12	7.5 mg/kg q8–12h	7.5 mg/kg q8–12h					
		0.2 PO/IV	24	24	24	24	0.4 q24h						
		10 mg/kg	24	24	7.5 mg/kg q24[h]								
		15 mg/kg[m]	8–12	12–18	18–48	Dose by levels[n]	0.25–1[o] after HD[n]	0.5 q48–96h[n]	7.21			50	Minimal

TABLE 54.25 Antiinfective Agent Pharmacology: Fluoroquinolones and Urinary Antiinfectives

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)						
				Oral	Parenteral		Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
Fluoroquinolones												
Ciprofloxacin[b] (50–85)	0.5 PO	1.6–2.9	350	0.5–0.75 q12h	0.4 q8–12h	1.5 PO	10–20 mg/kg q12h[c]	6–10 mg/kg q8–12h[c]	Not recommended	Not recommended	3–5	5–10
	0.75 PO	2.5–4.3										
	0.4 IV[f]	4.6				1.2 IV						
Delafloxacin (58.8)	0.45 PO	7.17		0.45 q12h	0.3 q12h	0.9 PO					4.2–8.5	14–15
	0.3 IV	8.94				0.6 IV					3.7[g]	
Gemifloxacin (71)	0.32 PO	1.48		0.32 q24h		0.32					6.65	
Levofloxacin (99)	0.5 PO	5.7		0.5–0.75 q24h	0.5–0.75 q24h	1	8 mg/kg q12h[i]	8 mg/kg 12h[i]	Not recommended	Not recommended	6–8	35
	0.75 PO	7.1										
	0.5 IV[f]	6.2										
Moxifloxacin (90)	0.4 PO	3.1		0.4 q24h	0.4 q24h	0.4					9–16	
	0.4 IV	3.9										
Ofloxacin[b] (85–100)	0.4 PO	2.9–5.6	200	0.2–0.4 q12h		0.8					4–8	16.9–28.4
	0.2 PO	1.5–2.7										
	0.4 IV[f]	4										
Urinary Antiinfectives												
Fosfomycin (37)	3 PO	26.1	706	3 × 1 dose		3					5.7	40–50
Methenamine hippurate[k]	1 PO		40 (formaldehyde)	1 q12h[l]		2	0.5–1 q12h[l]	Not recommended	Not recommended		3–6	
Methenamine mandelate[k]	1 PO	70–100 μmol/L	~50 (formaldehyde)	1 q6h[l]		4	0.5–1 q6h[l]	Not recommended	Not recommended		3–6	
Nitrofurantoin (40–94)[n]	0.1 PO	<2	50–150	0.05–0.1 q6–12h[o]		0.4	5–7 mg/kg/day q6h	Not recommended	Not recommended		0.3	1

[a]Inflamed meninges.
[b]Decreased rate and/or extent of absorption when given with food.
[c]Dose should not exceed the adult dose. Routine use in children is not recommended.
[d]3.2 h during dialysis/5.8 h in between sessions.
[e]Case report.
[f]Infused over 60 min.
[g]Multiple dose PO, single dose IV.
[h]Delafloxacin has not been studied with CrCl <15 mL/min. Recommended dose adjustments for the IV formulation occur for CrCl 15–30 mL/min.
[i]FDA-approved pediatric use is plague in children >6 mo of age. Weight-based dose should not exceed 250 mg/dose in children <50 kg.
[j]8–12 h during dialysis/13–48 h between sessions.
[k]Usually coadministered with an acidifying agent to convert the methenamine salts in urine to ammonia and bactericidal formaldehyde (pH <5.5). Mandelic acid and hippuric acid are mildly antiseptic and contribute to urine acidification.
[l]Use primarily for the prevention of urinary tract infections.
[m]Ineffective urinary concentrations expected with compromised renal function.
[n]Bioavailability is variable but generally sufficient for urinary activity.
[o]Nitrofurantoin is available in two formulations: macrocrystals and microcrystals. The macrocrystalline formulation is administered twice daily, whereas the microcrystalline formulation must be administered four times daily.
[p]Nitrofurantoin accumulates in the serum of patients with renal impairment, which may lead to systemic toxicity. The labeling states that this medication should not be used at CrCl <60 mL/min; however, recent data suggest that it may used until CrCl <30 mL/min.
[q]Although only small amounts of nitrofurantoin have been detected in breast milk, the drug could cause hemolytic anemia in a glucose-6-phosphate dehydrogenase–deficient infant exposed in this manner.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *FDA,* US Food and Drug Administration; *HD,* hemodialysis; *PD,* peritoneal dialysis.

With Dialysis		STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT					Dosage With Dialysis		Body Fluid Concentrations				
			For CrCl Ranges (mL/min)										
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
3.2/5.8[d]		0.5–0.75 PO	12	12	0.25–0.5 q12h	0.25–0.5 q18–24h	0.25–0.5 q24h	0.25–0.5 q24h	11–46		400	2800–4500	3–22[e]
		0.4 IV	8–12	8–12	12–24	18–24	0.2–0.4 q24h	0.2–0.4 q24h					
		0.45 PO	12	12	12[h]								
		0.3 IV	12	12	0.2 q12h[h]								
		0.32	24	24	0.16 q24h	0.16 q24h	0.16 q24h	0.16 q24h					
		0.5–0.75 PO/IV	24	24	24–48	0.25–0.5 q48h	0.25–0.5 q48h	0.25–0.5 q48h	15		100		
		0.4	24	24	24	24	24	24					
8–12/ 13–48[j]		0.2–0.4 PO	12	12	24	0.1–0.2 q24h	0.2 × 1, then 0.1 q24h	0.2 × 1, then 0.1 q24h	28–87		96–112	210–1886	
40–50		3	× 1	× 1	× 1								
		1	12	12	Avoid[m]								
		1	6	6	Avoid[m]					50	70–100		
		0.05–0.1[o]	6–12	6–12	6–12[m,p]					100	<25[q]	200–400	

TABLE 54.26 Antiinfective Agent Pharmacology: Antimycobacterial Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)			
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)		With Dialysis	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)								
				Oral	Parenteral		Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10	HD	PD
Aminosalicylic acid (60–65)	4 PO	76–104		8–12 g/day in 2–3 doses		12	200–300 mg/kg/day in 2–4 doses				1	23		
Bedaquiline[b]	0.4 PO	3		0.4 q24h for 2 wk, then 0.2 thrice weekly		0.4					5.5 mo	5.5 mo		
Capreomycin[c]	1 IM	20–47			0.75–1 IM/IV q24h[d]	1		15–30 mg/kg/day q24h[e]			4–6	29.4–55.5		
Clofazimine[b] (45–70)	0.1 PO[f]	0.76		0.1–0.2 q24h		0.2					8 days, 70 days[g]			
Cycloserine[h] (70–90)	0.25 PO	10		0.25–0.5 q12h[i]		1	10–15 mg/kg/day in 1–2 doses[e]				10–25			
Ethambutol (75–80)	25 mg/kg PO	2–5		15 mg/kg q24h		15 mg/kg	15–20 mg/kg q24h[e]				3.3	≥7		
Ethionamide (80)	1 PO	20		0.5–0.75 q24[i]		1	15–20 mg/kg/day[j] q24h[e]				3	9		
Isoniazid[k,l]	7 mg/kg PO	4.5, 1[m]		0.3 q24h	0.3 IM q24h	0.3	10–2 mg/kg/day in 1–2 doses	15 mg/kg/q24h			0.5–4	2–10		
Pyrazinamide	0.5 PO	9–12		15–30 mg/kg q24h		2	15–30 mg/kg/day in 1–2 doses[e]				10–16			
Rifabutin (≥20)	0.3 PO	0.375		0.3 q24h		0.3	4–18.5 mg/kg q24h[n]				16–69			
Rifampin (100)	0.6 PO	7		0.6 q24h	0.6 q24h	0.6	10–20 mg/kg/day in 1–2 doses				2–5	2–5	Minimal change	
	0.6 IV[o]	17.5												
Rifapentine (70)	0.6 PO	15.05		0.6 twice weekly		0.6					13.19			
Streptomycin	1 IM	25–50	≥1000		0.75–1 IM/IV q24h[d]	1		20–40 mg/kg/day q24h			2–3	100		

[a]Inflamed meninges.
[b]Should be taken with food.
[c]Pharmacokinetics similar to streptomycin.
[d]Dose is 15 mg/kg/day (max 1 g). Dose is reduced to 10 mg/kg/day (max 750 mg) in patients older than 59 years. Dosing is generally 5–7 days out of the week until 2–4 mo after culture conversion, then 2–3 times per week.
[e]Not FDA approved for use in pediatric patients.
[f]In leprosy patients.
[g]8-day serum half-life, 70-day tissue half-life.
[h]Patients are frequently unable to tolerate full dosing, and serum concentrations can be useful to assess exposure (target 20–35 μg/mL).
[i]Recommended dose is 15 mg/kg/day, generally administered as 500–700 mg/day divided in two doses.
[j]Limited evidence suggests that 20 mg/kg daily given as a single dose in children is more likely to produce cerebrospinal fluid concentrations exceeding the minimal inhibitory concentration of 2.5 μg/mL for *Mycobacterium tuberculosis*.
[k]Decreased rate and/or extent of absorption when given with food.
[l]To minimize risk of polyneuritis from isoniazid-induced pyridoxine deficiency, pyridoxine (15–50 mg) is often given concurrently.
[m]4.5 μg/mL in slow acetylators, 1.0 μg/mL in rapid acetylators.
[n]Dose varies significantly by age group; see manufacturer's recommendations before prescribing.
[o]Infused over 30 min.
[p]Desirable serum concentrations: peak, 5–25 μg/mL; trough, <5 μg/mL.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *FDA,* US Food and Drug Administration; *HD,* hemodialysis; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT

	For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
Usual Adult Dose (g)	**>80**	**80–50**	**50–10**	**<10 (Anuric)**	**HD (g)**	**PD (g)**	**CSF/ Serum (%)[a]**	**Newborn Serum/ Maternal Serum (%)**	**Breast Milk/ Maternal Serum (%)**	**Bile/ Serum (%)**	**Aqueous Humor/ Serum (%)**
4	8–12	8–12	12	12	4 q12h		10–50				
0.4, then 0.2	24, then thrice weekly	24, then thrice weekly	24, then thrice weekly	24, then thrice weekly	0.4 q24h for 2 wk, then 0.2 thrice weekly	0.4 q24h for 2 wk, then 0.2 thrice weekly					
0.75–1[d]	24	24	12–15 mg/kg 2–3 times weekly	12–15 mg/kg 2–3 times weekly	12–15 mg/kg 2–3 times weekly					Minimal	
0.1	24	24	24	24	24	24					
0.25–0.5[h]	12	12	0.25–0.5 q24h	0.25 q24h	0.25 q24h	0.25 q24h	80–100	100	72		
15 mg/kg	24	24	15–25 mg/kg thrice weekly	15–25 mg/kg thrice weekly	15–25 mg/kg thrice weekly after HD	15–25 mg/kg thrice weekly	25–50	~100			
0.5–0.75[i]	24	24	0.25–0.5 q24h	0.25–0.5 q24h	0.25–0.5 q24h	0.25–0.5 q24h	100				
0.3 PO/IM	24	24	24	24	0.3 q24h	0.3 q24h	100	High	100		
15–30 mg/kg	24	24	25–35 mg/kg thrice weekly	25–35 mg/kg thrice weekly	25–35 mg/kg thrice weekly	25–35 mg/kg thrice weekly	100				
0.3	24	24	0.15 q24h	0.15 q24	0.15 q24h	0.15 q24h					
0.6 PO/IV	24	24	24	24	24	24	10–20	33	20–60	10,000	
0.6	Twice weekly	Twice weekly									
1[p]	24	24	12–15 mg/kg 2–3 times weekly	12–15 mg/kg 2–3 times weekly	12–15 mg/kg 2–3 times weekly		20	10–40	<25	40–300	

TABLE 54.27 Antiinfective Agent Pharmacology: Antifungal Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)						
				Oral	Parenteral		Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
Polyenes												
Amphotericin B deoxycholate	0.03 IV[b] 0.05 IV[b]	1 2			0.25–1 mg/kg q24h[c,d]	1 mg/kg[e]		1–1.5 mg/kg q24–48h[c]	1 mg/kg q24h[c]	1 mg/kg q24h[c]	≥24, 15 days[f]	≥24, 15 days[f]
Amphotericin B lipid complex	5 mg/kg	1.7			5 mg/kg q24h	5 mg/kg		5 mg/kg q24h	Not recommended	Not recommedned		
Amphotericin B liposomal	5 mg/kg IV	57.6			3–5 mg/kg q24h	3–5 mg/kg		3–5 mg/kg q24h	Not recommended	Not recommended	100–153	
Nystatin (0)	All doses PO	Not detectable		0.4–1 MU q8h		3 MU	0.4–0.6 MU q6h		0.1–0.2 MU q6h	0.1–0.2 MU q6h		
Echinocandins												
Anidulafungin	0.1 IV	7.2			0.1–0.2 × 1, then 0.05–0.1 q24h	0.1		1.5–3 mg/kg ×1, then 0.75–1.5 mg/kg q24h[g]			26–50	26–50
Caspofungin	0.05 IV	8.7			0.07 × 1, then 0.05 q24h	0.05		70 mg/m^2 × 1, then 50 mg/m^2 q24h			9–11	9–11
Micafungin	0.1 IV	8.17			0.1–0.15 q24h	0.15		2–10 mg/kg q24h[h]			15	15
Azoles												
Fluconazole (≥90)	0.4 PO 0.1 IV[i]	6.72 3.86– 4.96		0.2–0.4 q24h	0.2–0.4 q24h	0.8	3–12 mg/kg q24h	3–12 mg/kg q24h			20–50	48
Isavuconazonium (98)	0.372 PO	7.499		0.372 q8h × 2 days, then 0.372 q24h	0.372 q8h × 2 days, then 0.372 q24h	0.372					130	
Itraconazole (99.8)[j,k]	0.2 PO[l]	0.23, 0.35[m1]		0.2 q12h		0.4					21–60[m2]	
Ketoconazole[k]	0.2 PO	4.2		0.2–0.4 q24h		0.4	3.3–6.6 mg/kg q24h				8	8
Posaconazole (54)[n]	0.2 PO[o] 0.3 PO[p]	0.512 1.580		0.2 q8h[o] 0.3 q24h[p]		0.8 0.3					35	35
Voriconazole[q] (96)	0.2 PO[r] 3 mg/kg IV[r]	2.08 3.06		0.4 q12h × 1 day, then 0.2 q12h	6 mg/kg q12h × 1 day, then 4 mg/kg q12h	8 mg/kg	9 mg/kg q12h[s]	9 mg/kg q12h × 1 day, then 8 mg/kg q12h[s]			6	
Allylamine												
Terbinafine (80)	0.25 PO	1		0.25–0.5 q24h		0.5	0.0675–0.25 q24h[u]				22–30	
Miscellaneous Antifungals												
Flucytosine[q,v] (75–90)	2 PO	30-–45		25 mg/kg q6h		150 mg/kg	50–150 mg/kg/day in 4 doses				3-–6	30-–250

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.25–1 mg/kg	24	24	24	24	0.25–1 mg/kg q24h	0.25–1 mg/kg q24h	3	50			25
		5 mg/kg	24	24	24	24	5 mg/kg q24h	5 mg/kg q24h					
		3–5 mg/kg	24	24	24	24	3–5 mg/kg q24h	3–5 mg/kg q24h					
		0.4–1 MU	8	8	8	8	0.4–1 MU q8h	0.4–1 MU q8h					
26–50	26–50	0.05–0.1	24	24	24	24	0.1–0.2 × 1, then 0.05–0.1 q24h	0.1–0.2 × 1, then 0.05–0.1 q24h					
9–11		0.05	24	24	24	24	0.07 × 1, then 0.05 q24h	0.07 × 1, then 0.05 q24h					
		0.1–0.15	24	24	24	24	0.1–0.15 q24h	0.1–0.15 q24h	Undetectable				Low
	71	0.2–0.4 IV/PO	24	24	0.1–0.2 q24h	0.1–0.2 q24h	0.1–0.2 q24h	0.1–0.2 q24h	50–94		85		
		0.372 IV/PO	24	24	24	24	0.372 q8h × 2 days, then 0.372 q24h	0.372 q8h × 2 days, then 0.372 q24h					
		0.2	12	12	12	12	0.2 q12h	0.2 q12h	<10				
		0.2–0.4	24	24	24	24	0.2–0.4 q24h	0.2–0.4 q24h	Minimal			Minimal	~10
35	35	0.2[o]	8	8	8	8	0.2 q8h[o]	0.2 q8h[o]					
		0.3[p]	24	24	24	24	0.3 q24h[p]	0.3 q24h[p]					
		0.2	12	12	12[t]	12[t]	12[t]	12[t]	42–67				
		4 mg/kg	12	12	12	12	12	12					
		0.25–0.5	24	24							Unsafe		
		25 mg/kg	6	6	12–-24	24–-48	25–-50 mg/kg q48–-72h	25–-50 mg/kg q48–-72h	60–-100				

Continued

TABLE 54.27 Antiinfective Agent Pharmacology: Antifungal Agents—cont'd

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
				Oral	Parenteral							
Griseofulvin (50[w],> 50[x])	0.5 PO[w]	0.4–2		0.5–1 q24h[v]		1	10–20 mg/kg/day in 2 doses[v]				24	24
	0.25 PO[x]	0.4–2		0.375–0.75 q24h[w]		0.75	5–15 mg/kg q24h[w]					

[a]Inflamed meninges.
[b]Infused over several hours.
[c]A test dose of 1 mg infused over 15 min is often given to assess febrile reactions before proceeding to higher doses.
[d]Should be administered by slow infusion; rapid IV infusion should be avoided because potentially serious adverse effects (e.g., hypotension, hypokalemia, arrhythmias, shock) may occur.
[e]Or 1.5 mg/kg every other day.
[f]Plasma half-life, terminal half-life.
[g]Experience in children is limited. Not FDA approved for pediatric patients.
[h]Higher doses need for patients younger than 8 years.
[i]Infused over 30 min; ascertained on days 6–7.
[j]When given with meals.
[k]Gastric acid–suppressing agents decrease bioavailability to <5%.
[l]Taken twice daily for 15 days.
[m1]Parent drug, active metabolite (hydroxyitraconazole).
[m2]Half-life extends as dosing continues.
[n]Bioavailability of the suspension is highly dependent on food; administration with a full meal is recommended.
[o]Oral suspension.
[p]Delayed-release tablet.
[q]Decreased rate and/or extent of absorption when given with food.
[r]Administered q12h for 10 days after 1 day of loading doses.
[s]Pediatric patients aged 2–12 years. Adult dosing should be used for pediatric patients older than 12 years.
[t]The intravenous formulation of voriconazole contains cyclodextrins, which may accumulate in renal impairment. Oral dosage formulations should be used whenever possible in these patients.
[u]Recommended doses are based on weight: <20 kg = 67.5 mg; 20–40 kg = 125 mg; >40 kg = 250 mg.
[v]Peak concentrations should be 25 μg/mL to avoid development of resistance but should not exceed 100–120 μg/mL to avoid side effects. Levels should be monitored routinely in renal dysfunction.
[w]Microsize.
[x]Ultramicrosize.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *FDA,* US Food and Drug Administration; *HD,* hemodialysis; *PD,* peritoneal dialysis.

With Dialysis		STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT					Dosage With Dialysis		Body Fluid Concentrations				
			For CrCl Ranges (mL/min)										
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.5–1[v]	24	24	24	24				80			
		0.375–0.75[iv]	24	24	24	24							

TABLE 54.28 Antiinfective Agent Pharmacology: Antiparasitic Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS						
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose			Up to 1 wk	1–4 wk
				Oral	Parenteral		Oral	Parenteral		
Anthelmintics										
Albendazole (minimal)[b,c]		0.4 PO	1.31[c]	0.4 q12h		0.8	15 mg/kg/day 2 doses			
Praziquantel (80)		40 mg/kg PO	0.8–3.57[d]	75 mg/kg/day in 3 doses		75 mg/kg	75 mg/kg/day in 3 doses[e]			
Diethylcarbamazine		0.5 PO	0.15–0.25	6–10 mg/kg/day in 3 doses		10 mg/kg	6 mg/kg/day in 3 doses			
Ivermectin		50–200 μg/kg PO	0.003–0.008	150–200 μg/kg × 1		200 μg/kg	150–200 μg/kg			
Mebendazole (5–10%)		0.1 PO	0.006–0.051	0.1 q12h		0.2				
Pyrantel pamoate				11 mg/kg[f] × 1		1	11 mg/kg[f] × 1			
Antimalarials										
Artemether-lumefantrine[g]		0.08/0.48 PO	0.06/ 7.38	4 tablets × 6 doses[g]		4 tablets × 6 doses[g]	1–4 tablets × 6 doses[g]			
Artesunate		2.4 mg/kg IV	4–5		2.4 mg/kg × 5 doses[h]	2.4 mg/kg		2.4 mg/kg × 5[h]		
Atovaquone-proguanil		0.5/0.2 q12h PO	0.908/0.17	1/0.4 q24h × 3 days		1–0.4	0.125/0.5 to 1/0.4 q24h × 3 doses[i]			
Chloroquine (89)		1 PO	1.0	0.5 × 5 doses[j]		1	5–10 mg/kg × 5 doses[j]		5 mg/kg × 5 doses[j]	5 mg/kg × 5 doses[j]
Hydroxychloroquine (75)		0.4 PO	1.22 nmol/mL	0.4 × 5 doses[j]		0.8	5–10 mg/kg × 5 doses[j]			
Mefloquine phosphate		12.2–18.3 mg/kg PO	1.8	0.75, then 0.5[k]		1.25	15 mg/kg, then 10 mg/kg[k]			
Primaquine phosphate (96)[l]		0.015 PO	0.053	0.015–0.03 q24h		0.03	0.5 mg/kg q24h[m]			
Quinine sulfate (89)[l]		0.648 PO	3.2	1.944/day in 3 doses		1.95	30 mg/kg/day in 3 doses			
Antiprotozoals										
Atovaquone (23–47)		0.75–1.5 PO	12	1.5/day in 1–2 doses		1.5	30–45 mg/kg/day in 2 doses[n]			
Benznidazole		0.1 PO	2.4	5–7 mg/kg/day in 2 doses[o]		7 mg/kg	5–8 mg/kg/day in 2 doses			
Eflornithine					400 mg/kg/day in 4 doses	400 mg/kg/day		400 mg/kg/day in 4 doses		
Iodoquinol (poor)				0.65 q8h		1.95	30–40 mg/kg/day in 3 doses			
Melarsoprol		3.6 mg/kg IV	4.7–6.7		2–3.6 mg/kg q24h	0.2		2–3.6 mg/kg q24h		
Miltefosine		0.050 q12h[p] PO	66.2	0.05 q8h		0.15	0.05 q8–12h[q]			
Nifurtimox				8–10 mg/kg/day in 3–4 doses		10 mg/kg	8–20 mg/kg/day in 3–4 doses[r]			
Nitazoxanide		0.5 PO	3.0	0.5 q12h		1	0.1–0.5 q12h			
Paromomycin (minimal)				25–35 mg/kg/day in 3 doses		35 mg/kg	25–35 mg/kg/day in 3 doses			
Pentamidine		4 mg/kg IV[s]	0.612		4 mg/kg q24h IM/IV	4 mg/kg		4 mg/kg q24h IM/IV		

SERUM HALF-LIFE (h)				STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT											
With Normal and Anuric CrCl Values (mL/min)		With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
>80	<10	HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
8–12[c]				0.4	12	12	12	12	0.4 q12h	0.4 q12h	25–50				
0.8–3				25 mg/kg	8	8	8	8	25 mg/kg q8h	25 mg/kg q8h	14				
10–12				6–10 mg/kg/ day											
18				150–200 µg/kg × 1											
3–6				0.1	12	12	12	12	0.1 q12h	0.1 q12h					
1.6/ 101				4 tablets × 6 doses[g]	4 tablets × 6 doses[g]	4 tablets × 6 doses[g]									
0.05–0.5				2.4 mg/kg × 5 doses[h]	2.4 mg/kg × 5 doses[h]	2.4 mg/kg × 5 doses[h]									
32–84/ 12–21				1–0.4	24	24									
6–60 days				0.5 × 5 doses[j]	0.5 × 5 doses	0.5 × 5 doses	0.5 × 5 doses	0.25–0.5							
40 days				0.4 × 5 doses[j]	0.4 × 5 doses[j]	0.4 × 5 doses[j]									
10–12 days				0.75, then 0.5[k]	0.75, then 0.5[k]	0.75, then 0.5[k]	0.75, then 0.5[k]	0.75, then 0.5[k]	0.75, then 0.5[k]	0.75, then 0.5[k]	High				
4–7				0.015–0.03	24	24									
9.7–20	26			0.648	8	8	0.324 q12h	0.324 q12h	0.324 q12h						
50–84				0.75	12	12	12	12	0.75 q12h	0.75 q12h	<1				
13													30–279%		
				100 mg/kg	6										
				0.65	8										
35				2–3.6 mg/kg	24										
30 days				0.05	8										
				8–10 mg/kg/ day											
1–1.6 h[c]				0.5	12										
				25–35 mg/kg/ day											
6.4				4 mg/kg	24										

Continued

TABLE 54.28 Antiinfective Agent Pharmacology: Antiparasitic Agents—cont'd

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS					
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose			
				Oral	Parenteral		Oral	Parenteral	Up to 1 wk / 1–4 wk
Pyrimethamine[t]		0.025–0.075 PO	0.26–4.7	0.05–0.075 q24h		0.75	1 mg/kg q24h		
Sodium Stibogluconate		20 mg/kg IV	9–12		20 mg/kg q24h IM/IV[u]	20 mg/kg/day[u]		20 mg/kg q24h IM/IV[u]	
Suramin[w]					1[x]			20 mg/kg q24h[x]	
Tinidazole		2 PO	42–60	2 q24h		2		50 mg/kg q24h	

[a]Inflamed meninges.
[b]Bioavailability is highly dependent on food. Administer with food.
[c]Rapidly converted to its active metabolite by first-pass hepatic metabolism. Plasma concentrations and pharmacokinetics reflect the active metabolite.
[d]Peak serum concentration increased significantly with impaired hepatic function.
[e]Not approved for children younger than 4 years.
[f]Dose expressed as mg/kg pyrantel base.
[g]A 3-day regimen of 6 doses of the coformulated artemether-lumefantrine (20 mg/120 mg per tablet) is recommended based on weight category (adult and pediatric) as an initial oral dose followed by an oral dose 8 h later, then the oral dose twice a day for the following 2 days. The dose is stratified by weight: 5 to <15 kg (1 tablet per dose); 15 to <25 kg (2 tablets per dose); 25 to <35 kg (3 tablets per dose); ≥35 kg (4 tablets per dose).
[h]5-dose regimen given at 0, 12, 24, 48, and 72 h.
[i]Dose depends on weight.
[j]4-dose regimen given at 0, 6, 24, 48 h. Initial loading dose is double subsequent doses.
[k]Initial dose followed by second dose given 6–12 h later.
[l]Used as part of a combination regimen in the treatment of malaria.
[m]Dose expressed as primaquine base.
[n]Dose depends on age and indication.
[o]FDA approved for children aged 2–12 years. Adult use is off label.
[p]After 4 wk of dosing.
[q]Dose based on weight: 30–44 kg (50 mg q12h); >45 kg (50 mg q8h).
[r]Dose based on age: 1–10 years (15–20 mg/kg/day); 11–16 years (12.5–15 mg/kg/day); >17 years (8–10 mg/kg/day).
[s]2-h infusion.
[t]Pyrimethamine is frequently administered with a loading dose on day 1 of therapy (200 mg adults, 2 mg/kg pediatrics). Leucovorin 10–25 mg/day is generally coadministered to prevent toxicity.
[u]Dose expressed in mg of pentavalent antimony.
[v]Beta elimination half-life, gamma elimination half-life.
[w]Suramin treatment courses require single-dose administrations on days 1, 3, 5, 14, and 21.
[x]Specified dose should be administered after a dialysis session to supplement drug clearance during dialysis.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *FDA,* US Food and Drug Administration; *HD,* hemodialysis; *PD,* peritoneal dialysis.

SERUM HALF-LIFE (h)				STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT											
With Normal and Anuric CrCl Values (mL/min)		With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis	Body Fluid Concentrations					
>80	<10	HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
80–96				0.05–0.075	24										
2, 76[v]				20 mg/kg	24										
50 days				1							1				
13.2				2	24	24	24	24	2 q24h, 1 after HD[y] if usual dose given prior						

TABLE 54.29 Antiinfective Agent Pharmacology: Antiviral Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF-LIFE (h)			
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)		With Dialysis	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval Oral	Dose (g)/Interval Parenteral	Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10	HD	PD
Acyclovir (15–30)[c]	0.2 PO[d]	0.83		0.2–0.8 2–5 times daily	5–10 mg/kg q8h	4 PO	1–4/day in 3–5 doses	30–45 mg/kg/day in 3 doses	60 mg/kg/day in 3 doses	60 mg/kg/day in 3 doses	2.1–3.5	19.5		Minimal change
	0.8 PO[d]	1.61				30 mg/kg IV								
	5 mg/kg IV[g]	7.7												
Adefovir (59)	0.01 PO	0.018		0.01 q24h		0.01	0.01 q24h				7.5			
Amantadine (85–90)	0.1 PO[d]	0.302		0.1 q12h		0.2	5 mg/kg/day in 2 doses				16–17		8.3 days	
Cidofovir	10 mg/kg IV	24			5 mg/kg weekly[h]	5 mg/kg					2.5			
Entecavir[i]	0.5 mg PO	0.004		0.5–1 mg q24h		1 mg					128–149			
	1 mg PO	0.008												
Famciclovir (75–77)	0.5 PO	4		0.25–0.5 q8–12h		1.5					2–2.3			
	0.75 PO	5.1–5.3												
Foscarnet	0.09 IV[d]	218 μmol/L			90 mg/kg q12h[k]	180 mg/kg					0.1–17			
Ganciclovir (5)	5 mg/kg IV[g]	9			5 mg/kg q12h[k]	10 mg/kg/day		5 mg/kg q12h	12 mg/kg/day in 2 doses	12 mg/kg/day in 2 doses	2.5–5	10		
	1.0 PO	0.98												
Oseltamivir (75)	0.075 PO	0.065		0.075 q12h		0.15	0.03–0.075 q12–24 h[m]		3 mg/kg q12h	3 mg/kg q12h	6–10			
Peramivir	0.6 IV	46.8			0.6 × 1	0.6		12 mg/kg × 1			20			
Ribavirin (64)	0.6 q12h PO	2.748		0.4–0.6 q12h		1.2 PO	15 mg/kg/day in 2 doses	6/day inhalation[n]			9.5, 298[o]			
	0.82 mg/kg/h[q]	0.275												
	0.82 mg/kg/h[r]	1.1												
Rimantadine (100)	0.2 PO	0.05–0.086		0.1 q12h		0.2	5 mg/kg/day in 1–2 doses				19.8–36.5			
Telbivudine	0.6 PO[d]	3.69		0.6 q24h		0.6					40–49			
Valacyclovir (55)	2 PO[d]	8.49		0.5–2 q8–12h		4	20 mg/kg q8h				2.5–3.6[s]	20		
Valganciclovir[t] (60)	0.45 PO	3.1		0.9 q12[k]		1.8 PO					3.7–4.6			
Zanamivir (2)	0.01 PO	0.017–0.142			0.01 q12h[u]			0.01 q12h[u]			1.6–5.1			

[a]Not including hepatitis C direct-acting antivirals and antiretrovirals, which are listed in Tables 54.30 and 54.31, respectively.
[b]Inflamed meninges.
[c]Bioavailability decreases as dosage is increased.
[d]At steady state.
[e]Specified dose should be administered after a dialysis session to supplement drug clearance during dialysis.
[f]Supplemental dose after dialysis is recommended based on simulation data when dose is 800 mg 5 times daily in normal renal function.
[g]Infused over 1 h.
[h]Weekly for 2 wk, then every other week.
[i]Cidofovir is contraindicated in preexisting renal impairment (SCr >1.5 mg/dL; CrCl <55 mL/min; urine protein >100 mg/dL).
[j]Decreased rate and/or extent of absorption when given with food.
[k]For 14–21 days as induction therapy. Dose should be reduced for maintenance therapy.
[l]Renal dose adjustments are based on modified Cockroft and Gault equation: ([140 – age/Scr[+] 72]). ([+], 0.85 if female). Refer to package insert for dosing table.
[m]Dosing is based on weight: <15 kg (30 mg q12h); 15.1–23 kg (45 mg q12h); 23.1–40 kg (60 mg q12h); >40 kg (75 mg q12h).
[n]Mist of 190 μg/L via SPAG-2 aerosol generator; rate of 12.5 L mist/min × 12–18 h/day for 3–7 days.
[o]Inhaled, oral.
[p]After administration for 4–7 wk in acquired immunodeficiency syndrome (AIDS) or AIDS-related complex patients.
[q]Inhaled over 5 h each day for 3 days.
[r]Inhaled over 8 h each day for 3 days.
[s]Half-life of valacyclovir is <30 min, but its metabolite, acyclovir, has a half-life of 2.5–3.6 h.
[t]Should be taken with food.
[u]Dose administered by oral inhalation.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HD,* hemodialysis; *PD,* peritoneal dialysis; *SCr,* serum creatinine.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT

	For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
Usual Adult Dose (g)	**>80**	**80–50**	**50–10**	**<10 (Anuric)**	**HD (g)**	**PD (g)**	**CSF/ Serum (%)[b]**	**Newborn Serum/ Maternal Serum (%)**	**Breast Milk/ Maternal Serum (%)**	**Bile/ Serum (%)**	**Aqueous Humor/ Serum (%)**
0.2–0.8 PO	2–5 times daily	2–5 times daily	2–5 times daily	0.2 q12h	0.2 q12h, 0.4[e] after HD[f]	0.2 q12h	50		≥100		37
5 mg/kg IV	8	8	12–24	2.5 mg/kg q24h	2.5 mg/kg q24h	2.5 mg/kg/day					
0.01	24	24	48–72	0.01 weekly	0.01 weekly	0.01 weekly					
0.1	12	12–24	48 – weekly	0.2 weekly	0.2 weekly	0.2 weekly	50				
5 mg/kg	weekly	weekly	Do not use[i]	Do not use[i]	Do not use[i]	Do not use[i]					
0.5–1.0 mg	24	24	48–72	weekly	0.5–1 weekly	0.5–1 weekly					
0.25–0.5	8–12	8–12	0.125–0.5 q12–24h	0.125–0.25 q24h	0.125–0.25 after HD[e]						
90 mg/kg[k,l]					45–60 mg/kg after HD[e]		13–103				
5 mg/kg[k]	12	2.5 mg/kg q12h	1.25–2.5 mg/kg q24h	1.25 mg/kg thrice weekly	1.25 mg/kg thrice weekly after HD[e]	1.25 mg/kg thrice weekly	24–68		40		
0.075	12	12	0.03 q12–24h	0.03 q48h	0.03 after HD[e]	0.03 q48h					
0.6 × 1	× 1	× 1	0.1–0.2 × 1	0.1 × 1	0.1 × 1 after HD						
0.4–0.6	12	12	0.2–0.4 q24h	0.2 q24h	0.2 q24h		70[p]				
0.1	12	12	12–24	24	0.1 q24h	0.1 q24h					
0.6	24	24	48–72	72	0.6 q96h	0.6 q96h					
0.5–1	8–12	8–12	12–24	0.5 q24h	0.5 q24h	0.5 q24h		170			
0.9[k]	12	12	0.45 q12–48h	Do not use	Do not use	Do not use					
0.01	12	12	12	12	0.05 q12h	0.05 q12h					

TABLE 54.30 Antiinfective Agent Pharmacology: Hepatitis C Direct-Acting Antivirals

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS						SERUM HALF-LIFE (h)	
				Adults			Children: Dose/Interval	Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
				Dose (g)/Interval		Serious Infection Daily Dose (g)					
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Oral	Parenteral		Oral Parenteral	Up to 1 wk	1–4 wk	>80	<10
Daclatasvir (67)				0.06 q24		0.06				12–15	
Elbasvir-grazoprevir[b]				1 tablet q24h		1 tablet				24/31	
Glecaprevir-pibrentasvir[c]	0.3/0.12 q24h PO[d]	0.725/0.018		3 tablets q24h		3 tablets				6–10/13–27	
Ombitasvir-paritaprevir-ritonavir[e] (48.1/52.6)[f]	0.0125/0.075/0.05 q24h PO[d]	0.082/0.194/0.543		2 tablets q24h		2 tablets				21–25/5.5/4	
Ombitasvir-paritaprevir-ritonavir- dasabuvir (48/53/70)[g]	0.0125/0.075/0.05 + 0.25 q24h PO[d,h]	0.068/0.262/0.682/0.667		1 kit q24h[h] 3 tablets q24h[i]		1 kit[h] 3 tablets[i]				21–25/5.5/4/5.5–6	
Simeprevir (62)	0.2 q24 PO[d]	10.9		0.15 q24h		0.15				10–13[j]	
Sofosbuvir	0.4 PO	1.26		0.4 q24h		0.4				0.4, 27[k]	
Sofosbuvir- ledipasvir[l]	0.4/0.09 q24h PO[d]	0.618/0.323		1 tablet q24h		1 tablet				0.5/47	
Sofosbuvir-velpatasvir[m]	0.4/0.1 PO q24h[d]	0.567/0.259		1 tablet q24h		1 tablet				0.5/15	
Sofosbuvir-velpatasvir-voxilaprevir[n]	0.4/0.1/0.1 q24h PO[d]	0.678/0.311/0.192		1 tablet q24h		1 tablet				0.5/17/33	

[a]Inflamed meninges.
[b]One tablet contains 50 mg of elbasvir and 100 mg of grazoprevir.
[c]One tablet contains 100 mg of glecaprevir and 40 mg of pibrentasvir.
[d]In subjects with HCV infection.
[e]One tablet contains 12.5 mg of ombitasvir, 75 mg of paritaprevir, and 50 mg of ritonavir.
[f]Bioavailability of ombitasvir-paritaprevir.
[g]Bioavailability of ombitasvir-paritaprevir-ritonavir reported for bilayer tablet.
[h]Kit composed of 2 tablets containing 50 mg of dasabuvir and 2 tablets containing 12.5 mg of ombitasvir, 75 mg of paritaprevir, and 50 mg of ritonavir. Dosing consists of 2 combination tablets in the morning and 1 tablet of dasabuvir twice daily in the morning and evening.
[i]Bilayer tablet composed of an extended-release layer containing 200 mg of dasabuvir and an immediate-release layer containing 8.33 mg of ombitasvir, 50 mg of paritaprevir, and 33.33 mg of ritonavir.
[j]May be prolonged up to 41 h in patients with hepatitis C.
[k]Parent drug, primary metabolite.
[l]One tablet contains 400 mg of sofosbuvir and 90 mg of ledipasvir.
[m]One tablet contains 400 mg of sofosbuvir, 100 mg of velpatasvir.
[n]One tablet contains 400 mg of sofosbuvir, 100 mg of velpatasvir, and 100 mg of voxilaprevir.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HCV,* hepatitis C virus; *HD,* hemodialysis; *PD,* peritoneal dialysis.

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD(g)	PD (g)	CSF/Serum (%)[a]	Newborn Serum/Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/Serum (%)	Aqueous Humor/ Serum (%)
		0.06	24	24	24	24	0.06 q24h	0.06 q24h					
		1 tablet	24	24	24	24	1 tablet q24h	1 tablet q24h					
		3 tablets	24	24	24	24	3 tablets q24h	3 tablets q24h					
		2 tablets	24	24	24								
		1 kit[h]	24	24	24								
		3 tablets[i]	24	24	24	24	3 tablets[i] q24h	3 tablets[i] q24h					
		0.15	24	24	24	24	0.15 q24h	0.15 q24h					
		0.4	24	24	24								
		1 tablet	24	24	24								
		1 tablet	24	24	24								
		1 tablet	24	24	24								

TABLE 54.31 Antiinfective Agent Pharmacology: Antiretroviral Agents

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF–LIFE (h)	
				Adults			Children: Dose/Interval		Newborn (Parenteral): Dose/Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval		Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
				Oral	Parenteral							
Abacavir (83)	0.3 PO	3.3		0.6/day in 1–2 doses		0.6	16 mg/kg/day in 1–2 doses				1.2	1.2
Atazanavir (60–70%)[b]	0.4 PO	5.226		0.4 q24h 0.3 q24h[c]		0.4	0.15–0.3 mg/kg q24h[c,d]				5–8	
Cobicistat	0.15 PO	0.99		0.15 q24h		0.15					3–4	
Darunavir (82)[b,e]	0.6 PO			0.8 q24[c] 0.6 q12h[c]		1.2	0.2–0.6 q12h[c,d]				15	
Delavirdine (60–100)	0.4 PO[f]	356		0.4 q8h		1.2					2–11	
Didanosine[g] (21–43)[h,i]	33 mg/kg	29.8 μmol/L		0.4/day in 1–2 doses[j]		0.4	120 mg/m^2 q12h			50 mg/m^2 q12h PO	1.3–1.6	4.5
Dolutegravir	0.05 PO	3.67		0.05 q12–24h[k]		0.1	0.035–0.05[d,k]				14	
Efavirenz	0.6 PO[f]	4.5		0.6 q24h		0.6	0.1–0.6 q24h[d]				40–55	
Elvitegravir	0.15 PO	1.7		0.15 q24h[l]		0.15 q24h[l]					12.9	
Emtricitabine (93)	0.2 PO[n] 6 mg/kg[o]	2.1 1.9		0.2 q24h[n] 0.24 q24h[o]		0.2[n] 0.24[o]	0.2 q24h[d,n] 6 mg/kg q24h[o]		3 mg/kg q24h[o] PO	3 mg/kg q24h[o] PO	2.5–7	
Enfuvirtide	0.09 SQ	4.59			0.09 q12h SQ	0.18		2 mg/kg q12h SQ				
Etravirine[b]	0.2 q12h PO	0.297		0.2 q12h		0.4	0.1–0.2 q12h[d]				41	
Fosamprenavir	1.4 PO[e]	7.9		1.4 q12h[p]		2.8	18–45 mg/kg q12h[d,e]				7.7	7.7
Indinavir[g] (30)	0.8 PO[f,j]	12,617 nmol/L		0.8 q8h		2.4					1.5–2	1.5–2
Lamivudine (82–87)	0.15 q12h PO	1.4		0.3/day in 1–2 doses		0.3	4 mg/kg q12h		2 mg/kg q12h PO	2 mg/kg q12h PO	3–7	
Lopinavir-ritonavir[b]	0.4/0.05 PO	6[bb]		0.4/0.1 q12h		0.8/0.2	0.3/0.075 mg/m^2 q12h			0.3/0.075 mg/m^2 q12h PO	5–6	
Maraviroc (23–33)	0.3 PO[f]	0.888		0.15–0.6 q12h[q]		1.2	0.05–0.3 q12h[d,q]				14–18	
Nelfinavir[b]	0.75 PO[f]	2.9		1.25 q12h		2.5	45–55 mg/kg q12h				3.5–5	3.5–5
Nevirapine (> 90)	0.4 PO	2.9–3.4		0.2 q12h[s]		0.4	120–200 mg/m^2 q12h[t]		4–6 mg/kg q12h PO	6 mg/kg q12h PO	25–30	25–30
Raltegravir	0.4 q12h PO[i]	4.5		0.4 q12h		0.8–1.2[u]	0.02–0.1 q12h[d]				9	9
Rilpivirine	0.025 PO	0.079		0.025 q24h		0.025					50	
Ritonavir (80)[v,w]	0.6 PO 1.2 PO	5 11.2		0.1–0.4/day in 1–2 doses		0.4					3–3.5	3–3.5
Saquinavir[b]	0.6 PO	0.066		1 q12h[e]		2					13	13
Stavudine (80)	4 mg/kg PO	4.2		0.04 q12h[x]		0.08	2 mg/kg/day[y]		0.5 mg/kg q12h PO	1 mg/kg q12h PO	0.9–1.6	5.7
Tenofovir alafenamide fumarate	0.0225 q24h PO	0.03		0.025 q24h		0.025					0.51	

STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT													
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.3–0.6	12–24	12–24	12–24	12–24	0.6/d in 1–2 doses	0.6/d in 1–2 doses	18–33				
		0.4[c]	24	24	24	24							
		0.15	24	24	24	24	0.15 q24h	0.15 q24h					
		0.8[c] 0.6[c]	24 12	24 12	24 12	24 12	0.8 q24h[c] 0.6 q24h[c]	0.8 q24h[c] 0.6 q24h[c]					
		0.4	8	8	8	8	0.4 q8h	0.4 q8h	0.4				
		0.4/day[j]	1–2 doses	1–2 doses	0.1–0.2 q24h	0.075–0.125 q24h	0.075–0.1 q24h	0.075–0.1 q24h	21–46				
		0.05	12–24	12–24	12–24	12–24	0.05 q12–24h	0.05 q12–24h	<2				
10		0.6	24	24	24	24	0.6 q24h	0.6 q24h	1.19				
		0.15[l]	24	24[m]	Do not use	Do not use	Do not use	Do not use					
		0.2[n] 0.24[o]	24 24	24 24	48–72 0.08–0.12 q24h	96 0.06 q24h	0.2 q96h[n] 0.06 q24h[o]	0.2 q96h[n] 0.06 q24h[o]					
		0.09	12	12	12	12	0.09 q12h SQ	0.09 q12h SQ					
		0.2	12	12	12	12	0.2 q12h	0.2 q12h					
		1.4[p]	12	12	12	12	1.4 q12h[p]	1.4 q12h[p]					
		0.8	8	8	8	8	0.8 q8h	0.8 q8h	5–9	Unsafe			
		0.15–0.3	12–24	12–24	0.05–0.15 q24h	0.025 q24h	0.025 q24h		6–11	~100	~100		
		0.4/0.1	12	12	12	12	0.4/0.1 q12h	0.4/0.1 q12h					
		0.15–0.6	12	12	0.3 q12h[r]	0.3 q12h[r]	0.3 q12h[r]						
3.5–5	3.5–5	1.25	12	12	12	12	1.25 q12h	1.25 q12h	0				
		0.2[s]	12	12	12	12	0.2 q12h	0.2 q12h		60			
		0.4	12	12	12	12	0.4 q12h	0.4 q12h					
		0.025	24	24	24	24	0.025 q24h	0.025 q24h					
		0.1–0.4	12–24	12–24	12–24	12–24	0.1–0.4/day in 1–2 doses	0.1–0.4/day in 1–2 doses	0.2				
		1	12	12	12	12	1 q12h	1 q12h	0.2				
5.3		0.04[x]	12	12	0.02 q12–24h	0.02 q24h[x]	0.02 q24h[x]		24–94				
		0.025	24	24	24								

Continued

TABLE 54.31 Antiinfective Agent Pharmacology: Antiretroviral Agents—cont'd

Drug (Oral Absorption, %)	Serum and Urine Concentration: Selected Doses			DOSAGE RECOMMENDATIONS							SERUM HALF–LIFE (h)	
				Adults			Children: Dose/ Interval		Newborn (Parenteral): Dose/ Interval		With Normal and Anuric CrCl Values (mL/min)	
	Dose (g)	Peak Serum (μg/mL)	Peak or Range, Urine (μg/mL)	Dose (g)/Interval Oral	Dose (g)/Interval Parenteral	Serious Infection Daily Dose (g)	Oral	Parenteral	Up to 1 wk	1–4 wk	>80	<10
Tenofovir disoproxil fumarate[b] (40)	0.3 PO	0.296		0.3 q24h		0.3	8 mg/kg q24h				4–8	
Tipranavir[b]	0.5 PO[e]	94.8 μmol/L		0.5 q12h[e]		1	14 mg/kg q12h[e]				4.8–6	
Zidovudine (50–76)[z]	2 mg/kg PO 1 mg/kg IV	0.41–0.54 0.4–0.68		0.3 q12h	1 mg/kg q4h[aa]	0.6	9–12 mg/kg[d]		2–4 mg/kg PO	2–4 mg/kg PO	0.5–3	1.4

[a]Inflamed meninges.
[b]Give with food.
[c]Administered with ritonavir or cobicistat as a boosting agent.
[d]Dose in pediatric patients depends on weight. Refer to guidelines or prescribing information for specific dosing nomograms.
[e]When administered with ritonavir.
[f]At steady state.
[g]Decreased rate and/or extent of absorption when given with food.
[h]Bioavailability decreases as dosage is increased.
[i]In human immunodeficiency virus (HIV)–positive patients.
[j]Delayed-release tablets administered once daily. Oral solution can be administered once daily or divided twice daily; however, divided dosing is preferred. Dose reduction is necessary for weight <60 kg and with concomitant tenofovir therapy.
[k]Administered once a day in HIV-1 integrase strand transfer inhibitor (INSTI)–naïve patients but should be used twice daily in INSTI experience with certain or clinically suspected resistance substitutions or used in combination with UGT1A/CYP3A inhibitors.
[l]Single-agent elvitegravir is no longer available. Dosing reflects the elvitegravir component of combination tablets, which is boosted with cobicistat.
[m]Renal adjustments for combination tablets depend on the tenofovir component: Tablets with tenofovir disoproxil fumarate should not be initiated with CrCl <70 mL/min and should be stopped if CrCl declines to <50 mL/min. Tablets containing tenofovir alafenamide fumarate should not be used with CrCl <30 mL/min.
[n]Capsule.
[o]Oral solution.
[p]Alternative dosage regimens are available with the addition of ritonavir. The preferred regimen for protease inhibitor–experienced patients is fosamprenavir 700 mg with ritonavir 100 mg twice daily.
[q]Dose depends on concomitant medications and resulting drug-drug interactions. Refer to guidelines or prescribing information to determine dose.
[r]Reduce dose to 150 mg q12h if postural hypotension occurs. Maraviroc is not recommended with CrCl <30 mL/min if patient is taking potent CYP3A inducers or inhibitors.
[s]Once-daily administration is possible with the extended-release formulation.
[t]Dose in pediatric patients depends on age.
[u]Isentress HD formulation can be administered as 1200 mg once daily. Other formulations may not be substituted for Isentress HD for this dosing.
[v]In animals.
[w]Ritonavir has antiretroviral activity but is no longer used as an antiretroviral. Doses listed reflect those used in combination with other antiretrovirals for pharmacologic boosting effect.
[x]Dosage should be reduced for patients weighing <60 kg.
[y]Pediatric patients weighing >30 kg should receive the adult dose for <60 kg.
[z]Reaches systemic circulation as unchanged drug.
[aa]An IV dose of 1 mg/kg q4h is equivalent to an oral dose of 100 mg q4h.
[bb]Lopinavir.
CrCl, Creatinine clearance; *CSF,* cerebrospinal fluid; *HD,* hemodialysis; PD, peritoneal dialysis.

		STANDARD DOSE WITH DOSING INTERVALS IN RENAL IMPAIRMENT										
With Dialysis			For CrCl Ranges (mL/min)				Dosage With Dialysis		Body Fluid Concentrations				
HD	PD	Usual Adult Dose (g)	>80	80–50	50–10	<10 (Anuric)	HD (g)	PD (g)	CSF/ Serum (%)[a]	Newborn Serum/ Maternal Serum (%)	Breast Milk/ Maternal Serum (%)	Bile/ Serum (%)	Aqueous Humor/ Serum (%)
		0.3	24	24	48–96		0.3 weekly						
		0.5	12	12	12	12	0.5 q12h	0.5 q12h					
		0.3	12	12	12	24	0.3 q24h	0.3 q24h	50–70	100	100		

TABLE 54.32 Key Drug Substrates, Organized by Cytochrome P450 (CYP) Drug Metabolizing Isoenzymes

CYP1A2	CYP2B6	CYP2C8	CYP2C9	CYP2C19	CYP2D6	CYP2E1	CYP3A	
amitriptyline	bupropion	amodiaquine	amitriptyline	carisoprodol	alprenolol	acetaminophen	alfentanil	lidocaine
caffeine	cyclophosphamide	**dasabuvir**	celecoxib	**chloramphenicol**	amitriptyline	chlorzoxazone	alprazolam	lovastatin
clomipramine	**efavirenz**	cerivastatin	diclofenac	citalopram	amphetamine	enflurane	amlodipine	**maraviroc**
clozapine	ifosfamide	paclitaxel	fluoxetine	clomipramine	aripiprazole	ethanol	aprepitant	midazolam
cyclobenzaprine	methadone	torsemide	fluvastatin	cyclophosphamide	atomoxetine	halothane	aripiprazole	nateglinide
estradiol		repaglinide	glipizide	esomeprazole	carvedilol	isoflurane	**artemisinins**	**nelfinavir**
fluvoxamine			glyburide	hexobarbital	chlorpheniramine	methoxyflurane	astemizole	nifedipine
haloperidol			ibuprofen	indomethacin	chlorpromazine	sevoflurane	**atazanavir**	nisoldipine
mexiletine			irbesartan	lansoprazole	clomipramine		atorvastatin	nitrendipine
naproxen			lornoxicam	moclobemide	codeine		**bedaquiline**	ondansetron
olanzapine			losartan	**nelfinavir**	debrisoquine		buspirone	**paritaprevir**
ondansetron			meloxicam	nilutamide	desipramine		Cafergot	pimozide
phenacetine			nateglinide	omeprazole	dexfenfluramine		chlorpheniramine	**praziquantel**
propranolol			omeprazole	pantoprazole	dextromethorphan		cilostazol	progesterone
riluzole			phenytoin	phenobarbital	duloxetine		**clarithromycin**	quetiapine
ropivacaine			piroxicam	phenytoin	encainide		cocaine	quinidine
tacrine			rosiglitazone	primidone	flecainide		cyclosporine	**quinine**
theophylline			rosuvastatin	progesterone	fluoxetine		**daclatasvir**	risperidone
tizanidine			S-warfarin	**proguanil**	fluvoxamine		**dapsone**	**ritonavir**
verapamil			tamoxifen	propranolol	haloperidol		**darunavir**	salmeterol
R-warfarin			tolbutamide	rabeprazole	imipramine		dexamethasone	**saquinavir**
zileuton			torsemide	teniposide	lidocaine		dextromethorphan	sildenafil
zolmitriptan				**voriconazole**	methoxyamphetamine		diltiazem	**simeprevir**
					metoclopramide		docetaxel	simvastatin
					paroxetine		domperidone	sirolimus
					perphenazine		**elbasvir**	tacrolimus
					propafenone		eplerenone	tadalafil
					S-metoprolol		**erythromycin**	taxol
					thioridazine		estradiol	terfenadine
					timolol		**etravirine**	terfenadine
							felodipine	testosterone
							fentanyl	**tipranavir**
							finasteride	trazodone
							fosamprenavir	triazolam
							grazoprevir	vardenafil
							haloperidol	verapamil
							hydrocortisone	vincristine
							imatinib	zaleplon
							indinavir	ziprasidone
							irinotecan	zolpidem

[a]Antiinfectives are **bold.**

TABLE 54.33 Drug Inhibitors by Cytochrome P450 (CYP) Drug Metabolizing Isoenzymes

CYP1A2	CYP2B6	CYP2C8	CYP2C9	CYP2C19	CYP2D6	CYP2E1	CYP3A
amiodarone cimetidine **ciprofloxacin** fluvoxamine **interferon** methoxsalen	ticlopidine thiotepa	gemfibrozil montelukast pioglitazone quercetin rosiglitazone **trimethoprim**	amiodarone fenofibrate **fluconazole** fluvastatin fluvoxamine **isoniazid** probenecid sertraline **sulfamethoxazole** teniposide **voriconazole** zafirlukast	cimetidine esomeprazole felbamate fluoxetine fluvoxamine indomethacin **ketoconazole** lansoprazole modafinil omeprazole oxcarbazepine pantoprazole probenecid rabeprazole ticlopidine topiramate	amiodarone bupropion celecoxib chlorpheniramine chlorpromazine cimetidine citalopram clemastine clomipramine cocaine diphenhydramine doxepin doxorubicin duloxetine escitalopram fluoxetine hydroxyzine metoclopramide mibefradil midodrine moclobemide paroxetine perphenazine quinidine ranitidine **ritonavir** sertraline terbinafine ticlopidine	disulfiram	amiodarone aprepitant cimetidine **clarithromycin** **cobicistat** **delavirdine** diltiazem **elvitegravir** **erythromycin** **fluconazole** fluvoxamine gestodene imatinib **indinavir** **isavuconazonium** **itraconazole** **ketoconazole** mibefradil mifepristone nefazodone **nelfinavir** norfluoxetine **posaconazole** **ritonavir** **saquinavir** verapamil **voriconazole**

[a]Antiinfectives are **bold.**

TABLE 54.34 Drug and Chemical Inducers by Cytochrome P450 (CYP) Drug Metabolizing Isoenzymes

CYP1A2	CYP2B6	CYP2C8	CYP2C9	CYP2C19	CYP2D6	CYP2E1	CYP3A
cigarette smoking marijuana smoking modafinil **nafcillin**	phenobarbital **rifampin**	**rifampin**	**rifampin** secobarbital	carbamazepine norethindrone prednisone **rifampin**	dexamethasone **rifampin**	ethanol **isoniazid**	barbiturates carbamazepine **efavirenz** glucocorticoids modafinil **nevirapine** oxcarbazepine phenobarbital phenytoin pioglitazone **rifabutin** **rifampin** St. John's wort

[a]Antiinfectives are **bold.**

TABLE 54.35 Select Drug Transporter Localization With Representative Substrates, Inducers, and Inhibitors

FAMILY	ATP-BINDING CASSETTE (ABC) TRANSPORTERS		SOLUTE-LIKE CARRIER (SLC) TRANSPORTERS				
SUBGROUP			ORGANIC ANION TRANSPORTERS (OAT)		ORGANIC ANION TRANSPORTER POLYPEPTIDE (OAT)		ORGANIC CATION TRANSPORTERS (OCT)
TRANSPORTER	BREAST CANCER RESISTANCE PROTEIN (BCRP)	P-GLYCOPROTEIN (P-gp)	OAT1	OAT3	OATP1B1	OATP1B3	OCT2
Organ or tissue localization	breast intestine liver placenta	adrenal brain intestine kidney liver placenta testes	brain kidney	brain kidney	liver	liver	brain kidney
Substrates	**dasabuvir**, **delafloxacin, glecaprevir**, imatinib, irinotecan, lapatinib, **ledipasvir**, methotrexate, mitoxantrone, **ombitasvir, paritaprevir, pibrentasvir**, rosuvastatin, **sofosbuvir**, sulfasalazine, topotecan, **velpatasvir**, **voxilaprevir**	colchicine, **dasabuvir**, **delafloxacin**, digoxin, fexofenadine, **glecaprevir**, **indinavir**, **ledipasvir**, **ombitasvir, paritaprevir,** paclitaxel**, pibrentasvir**, **sofosbuvir**, topotecan, vincristine, **velpatasvir**, **voxilaprevir**	**adefovir**, captopril, furosemide, **lamivudine**, methotrexate, **oseltamivir**, **tenofovir**, zalcitabine, **zidovudine**	**acyclovir**, bumetanide, **ciprofloxacin**, famotidine, furosemide, methotrexate, **oseltamivir carboxylate**, **penicillin G**, pravastatin, rosuvastatin, sitagliptin, **zidovudine**	atrasentan, atorvastatin, bosentan, ezetimibe, fluvastatin, glyburide, olmesartan, **paritaprevir**, pitavastatin, pravastatin, repaglinide, **rifampin**, rosuvastatin, simvastatin, valsartan, **voxilaprevir**	atorvastatin, **glecaprevir**, **grazoprevir,** olmesartan, **paritaprevir**, pitavastatin, rosuvastatin, telmisartan, valsartan, **voxilaprevir**	**amantadine**, amiloride, cimetidine, dopamine, famotidine, memantine, metformin, oxaliplatin, pindolol, procainamide, ranitidine, varenicline
Inhibitors	cyclosporine, **daclatasvir**, **dasabuvir**, eltrombopag, **glecaprevir**, gefitinib, **ledipasvir**, **paritaprevir**, **pibrentasvir**, **tedizolid, velpatasvir**, **voxilaprevir**	amiodarone, **azithromycin**, captopril, carvedilol, **clarithromycin**, conivaptan, cyclosporine, diltiazem, dronedarone, **erythromycin**, felodipine, **glecaprevir**, **itraconazole**, **ketoconazole**, **pibrentasvir**, quercetin, quinidine, ranolazine, **ritonavir**, **velpatasvir**, verapamil, **voxilaprevir**	**cefadroxil**, **cefamandole**, **cefazolin,** probenecid	cimetidine, diclofenac, probenecid	**atazanavir**, cyclosporine, **daclatasvir**, eltrombopag, gemfibrozil, **paritaprevir**, **rifampin**, **ritonavir**, **saquinavir**, **tipranavir, velpatasvir**, **voxilaprevir**	**atazanavir**, cyclosporine, **daclatasvir, glecaprevir, paritaprevir, pibrentasvir, rifampin**, **ritonavir**, **saquinavir**, **velpatasvir**, **voxilaprevir**	cimetidine, quinidine
Inducers	Not yet identified	avasimibe, carbamazepine, phenytoin, **rifampin**, St. John's wort, **tipranavir-ritonavir**	Not yet identified	Not yet identified	Not yet identified	Not yet identified	Not yet identified

[a]Antiinfectives are **bold.**

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Abacavir With		
Amprenavir	Increased amprenavir effect, toxicity	Increased bioavailability
Methadone	Decreased methadone effect	Mechanism not established
Ribavirin	Increased risk of lactic acidosis	Mechanism not established
Acyclovir, Valacyclovir With		
Aminoglycosides	Increased nephrotoxicity and/or neurotoxicity	Mechanism not established
Cimetidine	Increased acyclovir toxicity	Mechanism not established
Cyclosporine	Increased risk of nephrotoxicity	Mechanism not established
Meperidine	Increased meperidine effect	Decreased renal excretion
Phenytoin	Decreased phenytoin effect	Altered GI transit, pH
Probenecid	Possible increased acyclovir toxicity	Decreased renal excretion
Valproic acid	Decreased valproic acid effect	Altered GI transit, pH
Zidovudine	Increased neurotoxicity (profound drowsiness and lethargy)	Additive toxicity
Albendazole With		
Ginseng	Reduced intestinal albendazole concentration	Increased metabolism
Amantadine With		
Anticholinergics	Hallucinations, confusion, nightmares	Mechanism not established
Antihistamines	Increased CNS adverse reactions	Additive anticholinergic effects
Bupropion	Increased adverse events	Mechanism not established
CNS stimulants	Additive CNS stimulant effects	Mechanism not established
Triamterene	CNS toxicity	Decreased renal clearance
Trimethoprim	CNS toxicity	Decreased renal clearance
Aminoglycoside Antibiotics With		
Acyclovir	Increased nephrotoxicity and/or neurotoxicity	Additive toxicity
Amphotericin B	Increased nephrotoxicity	Synergistic toxicity
Anticoagulants, oral	Potentiation of anticoagulation effects	Decreased GI absorption or synthesis of vitamin K
Bacitracin	Increased nephrotoxicity	Additive toxicity
Capreomycin	Increased nephrotoxicity and/or neurotoxicity	Additive toxicity
Carboplatin	Increased ototoxicity	Additive toxicity
Cidofovir	Increased nephrotoxicity	Additive toxicity
Cisplatin	Increased nephrotoxicity	Mechanism not established
Cyclosporine	Increased nephrotoxicity	Possibly additive or synergistic toxicity
Digoxin	Probable decreased digoxin effect with oral gentamicin or neomycin	Decreased absorption
Loop diuretics	Increased ototoxicity and nephrotoxicity	Additive toxicity
Magnesium sulfate	Increased neuromuscular blockade	Additive toxicity
Methotrexate	Possible increased methotrexate toxicity with kanamycin Possible decreased methotrexate effect with oral aminoglycosides	Mechanism not established Decreased absorption
Methoxyflurane	Increased nephrotoxicity	Additive toxicity
Neuromuscular blocking agents	Neuromuscular blockade	Additive toxicity
NSAIDs	Possible aminoglycoside toxicity in preterm infants with indomethacin given for patent ductus closure	Decreased renal clearance
Polymyxins	Falsely low aminoglycoside levels Increased nephrotoxicity; neuromuscular blockade	In vitro inactivation Additive toxicity
Tacrolimus	Increased nephrotoxicity	Additive toxicity
Vancomycin	Possible increased nephrotoxicity and ototoxicity	Additive toxicity
Aminosalicylic Acid With		
Anticoagulants, oral	Enhanced hypoprothrombinemic effects	Mechanism not established
Ammonium chloride	Increased probability of crystalluria	Acidification of urine
BCG vaccine	Negates BCG vaccine effect	Negates immune response

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Digoxin	Decreased digoxin effect	Decreased absorption
Diphenhydramine	Decreased effect of aminosalicyclic acid	Decreases absorption
Ethionamide	GI distress, hepatotoxicity	Additive toxicity
Isoniazid	Increased isoniazid serum concentrations	Decreased metabolism
Probenecid	Increased aminosalicyclic acid toxicity	Decreased renal excretion
Rifampin	Rifampin effectiveness may be decreased; separate doses by 8–12 h	Decreased absorption due to excipient bentonite
Amphotericin B With		
Aminoglycoside antibiotics	Nephrotoxicity	Synergistic toxicity
Antineoplastics	Possible increased renal toxicity, bronchospasm, and hypotension	Mechanism not established
Capreomycin	Increased nephrotoxicity	Additive toxicity
Cidofovir	Increased nephrotoxicity	Additive toxicity
Cisplatin	Increased nephrotoxicity	Additive toxicity
Corticosteroids	Increased hypokalemia	Additive toxicity
Cyclosporine	Increased renal toxicity	Possible synergism
Digoxin	Increased digoxin toxicity	Hypokalemia
Imidazole antifungals	Possible antagonism in animal models	Mechanism not established
Methoxyflurane	Increased nephrotoxicity	Additive toxicity
Neuromuscular blocking agents	Increased neuromuscular blocking effects	Hypokalemia
Pentamidine	Increased nephrotoxicity	Additive toxicity
Polymyxins	Increased nephrotoxicity	Additive toxicity
Tacrolimus	Increased nephrotoxicity	Additive toxicity
Vancomycin	Increased nephrotoxicity	Additive toxicity
Zidovudine	Potential for increased myelotoxicity and nephrotoxicity	Mechanism not established
Anidulafungin With		
Cyclosporine	Increased anidulafungin exposure	Mechanism not established
Artemisinins With		
CYP3A inducers	Decreased artemether-lumefantrine exposure	Increased metabolism
CYP3A inhibitors	Increased artemether-lumefantrine exposure	Decreased metabolism
Atovaquone With		
Efavirenz	Decreased atovaquone exposure	Mechanism not established
Rifamycins	Decreased atovaquone exposure	Mechanism not established
Azithromycin With		
Aluminum-magnesium antacids	Decreased peak; no effect on overall exposure	Decreased absorption
Cyclosporine	Possible increased cyclosporine effect, toxicity	Mechanism not established
Digoxin	Increased digoxin concentrations	Destruction of intestinal *Eubacterium lentum* in 10% of digoxin patients
Nelfinavir	Increased azithromycin exposure	P-gp competition
Warfarin	Possible increased warfarin effect, toxicity	Decreased vitamin K–producing gut flora
Aztreonam With		
Chloramphenicol	Possible in vitro antagonism; administer a few hours apart	Mechanism not established
Bacitracin With		
Aminoglycosides	Increased nephrotoxicity	Additive toxicity
Anesthetics	Potentiation of neuromuscular blocking effects	Additive toxicity
Neuromuscular blocking drugs	Potentiation of neuromuscular blocking effects	Additive toxicity
Polymyxins	Increased nephrotoxicity	Additive toxicity
Bedaquiline With		
CYP3A inducers	Decreased bedaquiline exposure	Increased metabolism
CYP3A inhibitors	Increased bedaquiline exposure	Decreased metabolism

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Capreomycin With		
Aminoglycosides	Increased nephrotoxicity and/or ototoxicity	Additive toxicity
BCG vaccine	Negates BCG vaccine effect	Negates immune response
Polymyxins	Increased nephrotoxicity	Additive toxicity
Vancomycin	Increased nephrotoxicity and/or ototoxicity	Additive toxicity
Carbapenems With		
Cyclosporine	Increased cyclosporine and imipenem-cilastatin exposures, toxicities	Mechanism not established
Ganciclovir	Increased seizure risk with imipenem-cilastatin	Mechanism not established
Probenecid	Increased carbapenem exposure	Decreased tubular secretion
Theophylline	Increased CNS toxicity risk with imipenem-cilastatin	Mechanism not established
Valproic acid	Decreased valproic acid exposure	Mechanism not established
Caspofungin With		
Carbamazepine	Decreased caspofungin effect	Increased metabolism
Cyclosporine	Increased caspofungin effect, toxicity	Mechanism not established
Dexamethasone	Decreased caspofungin effect	Increased metabolism
Efavirenz	Decreased caspofungin effect	Increased metabolism
Nelfinavir	Decreased caspofungin effect	Increased metabolism
Nevirapine	Decreased caspofungin effect	Increased metabolism
Phenytoin	Decreased caspofungin effect	Increased metabolism
Rifamycins	Decreased caspofungin effect	Increased metabolism
Tacrolimus	Decreased tacrolimus effect	Mechanism not established
Cefditoren With		
Antacids	Decreased cefditoren effect	Decreased bioavailability
H_2 receptor antagonists	Decreased cefditoren effect	Decreased bioavailability
Proton pump inhibitors	Decreased cefditoren effect	Decreased bioavailability
Cephalosporins With		
Alcohol	Disulfiram-like effect with cefotetan	Inhibition of intermediary metabolism of alcohol
Ampicillin	In vitro antagonism with ceftazidime versus group B streptococci and *Listeria*	Mechanism not established
Chloramphenicol	In vitro antagonism	Mechanism not established
Diuretics	Increased nephrotoxicity with some cephalosporins	Mechanism not established
Polymyxins	Increased nephrotoxicity	Additive toxicity
Probenecid	Higher and prolonged cephalosporin concentrations	Competitive inhibition of tubular secretion
Salicylates	Decreased cefixime concentration and area under the serum antiinfective AUC	Displacement from protein binding sites
Warfarin	Increased bleeding risk with some cephalosporins	Mechanism not established
Chloramphenicol With		
Acetaminophen	Possible decreased chloramphenicol effect	Increased metabolism
Aminoglycosides	In vitro antagonism; not seen in vivo	Mechanism not established
Aztreonam	Antagonism; administer chloramphenicol separately a few hours later	Mechanism not established
Barbiturates	Increased barbiturate effect; decreased chloramphenicol effect	Decreased, increased metabolism
Cephalosporins	Antagonism	Mechanism not established
Cimetidine	Aplastic anemia	Possibly additive or synergistic toxicity
Cyclophosphamide	Decreased cyclophosphamide effect	Decreased clearance
Etomidate	Prolonged anesthesia	Decreased metabolism
Folic acid	Delayed response to folic acid	Mechanism not established
Iron	Delayed response to iron	Mechanism not established
Lincomycin	Decreased lincomycin effect	Target site antagonism
Penicillins	In vitro antagonism; not seen in vivo	Mechanism not established

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Phenytoin	Increased phenytoin toxicity Possible increased chloramphenicol toxicity	Decreased metabolism Mechanism not established
Rifamycins	Decreased chloramphenicol effect	Increased metabolism
Sulfonylureas	Increased hypoglycemic effect	Mechanism not established
Vitamin B_{12}	Delayed response to vitamin B_{12}	Mechanism not established
Warfarin	Increased warfarin effect	Mechanism not established
Chloroquine With		
Ampicillin	Decreased ampicillin effect	Decreased bioavailability
Cholestyramine	Decreased effect	Decreased bioavailability
Cimetidine	Increased toxicity	Decreased clearance
Cyclosporine	Increased cyclosporine toxicity	Decreased clearance
Magnesium antacids	Decreased efficacy	Decreased bioavailability
Methotrexate	Decreased methotrexate efficacy	Increased clearance
Rabies vaccine	Decreased vaccine effect	Interference with antibody response
Ritonavir	Increased chloroquine toxicity	Decreased metabolism
Succinylcholine	Increased neuromuscular blockade	Decreased clearance
Cidofovir With		
Aminoglycosides	Increased risk of nephrotoxicity	Additive toxicity
Foscarnet	Increased risk of nephrotoxicity	Additive toxicity
Pentamidine	Increased risk of nephrotoxicity	Additive toxicity
Clarithromycin With		
BZDs	Increased CNS toxicity	Decreased metabolism
CBZ	Increased CBZ toxicity	Decreased metabolism
Cimetidine	Decreased clarithromycin concentrations	Prolonged absorption
Cisapride	Increased cisapride effect, toxicity	Decreased metabolism
Clindamycin	In vitro antagonism; not documented clinically	Mechanism not established
Corticosteroids	Increased steroid effect, toxicity	Decreased excretion
Cyclosporine	Increased cyclosporine toxicity	Decreased metabolism
Delavirdine	Increased clarithromycin toxicity	Decreased metabolism
Digoxin	Increased digoxin effect	Decreased gut metabolism, increased absorption
Disopyramide	Increased disopyramide effect, toxicity	Mechanism not established
Ergot alkaloids	Increased ergot effect, toxicity	Mechanism not established
Fluoxetine	Increased fluoxetine effect, toxicity	Decreased metabolism
HMG-CoA reductase inhibitors	Increased risk of rhabdomyolysis	Decreased metabolism
Omeprazole	Increased omeprazole effect, toxicity; increased clarithromycin gastric tissue exposure	Decreased metabolism; mechanism not established
Phenytoin	Possible increased or decreased effect	Altered metabolism
Pimozide	Increased pimozide effect, toxicity	Decreased metabolism
Rifamycins	Decreased clarithromycin concentrations, increased rifamycin toxicity	Increased, decreased metabolism
Ritonavir	Increased clarithromycin effect, toxicity	Decreased metabolism
Saquinavir	Increased saquinavir effect, toxicity	Decreased metabolism
Sildenafil	Increased sildenafil effect, toxicity	Decreased metabolism
Tacrolimus	Increased tacrolimus effect, toxicity	Decreased metabolism
Theophylline	Increased theophylline effect, toxicity	Decreased metabolism
Warfarin	Increased warfarin effect, toxicity	Decreased metabolism
Zidovudine	Decreased zidovudine effect	Mechanism not established
Clindamycin With		
Neuromuscular blocking agents	Increased neuromuscular blockade	Additive toxicity
Saquinavir	Increased clindamycin toxicity	Decreased metabolism

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Clofazimine With		
Dapsone	Possible decrease or nullification of clofazimine's antiinflammatory activity	Opposing effects on neutrophil motility and lymphocyte transformation
Isoniazid	Increased clofazimine serum and urine concentrations, decreased skin concentrations	Mechanism not established
Phenytoin	Decreased efficacy	Increased phenytoin clearance
Rifampin	Decreased rate of absorption, time to reach peak, and AUC of rifampin	Mechanism not established
Cobicistat With		
CYP3A substrates	Increased substrate exposure	Decreased metabolism
CYP3A inducers	Decreased cobicistat exposure	Increased metabolism
Cycloserine With		
Alcohol	Increased alcohol effect or convulsions	Mechanism not established
Anticoagulants, oral	Increased effect	Mechanism not established
Ethionamide	Increased neurotoxicity	Additive toxicity
Isoniazid	CNS effects, dizziness, drowsiness; increased neurotoxicity	Mechanism not established, additive toxicity
Phenytoin	Increased phenytoin effect, toxicity	Decreased metabolism
Daclatasvir With		
Amiodarone	Symptomatic bradycardia	Mechanism not established
CYP3A inducers	Decreased daclatasvir exposure	Increased metabolism
CYP3A inhibitors	Increased daclatasvir exposure	Decreased metabolism
Digoxin	Increased digoxin exposure	Mechanism not established
HMG-CoA reductase inhibitors	Increased statin exposure	Decreased metabolism
Dapsone With		
Clofazimine	Possible decrease in or nullification of clofazimine's antiinflammatory activity	Opposing effects on neutrophil motility and lymphocyte transformation in vitro
Delavirdine	Increased dapsone toxicity	Decreased metabolism
Didanosine	Increased incidence of *Pneumocystis jirovecii* pneumonia recurrence	Mechanism not established
Folic acid antagonists	Increased risk of hematologic toxicity	Additive toxicity
Niridazole	Increased risk of hemolysis in G6PD deficiency	Additive toxicity
Nitrofurantoin	Increased risk of hemolysis in G6PD deficiency	Additive toxicity
Primaquine	Increased risk of hemolysis in G6PD deficiency	Additive toxicity
Pyrimethamine	Increased risk of hematologic toxicity	Additive toxicity
Rifamycins	Decreased dapsone serum concentrations	Hepatic enzyme induction
Saquinavir	Increased dapsone toxicity	Decreased metabolism
Trimethoprim	Increased dapsone serum concentrations; increased risk of adverse effects	Mechanism not established
Warfarin	Increased warfarin effect	Decreased metabolism
Zidovudine	Increased risk of hematologic toxicity	Additive toxicity
Daptomycin With		
HMG-CoA reductase inhibitors	Possible increased risk of myopathy	Additive toxicity
Tobramycin	Possible increased exposure to daptomycin, possible decreased exposure to tobramycin	Mechanism not established
Darunavir With		
Antihistamines	Increased antihistamine exposure, toxicity	CYP3A inhibition
Benzodiazepines	Increased benzodiazepine exposure, toxicity	CYP3A inhibition
Cisapride	Increased cisapride exposure, toxicity	CYP3A inhibition
CYP3A substrates	Increased exposure	CYP3A inhibition
Ergot derivatives	Increased ergot exposure, toxicity	CYP3A inhibition
Ombitasvir-paritaprevir-ritonavir	Decreased darunavir exposure	Mechanism not established
Pimozide	Increased pimozide exposure, toxicity	CYP3A inhibition

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Delavirdine With		
Alfentanil	Increased alfentanil effect, toxicity	Decreased metabolism
Amiodarone	Increased amiodarone effect, toxicity	Decreased metabolism
Amprenavir	Decreased amprenavir clearance; increased delavirdine clearance	Cytochrome P-450 (CYP) 3A4 interaction
Antacids	Decreased delavirdine effect	Decreased bioavailability
Anthracyclines	Increased anthracycline effect, toxicity	Decreased metabolism
Azole antifungals	Increased azole exposure, toxicity	Decreased metabolism
Barbiturates	Increased barbiturate effect, toxicity; decreased delavirdine effect	Decreased, increased metabolism
BZDs	Increased BZD effect, toxicity	Decreased metabolism
Calcium channel blockers	Increased calcium blocker effect, toxicity	Decreased metabolism
CBZ	Increased CBZ toxicity; decreased delavirdine effect	Decreased, increased metabolism
Clarithromycin	Increased clarithromycin, delavirdine effect, toxicity	Decreased metabolism
Clindamycin	Increased clindamycin effect, toxicity	Decreased metabolism
Corticosteroids	Increased steroid effect, toxicity	Decreased metabolism
Cyclosporine	Increased cyclosporine effect, toxicity	Decreased metabolism
Cyclophosphamide	Increased cyclophosphamide toxicity; decreased delavirdine effect	Decreased, increased metabolism
Dapsone	Increased dapsone effect, toxicity	Decreased metabolism
Ergot derivatives	Increased ergot effect, toxicity	Decreased metabolism
Erythromycin	Increased erythromycin, delavirdine effect, toxicity	Decreased metabolism
Fluoxetine	Increased delavirdine effect, toxicity	Decreased metabolism
Garlic supplements	Decreased delavirdine effect	Increased metabolism
H_2 receptor antagonists	Decreased delavirdine effect	Decreased bioavailability
HMG-CoA reductase inhibitors	Increased exposure and toxicity	Decreased metabolism
Ifosfamide	Increased ifosfamide effect, toxicity	Decreased metabolism
Lidocaine	Increased lidocaine effect, toxicity	Decreased metabolism
Metronidazole	Increased metronidazole effect, toxicity	Decreased metabolism
Nefazodone	Increased nefazodone effect, toxicity	Decreased metabolism
Paclitaxel	Increased paclitaxel toxicity	Decreased metabolism
Phenytoin	Increased phenytoin effect, toxicity; decreased delavirdine effect	Decreased, increased metabolism
Pimozide	Increased pimozide effect, toxicity	Decreased metabolism
Pioglitazone	Possible increased pioglitazone exposure, effects; possible decreased delavirdine exposure	CYP inhibition; CYP induction
Proton pump inhibitors	Decreased delavirdine effect	Decreased bioavailability
Quinidine	Increased quinidine effect, toxicity	Decreased metabolism
Repaglinide	Increased repaglinide exposure, effects	Decreased metabolism
Rifamycins	Increased rifamycin effect, toxicity; decreased delavirdine effect	Decreased, increased metabolism
Sildenafil	Increased sildenafil effect, toxicity	Decreased metabolism
Sirolimus	Increased sirolimus effect, toxicity	Decreased metabolism
St. John's wort	Decreased delavirdine effect	Increased metabolism
Sulfonylureas	Increased sulfonylurea exposure, effects	Decreased metabolism
Tacrolimus	Increased tacrolimus effect, toxicity	Decreased metabolism
Tolbutamide	Increased tolbutamide exposure, effects	Decreased metabolism
Warfarin	Increased warfarin effect, toxicity	Decreased metabolism
Zolpidem	Increased zolpidem effect, toxicity	Decreased metabolism
Didanosine With		
Allopurinol	Increased didanosine effect, toxicity	Decreased didanosine clearance
Antacids	Increased toxicity caused by ingredients in both	Additive toxicity
BZDs	Increased confusion	Mechanism not established
Bisphosphonates	Decreased effect of bisphosphonates	Decreased bioavailability

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Chloramphenicol	Increased peripheral neuropathy	Additive toxicity
Cisplatin	Increased peripheral neuropathy	Additive toxicity
Dapsone	Decreased dapsone effect, increased peripheral neuropathy	Decreased dapsone bioavailability, additive toxicity
Delavirdine	Decreased delavirdine, didanosine effect	Mechanism not established
Disulfiram	Increased peripheral neuropathy	Additive toxicity
Ethambutol	Increased peripheral neuropathy, ocular toxicity	Additive toxicity
Ethionamide	Increased peripheral neuropathy	Additive toxicity
Fluoroquinolones	Decreased fluoroquinolone, didanosine effects	Decreased bioavailability
Ganciclovir	Increased peripheral neuropathy, pancreatitis	Altered bioavailability of both
Hydralazine	Increased peripheral neuropathy	Additive toxicity
Indinavir	Decreased indinavir effect	Decreased bioavailability
Iodoquinol	Increased peripheral neuropathy	Additive toxicity
Isoniazid	Increased peripheral neuropathy	Additive toxicity
Itraconazole	Decreased itraconazole effect	Decreased bioavailability
Ketoconazole	Decreased ketoconazole effect	Decreased bioavailability
Methadone	Decreased didanosine effect	Decreased bioavailability
Metronidazole	Increased peripheral neuropathy	Additive toxicity
Nitrofurantoin	Increased peripheral neuropathy	Additive toxicity
Pentamidine	Increased risk of pancreatitis	Additive toxicity
Phenytoin	Increased peripheral neuropathy	Additive toxicity
Ribavirin	Increased risk of toxicity	Additive toxicity
Tetracyclines	Decreased tetracycline effect	Decreased bioavailability
Trimethoprim-sulfamethoxazole	Increased pancreatitis	Additive toxicity
Vincristine	Increased peripheral neuropathy	Additive toxicity
Zalcitabine	Increased neurotoxicity	Additive toxicity
Dolutegravir With		
Antacids	Decreased dolutegravir exposure with polyvalent cation–containing medications	Decreased absorption
Carbamazepine	Decreased dolutegravir exposure	Increased metabolism
Efavirenz	Decreased dolutegravir exposure	Increased metabolism
Etravirine	Decreased dolutegravir exposure	Increased metabolism
Fosamprenavir	Decreased dolutegravir exposure	Increased metabolism
Metformin	Increased metformin exposure	Tubular secretion inhibition
Nevirapine	Decreased dolutegravir exposure	Increased metabolism
Oxcarbazepine	Decreased dolutegravir exposure	Increased metabolism
Phenobarbital	Decreased dolutegravir exposure	Increased metabolism
Phenytoin	Decreased dolutegravir exposure	Increased metabolism
St. John's wort	Decreased dolutegravir exposure	Increased metabolism
Tipranavir	Decreased dolutegravir exposure	Increased metabolism
Efavirenz With		
Amiodarone	Decreased amiodarone effect	Increased metabolism
Azole antifungals	Increased efavirenz effect, decreased azole effect, toxicity	Decreased, increased metabolism
Barbiturates	Decreased barbiturate, efavirenz effects	Increased metabolism
Bupropion	Decreased bupropion effect	Increased metabolism
BZDs	Decreased BZD effect	Increased metabolism
CBZ	Decreased CBZ, efavirenz effects	Increased metabolism
Clarithromycin	Increased efavirenz effect, toxicity	Decreased metabolism
Corticosteroids	Decreased efavirenz, steroid effects	Increased metabolism
Cyclosporine	Decreased cyclosporine effect; increased efavirenz effect, toxicity	Increased, decreased metabolism

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Elbasvir-grazoprevir	Decreased elbasvir and grazoprevir exposure	Increased metabolism
Ergot alkaloids	Increased ergot effect, toxicity	Decreased metabolism
Erythromycin	Increased efavirenz effect, toxicity	Decreased metabolism
Fluoxetine	Increased risk of serotonin syndrome	Decreased metabolism
Garlic supplements	Decreased efavirenz effect	Increased metabolism
Indinavir	Decreased indinavir concentrations	Increased metabolism
Methadone	Decreased methadone effect; withdrawal	Increased metabolism
Oral contraceptives	Decreased contraceptive effect	Increased metabolism
Paclitaxel	Decreased paclitaxel effect	Increased metabolism
Phenytoin	Decreased phenytoin, efavirenz effects	Increased metabolism
Repaglinide	Decreased repaglinide effect	Increased metabolism
Rifamycins	Decreased efavirenz effect	Increased metabolism
Ritonavir	Decreased ritonavir concentration	Increased metabolism
St. John's wort	Decreased efavirenz effect	Increased metabolism
Terfenadine	Increased risk of cardiotoxicity	Decreased metabolism
Warfarin	Decreased warfarin effect	Increased metabolism
Zidovudine	Decreased zidovudine concentration	Increased metabolism
Elbasvir-Grazoprevir With		
Cyclosporine	Increased grazoprevir exposure and ALT elevation	OATP1B1/3 inhibition
CYP3A inducers	Decreased elbasvir and grazoprevir exposure	Increased metabolism
Efavirenz	Decreased elbasvir and grazoprevir exposure	Increased metabolism
Eltrombopag	Increased grazoprevir exposure and ALT elevation	OATP1B1/3 inhibition
Etravirine	Decreased elbasvir and grazoprevir exposure	Increased metabolism
HMG-CoA reductase inhibitors	Increased statin exposure	Mechanism not established
Protease inhibitors	Increased grazoprevir exposure and ALT elevation	Mechanism not established
Tacrolimus	Increased tacrolimus exposure	Mechanism not established
Elvitegravir-Cobicistat-Emtricitabine-Tenofovir With		
Alfuzosin	Increased alfuzosin exposure	Decreased metabolism
BZDs	Prolonged sedation or respiratory depression	Decreased metabolism
Ergotamine derivatives	Life-threatening ergot toxicity	Decreased metabolism
HMG-CoA reductase inhibitors	Myopathy including rhabdomyolysis	Decreased metabolism
Pimozide	Cardiac arrhythmias	Decreased metabolism
Rifampin	Decreased elvitegravir exposure	Increased metabolism
Sildenafil	Visual disturbance, syncope, priapism, and hypotension	Decreased metabolism
St. John's wort	Decreased elvitegravir exposure	Increased metabolism
Enfuvirtide With		
Tipranavir	Increased tipranavir exposure	Mechanism not established
Entecavir With		
Probenecid	Increased entecavir exposure	Tubular secretion inhibition
Erythromycin With		
Alfentanil	Increased alfentanil toxicity	Decreased metabolism
Bromocriptine	Increased toxicity	Increased bioavailability
BZDs	Increased BZD toxicity	Decreased metabolism
CBZ	Increased CBZ toxicity	Decreased metabolism
Clindamycin	Antagonism	Target site competition
Clozapine	Increased clozapine toxicity	Decreased metabolism
Corticosteroids	Increased steroid effect, toxicity	Decreased excretion
Cyclosporine	Increased cyclosporine toxicity	Decreased metabolism

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Digoxin	Increased digoxin effect	Decreased GI metabolism and increased absorption
Disopyramide	Cardiac arrhythmias	Decreased metabolism
Ergot alkaloids	Increased ergot toxicity	Mechanism not established
Felodipine	Increased toxicity	Decreased metabolism
HMG-CoA reductase inhibitors	Increased risk of rhabdomyolysis	Decreased clearance
Lidocaine	Decreased clearance; increased monoethylglycinexylidide (MEGX) concentration	Decreased metabolism
Phenytoin	Possible increased or decreased effect	Altered metabolism
Quinidine	Increased quinidine effect, toxicity	Decreased metabolism
Ritonavir	Increased erythromycin toxicity	Decreased metabolism
Sildenafil	Increased sildenafil effect, toxicity	Decreased metabolism
Tacrolimus	Increased tacrolimus toxicity	Decreased metabolism
Theophylline	Increased theophylline effect and possible toxicity	Decreased metabolism
Trimetrexate	Increased trimetrexate toxicity	Decreased metabolism
Valproic acid	Increased toxicity	Decreased metabolism
Vinblastine	Increased vinblastine toxicity	Decreased metabolism
Warfarin	Increased warfarin effect, toxicity	Decreased metabolism
Zafirlukast	Decreased zafirlukast effect	Mechanism not established
Ethambutol With		
Aluminum-containing antacids	Decreased ethambutol exposure	Decreased absorption
Ethionamide With		
Aminosalicylic acid	Increased GI distress, hepatotoxicity	Mechanism not established
BCG vaccine	Negates BCG vaccine effect	Negates immune response
Cycloserine	Increased neurotoxicity	Additive toxicity
Ethambutol	Increased ethambutol toxicity	Mechanism not established
Isoniazid	Increased neurotoxicity	Additive toxicity
Pyrazinamide	Increased hepatotoxicity	Additive toxicity
Rifamycins	Increased hepatotoxicity	Additive toxicity
Etravirine With		
Antiarrhythmic agents	Decreased antiarrhythmic exposure	Metabolism induction
Anticonvulsants	Decreased etravirine exposure, effect	Metabolism induction
Atazanavir-ritonavir	Increased etravirine and decreased atazanavir concentrations, effects	Metabolism inhibition and induction
Azole antifungals	Increased etravirine, decreased azole exposure	Decreased, increased metabolism
Clarithromycin	Decreased clarithromycin and increased 14-hydroxyclarithromycin exposures	Metabolism induction
Darunavir-ritonavir	Decreased etravirine exposure	Metabolism induction
Dexamethasone	Decreased etravirine exposure	Mechanism not established
Diazepam	Increased diazepam exposure	Metabolism inhibition
Elbasvir-grazoprevir	Decreased elbasvir and grazoprevir exposure	Increased metabolism
Fosamprenavir-ritonavir	Increased amprenavir exposure, toxicity	Metabolism inhibition
HMG-CoA reductase inhibitors	Decreased lovastatin, simvastatin, increased fluvastatin exposures	Metabolism induction, inhibition
Immunosuppressants	Possible decreased cyclosporine, sirolimus, and tacrolimus exposures	Metabolism induction
Lopinavir-ritonavir	Increased etravirine exposure	Metabolism inhibition
Methadone	Minimal change	—
NNRTIs	Decreased etravirine exposure with efavirenz or nevirapine, increased etravirine exposures with delavirdine	Metabolism induction, inhibition
Phosphodiesterase inhibitors	Possible decreased sildenafil effect	Mechanism not established
Protease inhibitors	Must ensure low-dose ritonavir is given with any etravirine–protease inhibitor combinations	Mechanism not established
Rifamycins	Decreased etravirine exposures	Metabolism induction

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Ritonavir	Significant decrease in etravirine exposure	Metabolism induction
Saquinavir-ritonavir	Decrease etravirine exposure	Metabolism induction
St. John's wort	Decreased etravirine exposure	Metabolism induction
Tipranavir-ritonavir	Decreased etravirine effect	Metabolism induction
Warfarin	Increased warfarin exposure	Metabolism inhibition
Fluconazole With		
Amitriptyline	Increased amitriptyline toxicity	Decreased metabolism
Amphotericin B	Possible antagonism in animal models	Mechanism not established
BZDs	Increased CNS toxicity	Decreased metabolism
Cimetidine	Decreased fluconazole effect	Decreased bioavailability
Cisapride	Increased risk of cardiotoxicity	Decreased metabolism
Cyclosporine	Increased cyclosporine concentration	Mechanism not established
DHP CCB	Increased DHP CCB toxicity	Decreased metabolism
Etravirine	Increased etravirine concentration	Metabolism inhibition
HMG-CoA reductase inhibitors	Increased risk of rhabdomyolysis	Mechanism not established
Phenytoin	Increased phenytoin concentration	Decreased metabolism
Quetiapine	Possible increased quetiapine concentration	Decreased metabolism
Rifamycins	Decreased fluconazole concentration	Mechanism not established
Sulfonylureas	Increased plasma concentration; decreased metabolism of tolbutamide, glyburide, glipizide	Mechanism not established
Tacrolimus	Increased tacrolimus toxicity	Decreased metabolism
Terfenadine	Increased risk of cardiotoxicity	Decreased metabolism
Thiazides	Increased fluconazole concentrations and AUC of fluconazole	Decreased renal clearance
Warfarin	Increased warfarin effect	Metabolism inhibition
Zidovudine	Increased zidovudine concentrations	Decreased metabolism
Flucytosine With		
Amphotericin B	Increased flucytosine toxicity	Increased cellular flucytosine uptake
Zidovudine	Increased hematologic toxicity	Additive toxicity
Fluoroquinolones With		
Antacids	Decreased fluoroquinolone effect with aluminum or magnesium antacids	Decreased absorption
BCG vaccine	Negates BCG vaccine effect	Negates immune response
Chloramphenicol	Inhibition in vitro of norfloxacin bactericidal activity	Mechanism not established
Cyclosporine	Increased risk of nephrotoxicity; increased serum cyclosporine concentration	Mechanism not established
Didanosine	Decreased fluoroquinolone effect	Decreased GI absorption
Iron	Decreased serum fluoroquinolone concentration	Decreased GI absorption
Mineral fortified foods	Decreased fluoroquinolone concentration	Decreased GI absorption
NSAIDs	Possible increased risk of CNS stimulation	Mechanism not established
Oral contraceptives	Possible decreased effect of moxifloxacin	Increased metabolism
Oral hypoglycemics	Increased incidence, severity of hypoglycemia	Mechanism not established
Probenecid	Increased serum concentration and AUC	Decreased tubular secretion
Rifamycins	Inhibition in vitro of norfloxacin bactericidal activity	Mechanism not established
Riluzole	Increased risk of riluzole toxicity	Decreased elimination
Ropivacaine	Increased risk of ropivacaine toxicity	Decreased metabolism
Scopolamine	Decreased rate of fluoroquinolone absorption	Mechanism not established
Sucralfate	Decreased serum fluoroquinolone concentration	Decreased GI absorption
Tetracycline	Inhibition in vitro of norfloxacin bactericidal activity	Mechanism not established
Theophylline	Possible theophylline toxicity	Decreased metabolism

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Tizanidine	Increased tizanidine concentrations, toxicity with ciprofloxacin	Metabolism inhibition
Warfarin	Increased warfarin effect	Disruption of vitamin K synthesis
Zinc	Decreased serum fluoroquinolone concentrations	Decreased GI absorption
Fosamprenavir With		
Antacids	Decreased amprenavir exposure	Mechanism not established
Antiarrhythmics	Increased antiarrhythmic exposure, toxicity	Metabolism interaction
Anticonvulsants	Decreased amprenavir exposure, increased anticonvulsant exposure	Metabolism site competition
Azole antifungals	Increased azole and amprenavir exposures	Metabolism interaction
BZDs	Increased benzodiazepine exposure, toxicity	Metabolism interaction
CCBs	Increased CCB exposures, toxicity	Metabolism interaction
Cisapride	Increased cisapride exposure, toxicity	Metabolism interaction
Contraceptives, oral	Decreased amprenavir concentration, change in oral contraceptive exposure	Metabolism interaction
Corticosteroids	Increased corticosteroid exposure	Metabolism interaction
CYP3A inhibitors	Increased amprenavir exposure	Metabolism interaction
Delavirdine	Increased amprenavir and decreased delavirdine exposures	Metabolism interaction
Dexamethasone	Decreased amprenavir exposure	Metabolism interaction
Efavirenz-ritonavir	Increased amprenavir exposure	Metabolism interaction
Ergot derivatives	Increased ergot exposure, toxicity	Metabolism interaction
Esomeprazole	Increased esomeprazole exposure	Metabolism interaction
H_2 receptor antagonists	Decreased amprenavir exposure	Mechanism not established
HMG-CoA reductase inhibitors	Increased HMG-CoA exposure, toxicity; decreased amprenavir exposure	Metabolism interaction
Immunosuppressants	Increased immunosuppressant exposure	Metabolism interaction
Indinavir	Increase in amprenavir and decrease in indinavir exposures	Metabolism interaction
Lopinavir-ritonavir	Decreased amprenavir, increased lopinavir-ritonavir exposures	Metabolism interaction
Methadone	Decreased amprenavir and methadone exposures	Metabolism interaction
Nevirapine	Decreased amprenavir, increased nevirapine exposures	Metabolism interaction
Opiates	Increased opiate exposure, toxicity	Metabolism interaction
Paroxetine	Decreased paroxetine exposure	Metabolism interaction
Phenytoin	Decreased phenytoin exposure	Metabolism interaction
Phosphodiesterase inhibitors	Increased phosphodiesterase inhibitor exposure, toxicity	Metabolism interaction
Pimozide	Increased pimozide exposure, toxicity	Metabolism interaction
Ranolazine	Increased ranolazine exposure, toxicity	Metabolism interaction
Rifabutin	Increased rifabutin and amprenavir exposures	Metabolism interaction
Rifampin	Decreased amprenavir exposure	Metabolism interaction
Saquinavir	Decreased amprenavir exposure	Metabolism interaction
St. John's wort	Decreased amprenavir exposure	Metabolism interaction
Trazodone	Increased trazodone exposure, toxicity	Metabolism interaction
Tricyclic antidepressants	Increased tricyclic exposure, toxicity	Metabolism interaction
Warfarin	Possible change in warfarin exposure	Mechanism not established
Zidovudine	Increased amprenavir and zidovudine exposures	Metabolism interaction
Foscarnet With		
Acyclovir	Increased nephrotoxicity	Additive toxicity
Cidofovir	Increased nephrotoxicity	Additive toxicity
Pentamidine	Increased nephrotoxicity; increased hypocalcemia	Additive toxicity
Probenecid	Increased foscarnet serum concentration; increased possibility of adverse effects	Decreased tubular secretion
Suramin	Increased nephrotoxicity	Additive toxicity
Trimethoprim-sulfamethoxazole	Increased nephrotoxicity	Additive toxicity

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Ganciclovir/Valganciclovir With		
Aminoglycosides	Increased nephrotoxicity	Additive toxicity
Amphotericin B	Increased nephrotoxicity; replication inhibition of rapidly dividing host cells	Additive toxicity; additive
Cyclosporine	Increased nephrotoxicity	Additive toxicity
Cytotoxic antineoplastics	Replication inhibition of rapidly dividing host cells	Additive
Dapsone	Replication inhibition of rapidly dividing host cells	Additive
Didanosine	Increased didanosine effect, toxicity	Increased bioavailability
Flucytosine	Replication inhibition of rapidly dividing host cells	Additive
Imipenem-cilastatin	Generalized seizures	Mechanism not established
Immunosuppressives	Increased suppression of bone marrow and immune system	Additive toxicity
Nucleoside analogues	Replication inhibition of rapidly dividing host cells	Additive
Pentamidine	Replication inhibition of rapidly dividing host cells	Additive
Probenecid	Increased ganciclovir concentration; prolonged AUC	Decrease in tubular secretion
Pyrimethamine	Replication inhibition of rapidly dividing host cells	Additive
Tacrolimus	Increased risk of nephrotoxicity	Additive toxicity
Trimethoprim-sulfamethoxazole	Replication inhibition of rapidly dividing host cells	Additive
Zidovudine	In vitro antiretroviral antagonism; increased risk of hematologic toxicity	Mechanism not established; additive toxicity
Glecaprevir-Pibrentasvir With		
Atazanavir	Increased ALT	Mechanism not established
CBZ	Decreased glecaprevir and pibrentasvir exposure	Increased P-gp–mediated efflux
Cyclosporine	Decreased glecaprevir and pibrentasvir exposure	Mechanism not established
Dabigatran	Increased dabigatran exposure and risk of bleeding	Decreased P-gp–mediated efflux
Estrogens	Increased ALT	Mechanism not established
HMG-CoA reductase inhibitors	Increased statin toxicities	Mechanism not established
Rifampin	Decreased glecaprevir and pibrentasvir exposure	Increased P-gp–mediated efflux
Ritonavir	Increased glecaprevir and pibrentasvir exposure	Decreased P-gp–mediated efflux
St. John's wort	Decreased glecaprevir and pibrentasvir exposure	Increased P-gp–mediated efflux
Griseofulvin With		
Alcohol	Increased alcohol effects, tachycardia and flushing	Mechanism not established
Anticoagulants, oral	Decreased anticoagulant effect	Mechanism not established
Contraceptives, oral	Decreased contraceptive effect	Increased metabolism
Phenobarbital	Decreased griseofulvin concentrations	Decreased absorption or hepatic enzyme induction
Hydroxychloroquine With		
Digoxin	Increased digoxin effect	Mechanism not established
Imipenem-Cilastatin With		
Chloramphenicol	Antagonism; administer a few hours after imipenem-cilastatin	Mechanism not established
Cyclosporine	Increased cyclosporine and imipenem-cilastatin exposures, toxicities	Mechanism not established
Ganciclovir	Generalized seizures	Mechanism not established
Probenecid	Increased imipenem-cilastatin exposure	Decreased tubular secretion
Valproic acid	Decreased valproic acid exposure	Mechanism not established
Isavuconazonium With		
Bupropion	Decreased bupropion exposure	Mechanism not established
CYP3A inducers	Decreased isavuconazonium exposure	Increased metabolism
CYP3A substrates	Increased substrate exposure	Decreased metabolism
Digoxin	Increased digoxin exposure	Mechanism not established
HMG-CoA reductase inhibitors	Increased statin exposure	Decreased metabolism
Immunosuppressants, oral	Increased immunosuppressant exposure	Decreased metabolism

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Isoniazid With		
Alcohol	Increased incidence of hepatitis Decreased isoniazid effect in some alcoholic patients	Additive toxicity Increased metabolism
Aluminum antacids	Decreased isoniazid effect	Decreased absorption
Aminosalicylic acid	Increased isoniazid concentration	Reduced acetylation
BCG vaccine	Vaccine may be ineffective	Isoniazid inhibits multiplication of BCG
BZDs	Pharmacologic effects of BZDs may be increased; documented with diazepam and triazolam	Decreased metabolism
CBZ	Increased toxicity of both drugs	Altered metabolism
Cycloserine	CNS effects, dizziness, drowsiness	Mechanism not established
Disulfiram	Psychotic episodes, ataxia	Altered dopamine metabolism
Enflurane	Possible nephrotoxicity	Increased metabolism of enflurane caused increased fluoride concentration
Ethionamide	Increased CNS adverse effects	Additive toxicity
Itraconazole	Decreased itraconazole activity	Increased metabolism
Ketoconazole	Decreased ketoconazole effect	Decreased concentration
Meperidine	Increased risk of serotonin syndrome	Additive toxicity
Phenytoin	Increased phenytoin toxicity	Decreased metabolism
Rifamycins	Possible increased isoniazid hepatotoxicity	Possible increased toxic metabolites
SSRI antidepressants	Increased risk of serotonin syndrome	Additive toxicity
Warfarin	Possible increased anticoagulant effect	Decreased metabolism
Itraconazole With		
Alfentanil	Increased alfentanil exposure	Decreased metabolism
Amphotericin B	In vitro antagonism	Mechanism not established
Antacids	Possible decreased itraconazole bioavailability	Mechanism not established
Aripiprazole	Increased aripiprazole exposure	Decreased metabolism
Barbiturates	Decreased itraconazole effect	Increased metabolism
Buspirone	Increased buspirone exposure	Metabolism interaction
BZDs	Increased CNS effects	Decreased metabolism
CBZ	Decreased itraconazole effect	Increased metabolism
Clarithromycin	Increased itraconazole exposure	Decreased metabolism
Corticosteroids	Increased corticosteroid exposure	Metabolism interaction
Cyclosporine	Possible increased cyclosporine concentrations	Mechanism not established
Didanosine	Decreased itraconazole effect	Decreased bioavailability
Digoxin	Increased digoxin toxicity	Decreased metabolism
DHP CCBs	Increased DHP CCB effect	Decreased metabolism
Docetaxel	Increased docetaxel exposure	Decreased metabolism
Dofetilide	Increased dofetilide effect, toxicity	Decreased metabolism
Eletriptan	Increased eletriptan exposure	Decreased metabolism
Ergot alkaloids	Increased ergot alkaloid exposure, toxicity	Metabolism interaction
Erythromycin	Increased itraconazole exposure	Decreased metabolism
H_2 receptor antagonists	Decreased itraconazole bioavailability	Decreased gastric acidity
HMG-CoA reductase inhibitors	Increased risk of rhabdomyolysis	Decreased metabolism
Indinavir	Increased indinavir toxicity	Decreased metabolism
Nevirapine	Decreased itraconazole exposure	Increased metabolism
Oral hypoglycemics	Increased oral hypoglycemic effects	Decreased metabolism
Phenytoin	Decreased itraconazole effect	Increased metabolism
Phosphodiesterase inhibitors	Increased phosphodiesterase inhibitor exposure	Decreased metabolism

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Pimozide	Increased pimozide effect, toxicity	Decreased metabolism
Protease inhibitors	Increased protease inhibitor exposure, increased itraconazole exposure	Decreased metabolism
Proton pump inhibitors	Decreased itraconazole bioavailability	Decreased gastric acidity
Quinidine	Increased quinidine effect, toxicity	Decreased metabolism
Rifamycins	Decreased systemic bioavailability of itraconazole	Hepatic enzyme induction
Ritonavir	Increased itraconazole concentrations	Decreased metabolism
Saquinavir	Increased saquinavir concentration	Decreased metabolism
Sirolimus	Increased sirolimus exposure	Decreased metabolism
Tacrolimus	Increased tacrolimus toxicity	Decreased metabolism
Terfenadine	Increased risk of cardiotoxicity	Decreased metabolism
Tolterodine	Increased tolterodine exposure	Decreased metabolism
Trimetrexate	Increased trimetrexate exposure	Decreased metabolism
Vinca alkaloids	Increased vinca toxicity	Mechanism not established
Warfarin	Increased warfarin effect	Decreased metabolism
Ivermectin		
Dasabuvir	Increased ivermectin exposure	Decreased BCRP-mediated efflux
Warfarin	Increased warfarin effect	Mechanism not established
Lincomycin With		
Neuromuscular blocking agents	Increased neuromuscular blockade	Mechanism not established
Ketoconazole: Same as Itraconazole *Plus*		
Alcohol	Possible disulfiram-like reaction	Mechanism not established
Delavirdine	Increased delavirdine concentration	Mechanism not established
Donepezil	Increased cholinomimetic effects	Decreased metabolism
Hepatotoxic agents	Increased hepatotoxicity	Additive toxicity
Isoniazid	Decreased ketoconazole effect	Decreased blood concentrations
Quetiapine	Increased risk of quetiapine toxicity	Decreased metabolism
Theophylline	Decreased theophylline concentration	Mechanism not established
Lamivudine With		
Nelfinavir	Increased lamivudine concentration	Decreased clearance
Pentamidine	Increased risk of pancreatitis	Additive toxicity
Sulfonamides	Increased lamivudine concentration	Decreased clearance
Trimethoprim	Increased lamivudine concentration	Decreased clearance
Trimethoprim-sulfamethoxazole	Increased risk of pancreatitis	Additive toxicity
Zidovudine	Increased zidovudine concentration	Mechanism not established
Linezolid With		
Adrenergic agents	Increased adrenergic agent effects	Monoamine oxidase (MAO) inhibition
Bupropion	Increased bupropion exposure, toxicity	Mechanism not established
Entacapone or tolcapone	Decreased catecholamine metabolism	MAO inhibition
MAO inhibitors	Increased MAO inhibitor actions, toxicity	Additive toxicity
Meperidine	Increased risk of serotonin syndrome	MAO inhibition
SNRI antidepressants	Increased risk of serotonin syndrome	MAO inhibition
SSRI antidepressants	Increased risk of serotonin syndrome	MAO inhibition
Tramadol	Increased risk of seizures	Mechanism not established
Tricyclic antidepressants	Increased risk of serotonin syndrome	MAO inhibition
Triptans	Increased triptan exposure, toxicity	MAO inhibition
Maraviroc With		
CYP3A inhibitors	Increased maraviroc exposure	CYP3A inhibition
CYP3A inducers	Decreased maraviroc exposure	CYP3A induction

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Mebendazole With		
CBZ	Decreased mebendazole concentrations	Increased metabolism
Phenytoin	Decreased mebendazole concentrations	Increased metabolism
Mefloquine With		
Anticonvulsants	Increased seizure frequency	Mechanism not established
Lumefantrine	Decreased lumefantrine exposure	Decreased absorption
Rifampin	Decreased mefloquine exposure	Increased metabolism
Methenamine With		
Sulfonamides	Increased risk of crystalluria; precipitate formation between formaldehyde and sulfamethizole	Acidification of the urine
Metronidazole With		
Alcohol	Mild disulfiram-like symptoms	Possible inhibition of intermediary metabolism of alcohol
Azathioprine	Transient neutropenia	Mechanism not established
Barbiturates	Decreased metronidazole effect with phenobarbital	Probably increased metabolism
CBZ	Increased CBZ toxicity	Decreased metabolism
Cimetidine	Possible increased metronidazole toxicity	Decreased metabolism
Disulfiram	Organic brain syndrome	Mechanism not established
Fluorouracil	Transient neutropenia	Mechanism not established
Lithium	Lithium toxicity	Mechanism not established
Warfarin	Increased warfarin effect	Decreased metabolism
Micafungin With		
Cyclosporine	Increased cyclosporine exposure	Mechanism not established
Itraconazole	Increased itraconazole exposure	Mechanism not established
Nifedipine	Increased nifedipine exposure	Mechanism not established
Sirolimus	Increased sirolimus exposure	Mechanism not established
Nafcillin With		
CYP3A substrates	Decreased effect	Increased metabolism
Warfarin	Decreased warfarin effect	Increased metabolism
Nevirapine With		
Amiodarone	Decreased amiodarone effect	Increased metabolism
Azole antifungals	Decreased azole effect; increased nevirapine effect, toxicity	Increased, decreased metabolism
Barbiturates	Decreased barbiturate, nevirapine effects	Increased metabolism
Bupropion	Decreased bupropion effect	Increased metabolism
BZDs	Decreased BZD effect	Increased metabolism
CBZ	Decreased CBZ, nevirapine effects	Increased metabolism
Cimetidine	Increased nevirapine effect, toxicity	Decreased metabolism
Clarithromycin	Increased nevirapine effect, toxicity	Decreased metabolism
Corticosteroids	Decreased nevirapine, steroid effects	Increased metabolism
Cyclosporine	Decreased cyclosporine effect; increased nevirapine effect, toxicity	Increased, decreased metabolism
Erythromycin	Increased nevirapine effect, toxicity	Decreased metabolism
Garlic supplements	Decreased nevirapine effect	Increased metabolism
Indinavir	Decreased indinavir concentration	Increased metabolism
Methadone	Decreased methadone effect; withdrawal	Increased metabolism
Oral contraceptives	Decreased contraceptive effect	Increased metabolism
Paclitaxel	Decreased paclitaxel effect	Increased metabolism
Phenytoin	Decreased phenytoin, nevirapine effects	Increased metabolism
Repaglinide	Decreased repaglinide effect	Increased metabolism
Rifamycins	Decreased nevirapine effect	Increased metabolism

Continued

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Ritonavir	Decreased ritonavir concentration	Increased metabolism
St. John's wort	Decreased nevirapine effect	Increased metabolism
Warfarin	Decreased warfarin effect	Increased metabolism
Zidovudine	Decreased zidovudine concentration	Increased metabolism
Nitrofurantoin With		
Antacids	Possible decreased nitrofurantoin effect	Decreased absorption
Fluoroquinolones	In vitro antagonism of fluoroquinolone activity	Mechanism not established
Probenecid	Increased nitrofurantoin serum concentration	Inhibition of renal excretion
Voriconazole	Decreased voriconazole exposure	Mechanism not established
Ombitasvir-Paritaprevir-Ritonavir ± Dasabuvir With		
Angiotensin receptor blockers	Increased angiotensin receptor blocker exposure	Mechanism not established
Antiarrhythmics	Increased antiarrhythmic exposure	Mechanism not established
Atazanavir	Increased paritaprevir exposure	Decreased metabolism
CCBs	Increased CCB effect	Mechanism not established
CYP3A substrates	Increased substrate exposure	Decreased metabolism
Darunavir	Decreased darunavir exposure	Mechanism not established
Digoxin	Increased digoxin exposure	Decreased P-gp–mediated efflux
HMG-CoA reductase inhibitors	Increased statin effect	Decreased metabolism
Immunosuppressants, oral	Increased immunosuppressant exposure	Decreased metabolism
Lopinavir-ritonavir	Increased paritaprevir exposure	Decreased metabolism and P-gp–mediated efflux
Metformin	Increased risk of lactic acidosis	Mechanism not established
Quetiapine	Increased quetiapine exposure	Decreased metabolism
Rilpivirine	Increased rilpivirine exposure	Mechanism not established
Voriconazole	Decreased voriconazole exposure	Mechanism not established
Oritavancin With		
Heparin	Falsely elevated aPTT results	Mechanism not established
Warfarin	Increased warfarin exposure and unreliable PT/INR results	Mechanism not established
Oseltamivir With		
Warfarin	Increased risk of bleeding	Mechanism not established
Oxacillin With		
Same as nafcillin		
Penicillins (Except Nafcillin or Oxacillin) With		
Methotrexate	Increased methotrexate toxicity	Inhibition of renal excretion
Probenecid	Increased penicillin serum concentration	Inhibition of renal excretion
Tetracyclines	Possible decreased penicillin effectiveness	Decreased bactericidal activity
Vancomycin	Increased renal toxicity with piperacillin-tazobactam and vancomycin	Mechanism not established
Warfarin	Increased warfarin effect	Disruption of gut vitamin K synthesis
Pentamidine With		
Aminoglycosides	Increased nephrotoxicity	Additive toxicity
Amphotericin B	Increased nephrotoxicity	Additive toxicity
Capreomycin	Increased nephrotoxicity	Additive toxicity
Cidofovir	Increased nephrotoxicity	Additive toxicity
Cisplatin	Increased nephrotoxicity	Additive toxicity
Foscarnet	Hypocalcemia	Mechanism not established
Methoxyflurane	Increased nephrotoxicity	Additive toxicity
Polymyxins	Increased nephrotoxicity	Additive toxicity
Vancomycin	Increased nephrotoxicity	Additive toxicity

TABLE 54.36 Adverse Drug Interactions Involving Antiinfective Agents[a]—cont'd

INTERACTING DRUGS	ADVERSE EFFECT	PROBABLE MECHANISM
Polymyxins With		
Aminoglycoside antibiotics	Increased nephrotoxicity; increased neuromuscular blockade	Additive toxicity
Neuromuscular blocking agents	Increased neuromuscular blockade	Additive toxicity
Parenteral quinine/quinidine	Increased neurotoxicity	Additive toxicity
Vancomycin	Increased nephrotoxicity	Additive toxicity
Posaconazole With		
BZDs	Increased benzodiazepine effect, toxicity	Decreased metabolism
CCBs	Increased CCB effect, toxicity	Decreased metabolism
Cimetidine	Decreased posaconazole effect	Unknown mechanism
Ergot alkaloids	Increased ergot effect, toxicity	Decreased metabolism
Halofantrine	Increased halofantrine effect, toxicity	Decreased metabolism
HMG-CoA reductase inhibitors	Increased statin effect, toxicity	Decreased metabolism
Immunosuppressants	Increased immunosuppressant effect, toxicity	Decreased metabolism
Phenytoin	Decreased posaconazole effect, increased phenytoin effect, toxicity	Metabolism interaction
Pimozide	Increased pimozide effect, toxicity	Decreased metabolism
Rifamycins	Decreased posaconazole effect, increased rifamycin effect, toxicity	Metabolism interaction
Quinidine	Increased quinidine effect, toxicity	Decreased metabolism
Vinca alkaloids	Increased vinca effect, toxicity	Decreased metabolism
Praziquantel With		
CBZ	Decreased praziquantel exposure	Increased metabolism
Dexamethasone	Decreased praziquantel exposure	Increased metabolism
Phenytoin	Decreased praziquantel exposure	Increased metabolism
Rifampin	Decreased praziquantel exposure	Increased metabolism
Primaquine With		
Ritonavir	Increased primaquine concentrations	Decreased metabolism
Proguanil With		
Chloroquine	Increased incidence of mouth ulcers	Mechanism not established
Efavirenz	Decreased exposure of active metabolite	Mechanism not established
Warfarin	Increased bleeding risk	Mechanism not established
Protease Inhibitors (Except Ritonavir) With		
Alfentanil	Increased alfentanil effects, toxicity	Decreased metabolism
Antacids	Decreased efficacy of indinavir, tipranavir	Decreased bioavailability
Antiarrhythmic agents	Increased antiarrhythmic effects, toxicities	Decreased metabolism
Azithromycin	Possible decreased nelfinavir efficacy	P-gp interaction
Azole antifungals	Increased azole and protease inhibitor effect, toxicity	Decreased metabolism
Barbiturates	Decreased protease effect, increased barbiturate effect, toxicity	Increased, decreased metabolism
Bupropion	Possible increased bupropion toxicity	Decreased metabolism
BZDs	Increased CNS BZD toxicity	Decreased metabolism
CCBs	Increased CCB effects	Decreased metabolism
CBZ	Decreased protease effect, increased CBZ effect	Increased, decreased metabolism
Clarithromycin	Increased protease toxicity	Decreased metabolism
Clindamycin	Increased clindamycin toxicity	Decreased metabolism
Corticosteroids	Increased risk of hypercorticoidism	Decreased metabolism
Cyclophosphamide	Increased cyclophosphamide toxicity, decreased protease effect	Decreased, increased metabolism
Dapsone	Increased dapsone toxicity with saquinavir	Decreased metabolism
Daunorubicin	Increased risk of cardiotoxicity	Decreased metabolism
Delavirdine	Increased protease toxicity, increased hepatotoxicity, decreased delavirdine effect	Decreased metabolism

Continued