Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose	Reference
Antibiotic/Antiviral/Antifungal									
Amantadine	—	4.75	20.0	190	—	<10% Hepatic >90% Renal	Negligible unless renal function decreased	None	
Amikacin	5	0.26	2.5	85	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None	
Ampicillin	30	0.28	1.0	340	—	<10% Hepatic >90% Renal	$t_{1/2}\uparrow$; $V_d\uparrow$; $Cl\rightarrow$; f_p ? $\rightarrow$	None	83
Aztreonam	56	0.15	1.9	70	—	33% Hepatobiliary 66% Renal	$t_{1/2}\uparrow$; $V_d\rightarrow$; $Cl\rightarrow$	Decrease if chronic, high-dosing	86
Carbenicillin	48	0.16	1.0	130	—	<10% Hepatic >90% Renal	Negligible unless renal function decreased	None	52
Cefaclor	24	0.35	1.0	280	—	<10% Hepatic >90% Renal	Negligible unless renal function decreased	None	
Cefamandole	74	0.16	1.0	130	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None	
Cefazolin	84	0.15	1.8	68	—	<5% Hepatic >95% Renal	$t_{1/2}\downarrow$; $f_p\uparrow$	None	113
Cefoperazone	90	non-linear 0.20	1.7	80	Enzyme-limited, binding-sensitive	75% Hepatic 25% Renal	$t_{1/2}\uparrow$; $V_d\rightarrow$; $Cl\downarrow$ 60%; f_p ?	Decrease dose	
Cefotaxime	36	0.24	1.2	94	—	40% Hepatic 60% Renal	$t_{1/2}\uparrow$; V_d ?; Cl ?	Unknown	
Cefotetan	83	0.15	3.7	39.5	—	80% Renal 20% Biliary (unchanged)	Negligible unless renal function decreased	None	
Cefoxitin	73	0.12	1.0	98	—	15% Hepatic 85% Renal	Negligible unless renal function decreased	None	
Ceftazidime	17	0.2	1.7	75	—	10% Hepatic 90% Renal	$t_{1/2}\uparrow$; V_d ?; Cl slight $\downarrow$	Negligible unless renal function decreased	
Ceftriaxone	90	0.14	8.4	16	Enzyme-limited, binding-sensitive	60% Hepatobiliary 40% Renal	$t_{1/2}\rightarrow$; $V_d\uparrow$ if ascites present; $Cl\rightarrow$; $fp\uparrow$	None	
Cefuroxime	30	0.33	1.2	210	—	<1% Hepatic >99% Renal	Negligible unless renal function decreased	None	
Cephalothin	75	0.30	0.60	470	—	30–50% Hepatic 50–70% Renal	$t_{1/2}$ slight $\uparrow$; $V_d\rightarrow$; $Cl\downarrow$	None	
Chloramphenicol	70	1.0	3.0	170	Enzyme-limited, binding-sensitive	>90% Hepatic <10% Renal Glucuronidation of drug	$t_{1/2}\uparrow$; V_d slight $\downarrow$; $Cl\downarrow$ 65%; f_p ? $\rightarrow$; unknown if f_p changes	Decrease dose	
Ciprofloxacin	30	2.3	4.0	350	—	40% Renal (unchanged) 15% Hepatic	Negligible unless renal function decreased	None	

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose
Clindamycin	79	0.58	2.0	160	Enzyme-limited, binding-sensitive	90% Hepatic 10% Renal	$t_{1/2}$ slight ↑; V_d →; Cl ↓ 23%; f_p →	Decrease dose in severe cases
Doxycycline	82	—	12.0	195	—	<10% Hepatic >90% Renal	Negligible unless renal function decreased	None
Erythromycin	80	0.77	1.6	600	Enzyme-limited, binding-sensitive	>90% Hepatic <10% Renal	$t_{1/2}$ ↑; no other information	Decrease dose in moderate or severe disease
Fluconazole	12	0.8	35	20	—	70% Renal (unchanged) 10% Hepatic	Negligible unless renal function decreased	None
Ganciclovir	2	0.5	3.0	185/ 1.73m²	—	>90% Renal (unchanged)	Negligible unless renal function decreased	None
Gentamicin	<5	0.25	2.0	100	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None
Imipenem	25	0.33	1.1	186	—	70% Renal (unchanged) 25% Nonspecific hydrolysis	Negligible unless renal function decreased	None
Isoniazid	<10	0.6	2.0 fast 6.0 slow	480 fast 170 slow	Enzyme-limited, binding-insensitive	85% Hepatic 15% Renal Drug acetylated	$t_{1/2}$ ↑; some assume Cl ↓; genetic differences more important than disease	Decrease dose in severe cases
Kanamycin	<10	0.20	3.0	55	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None
Metronidazole	10	0.75	8.0	85	—	>90% Hepatic <10% Renal	$t_{1/2}$ ↑; V_d ↓; Cl ↓	Decrease dose
Nafcillin	90	0.4	1.0	580	Enzyme-limited, binding-sensitive	70% Hepatic 30% Renal	$t_{1/2}$ ↑ but little change; V_d ↓; Cl ↓ 50–60%; fp ?→	Decrease dose in moderate or severe disease
Neomycin	40	—	2.0	—	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None
Rifampin	85	0.4	2.5	180	Enzyme-limited, binding-sensitive	90% Hepatic 10% Renal	$t_{1/2}$ ↑; V_d ?; Cl ↓; f_p ?	Decrease in severe disease
Streptomycin	35	0.26	2.5	85	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None
Sulfamethoxazole	66	0.17	9.0	15	Enzyme-limited, binding-sensitive	70% Hepatic 30% Renal Drug acetylated	Unknown, but probably little change unless there is severe liver disease	Slight decrease
Tobramycin	<5	0.24	2.5	80	—	<5% Hepatic >95% Renal	Negligible unless renal function decreased	None

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose	
Trimethoprim	45	1.5	12.0	96	—	30% Hepatic 70% Renal	Slight unless renal function decreased	None	
Vancomycin	55	0.4	5.0	80	—	<10% Hepatic >90% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$	Decrease dose	2
Zidovudine	36	1.6	1.1	1900	Flow-limited	14% Renal (unchanged) 74% Hepatic	$t_{1/2}$, Cl, V_d	Decrease dose	1
Analgesic									
Acetaminophen	20	0.9	2.2	350	Flow/enzyme-sensitive	>95% Hepatic <5% Renal Mostly conjugated	$t_{1/2} \uparrow$; V_d ?; $Cl \downarrow$ 54%; assume $f_p \rightarrow$; little change in Cl if albumin >3.5 g/100 ml	Avoid chronic use; single dose—no change	9,
Meperidine	65	4.5	4.5	900	Flow/enzyme-sensitive	>95% Hepatic <5% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 50%; $f_p \rightarrow$	Decrease oral dose by 50% in cirrhosis or acute viral hepatitis	10
Methadone	80	4.0	28	150	Enzyme-limited, binding-sensitive	80% Hepatic 20% Renal	$t_{1/2} \uparrow$ with severe liver disease; $Cl \rightarrow$; $V_d \uparrow$ slightly	None or decrease	10
Morphine	35	3.7	2.0	1200	Flow-limited	90% GI tract and liver, 10% renal Extensive glucuronidation	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \rightarrow$, by some reports $f_p \uparrow$	None, but avoid in severe liver disease	
Pentazocine	65	5.4	4.5	1000	Flow-limited	>95% Hepatic <5% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 50%	Decrease oral dose by $\frac{2}{3}$	
Propoxyphene	75	16	12	1200	Flow-limited	>95% GI tract and liver; <2% renal	$t_{1/2} \uparrow$ slightly; V_d ?; $Cl \downarrow$ 25%; $f_p \rightarrow$	Decrease oral dose by 50%	
Anticancer									
Adriamycin	50	2.5	20	100	Enzyme-limited, binding-insensitive	>95% Hepatic <5% Renal Most biliary Active metabolite	$t_{1/2} \uparrow$; V_d ?; Cl ?; f_p ?, assume $f_p \rightarrow$	Unknown	
Bleomycin	0	0.3	2.0	120	—	40% Hepatic 60% Renal	Unknown; probably not altered greatly	None ? Perhaps decrease	
Cyclophosphamide	14	0.6	5.0	120	Enzyme-limited, binding-insensitive	90% Hepatic 10% Renal Active metabolite	$t_{1/2} \uparrow$; V_d ?$\rightarrow$; $Cl \downarrow$ 43%; f_p ?$\rightarrow$	Unknown	
Cytosine arabinoside	13	2.5	2.5	800	—	Extensive extrahepatic elimination; 40% renal	No data; probably little effect	None	
Etoposide	—	.28	5.6	39	—	65% Hepatic 35% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$	None	
5-Fluorouracil	—	0.5	0.1	—	Flow-limited	Hepatic and extrahepatic; <5% Renal	Some decrease in clearance expected	Probable slight decrease	

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustmer of Dose
Methotrexate	50	0.5	9.0	80	—	15% Hepatic; mostly biliary; 85% Renal	No data; probably little effect. Drug is hepatotoxic and should be avoided if possible.	None
Antiepileptic								
Carbamazepine	75	1.1	18.0 induced	—	Enzyme-limited, binding-sensitive	>98% Hepatic <2% Renal	No data; expect a decrease in clearance and increase in $t_{1/2}$	Probably de crease dose
Diphenylhydantoin	92	0.65	15.0 non-linear	40	Enzyme-limited, binding-sensitive	>95% Hepatic <5% Renal	AVH $t_{1/2} \rightarrow$; $Cl \rightarrow$; $f_p \uparrow$. Cirrhosis $f_p \uparrow$	Decrease dose in mod erate to se-vere liver disease
Phenobarbital	50	0.8	100	8	Enzyme-limited, binding-insensitive	75% Hepatic 25% Renal	$t_{1/2} \uparrow$; presumed $Cl \downarrow$	Decrease with severe liver disease
Valproic acid	89 non-linear	12	0.14	30	Enzyme-limited, binding-sensitive	>98% Hepatic <25% Renal	$t_{1/2} \uparrow$; V_d slightly $\uparrow$; $Cl \downarrow$ 40%; $f_p \uparrow$	Decrease dose
Antipyretic/ Antiinflammatory								
Antipyrine	<10	0.58	12	50	Enzyme-limited, binding-insensitive	92% Hepatic 8% Renal	$t_{1/2} \uparrow$; $V_d \uparrow$ or $\rightarrow$; $Cl \downarrow$ 60% or more, but actual decrease in Cl depends on disease	Not used clinically
Dexamethasone	68	0.75	3.25	260	Flow/enzyme-sensitive	>97% Hepatic <3% Renal	$f_p \rightarrow$; $V_d \rightarrow$; $t_{1/2} \uparrow$; $Cl \downarrow$	Decrease dose
Fenprofen	>99	0.10	1.5	200	Enzyme-limited, binding-sensitive	>98% Hepatic <2% Renal	No data; would expect $fp \uparrow$; $t_{1/2} \uparrow$; $Cl \uparrow$ or $\rightarrow$	Decrease dose
Ibuprofen	>99	0.15 V area F	2.0	52	Enzyme-limited, binding-sensitive	>99% Hepatic <1% Renal	$t_{1/2}$ slightly $\uparrow$ in severe LD; V_d ?; Cl ?	Decrease in severe liver disease if high doses
Indomethacin	90	0.17	8.0	125	Enzyme-limited, binding-sensitive	>98% Hepatic <2% Renal	$t_{1/2} \uparrow$; no other information. Assume $Cl \downarrow$, $f_p \uparrow$	Decrease dose as required
Naproxen	99.6	0.10	14.0	5	Enzyme-limited, binding-sensitive	>90% Hepatic <10% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 28%; f_p ?	Decrease dose in moc erate to se-vere diseas
Phenylbutazone	98.5	0.17	70	2	Enzyme-limited, binding-sensitive	>99% Hepatic <1% Renal	$t_{1/2} \uparrow$ or $\rightarrow$; $f_p \uparrow$; V_d ?; Cl ? Assume $Cl \downarrow$ with liver disease	Decrease dose

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose
Prednisolone	80	0.6	3.0	180	Enzyme-limited, binding-sensitive	>85% Hepatic <15% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \rightarrow$ or $\uparrow$. Drug little affected by liver disease.	None
Salicylic acid	80–95 dose dependent	0.17 dose dependent	2.4–19	13 in therapeutic range	—	2–30% Renal; dose dependent	$t_{1/2} \rightarrow$; $V_d \rightarrow$; Cl ?; $f_p \uparrow$	None
Sulfinpyrazone	99	0.06	6.0	23	Enzyme-limited, binding-sensitive	65% Hepatic 35% Renal	No data; would expect some decrease in Cl with liver disease	Slight decrease in dose
Cardiovascular								
Atenolol	<5	0.55	6.5	55–130	—	10% Hepatic 90% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$	None
Captopril	27	0.7	1.9	13.3/kg	—	40% Renal 50% Hepatic	Negligible unless renal function decreased	None
Digitoxin	95	0.60	180	2.5	Enzyme-limited, binding-sensitive	70% Hepatic 30% Renal	$t_{1/2} \rightarrow$ or $\downarrow$; $Cl \uparrow$ or $\rightarrow$; $f_p \uparrow$	None
Digoxin	30	6.0	35	150	—	30% Hepatic 70% Renal	Appears negligible	None
Disopyramide	80	non-linear 1.0	8	100	—	45% Hepatic 55% Renal	No data; would not expect a tremendous change in liver disease	Probably slight decrease
Enalapril	50	1.0	4.0	125	Flow/enzyme-sensitive	Rapidly hydrolyzed to active enalaprilat in the liver, 60% excreted in the urine	$t_{1/2}$ enalaprilat C_{max} enalaprilat	None
Esmolol	55	1.2	0.15	310/kg	—	80% Renal (rapidly hydrolyzed to inactive product in blood)	Negligible	None
Isradipine	95	3.0	8.0	1400	Flow-limited	<90% Hepatic	Cl, C_{max}, AUC, $t_{1/2}$, V_d	Decrease dose
Labetalol	50	11.5	3.0	1600	Flow-limited	>95% Hepatic <5% Renal	$t_{1/2} \rightarrow$; $V_d \downarrow$; $Cl \rightarrow$ or $\downarrow$; f_p ?, assume $\uparrow$	Decrease oral dose; decrease i.v. dose to much smaller extent
Lidocaine	65	non-linear 1.1	2.0	1000	Flow-limited	97% Hepatic 3% Renal	$t_{1/2} \uparrow$; $V_d \uparrow$ or $\rightarrow$; $Cl \downarrow \sim 50\%$; f_p ? Low therapeutic ratio. Decrease in Cl depends on severity of disease	Decrease dose by 50% in severe liver disease

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose	
Lisinopril	<10	1.8	12	106	—	3% Hepatic 97% Unchanged 70% Fecal 30% Renal	Negligible unless renal function decreased	None	
Lorcainide	70	12.9	8.0	1700	Flow-limited	98% Hepatic 2% Renal	$t_{1/2}$ ↑; V_d →; Cl ↓ 29%; f_p ↑ slightly. Cl_{int} exhibits a very large decrease	Decrease dose	2
Metoprolol	10	3.2	4.0	800	Flow-limited	95% Hepatic 5% Renal	$t_{1/2}$ ↑; V_d ↑ slightly; Cl ↓ 23%; f_p ? assumed unaffected	Decrease dose slightly	1
N-Acetyl-procainamide	10	1.4	8.0	210	—	20% Hepatic 80% Renal	No data; expect little change unless renal function altered	None	
Nifedipine	98	1.0	3.0	600	Flow-limited, binding-sensitive	100% Hepatic	$t_{1/2}$ ↑; V_d →; Cl ↓; f_p ↑	Decrease dose	7
Pindolol	57	6.2	3.5	300	Enzyme-limited, binding-insensitive	70% Hepatic 30% Renal	Not affected by AVH. Cirrhosis Cl ↓ slightly and renal excretion of drug is increased	Some decrease in severe liver disease	1
Prazosin	97	1.3	3.0	450	Flow-limited	95% Hepatic 5% Renal	No data—would expect $t_{1/2}$ ↑; Cl ↓; f_p ↑	Decrease dose	
Procainamide	15	2.2	3.0	600	—	45% Hepatic 55% Renal Drug acetylated	$t_{1/2}$ ↑; V_d ?; Cl ? probably decreased slightly	Some minor decrease in dose	33
Propranolol	95	4.0	4.0	850	Flow-limited	>95% Hepatic <5% Renal	$t_{1/2}$ ↑; V_d ↑; Cl ↓ ~ 60%; f_p ↑. Tremendous decrease in Cl_{int}. Flow/enzyme-limited in cirrhosis	Decrease dose depending on extent of damage	19
Quinidine	85	3.0	6.0	330	Flow/enzyme-sensitive	80% Hepatic 20% Renal	$t_{1/2}$ ↑; V_d ↑; Cl →; f_p ↑; Cl_{int} decreased significantly	Decrease dose	5
Tocainide	10	3.0	13	150	Enzyme-limited	60% Hepatic 40% Renal	$t_{1/2}$ ↑; V_d ?; Cl ↓	Decrease dose	1
Verapamil	92	6.7	3.5	1570	Flow-limited	95% Hepatic 5% Renal	$t_{1/2}$ ↑; V_d ↑; Cl ↓ 60%; f_p →; Cl_{int} decreases even more than 60%	Decrease dose by 50% in severe liver disease	1
Diuretic									
Bumetanide	?	9.45	1.0	129	—	36% Hepatic 64% Renal	$t_{1/2}$ ↑; V_d ↓; Cl ↓	Minor decrease in dose	8
Furosemide	95	0.15	1.0	170	—	35% Hepatic 65% Renal	$t_{1/2}$ ↑ or →; V_d ↑ or →; Cl →; f_p ↑; the change in f_p compensates for decrease in Cl_{int} of liver	None or slight decrease in severe cases	4

TABLE 4.2. (Continued)

Drug	Protein Binding (%)	Volume of Distribution (V_d) (liter/kg)	Half-life ($t_{1/2}$) (h)	Clearance (Cl) (ml/min)	Class	Hepatic/Renal Elimination	Effect of Liver Disease on Drug Disposition	Adjustment of Dose	
Hydrochlorothiazide	95	1.5	2.5	480	—	<10% Hepatic >90% Renal	No data; probably little affected unless renal function altered	None	
Spironolactone	98	—	20	—	Enzyme-limited, binding-sensitive, and extrahepatic metabolism	>85% Hepatic <15% Renal	No apparent change in drug disposition with liver disease; $t_{1/2} \rightarrow$	None	2,
Triamterene	50	2.5	2.0	1000	Flow-limited	95% Hepatic 5% Renal	$Cl \downarrow$; $f_p \rightarrow$; expect $t_{1/2} \uparrow$	Decrease dose	1
Sedative/Hypnotic Amylobarbital	60	1.2	21	35	Enzyme-limited, binding-insensitive	>95% Hepatic <5% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 55%; $f_p \uparrow$. Little change if albumin >3.5 g/100 ml	Decrease dose	9
Chlordiazepoxide	96	0.3	12 age-dependent	20	Enzyme-limited, binding-sensitive	>99% Hepatic <1% Renal	$t_{1/2} \uparrow$; $V_d \uparrow$; $Cl \downarrow$ 60%; $f_p \uparrow$. Both AVH and cirrhosis affect drug	Decrease dose	1
Diazepam	99	1.2	45	28	Enzyme-limited, binding-sensitive	>97% Hepatic <3% Renal	$t_{1/2} \uparrow$; $V_d \uparrow$; $Cl \downarrow$ 50%; $f_p \uparrow$. AVH and cirrhosis increase $t_{1/2}$. Large therapeutic index—safe	Single dose, no change; chronic, decrease dose	
Flumazenil	40	0.85	0.8	1201	Flow-limited	>90% Hepatic	$t_{1/2}$, Cl, V_d	? Decrease dose	
Hexobarbital	47	1.2	6.0	232	Enzyme-limited, binding-insensitive	>99% Hepatic <1% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 62% (Cl decreased in AVH and cirrhosis, $Cl \rightarrow$ in cholestasis); $f_p \rightarrow$	Decrease during chronic dosing	
Lorazepam	90	1.3	12.0	53	Enzyme-limited, binding-sensitive	>98% Hepatic <2% Renal Extensive glucuronidation	$t_{1/2} \uparrow$; $V_d \uparrow$; $Cl \rightarrow$; $f_p \uparrow$. Neither AVH nor cirrhosis affects drug dosing	None	
Methohexital	—	61	2.0	829	Flow/enzyme-sensitive	>90% Hepatic <10% Renal	No data; assume $Cl \downarrow$, $t_{1/2} \uparrow$	Probably decrease dose	
Midazolam	—	1.3	1.6	624	Flow-limited	>95% Hepatic <5% Renal	$t_{1/2} \uparrow$; V_d slightly $\uparrow$; $Cl \downarrow$	Decrease dose	
Nitrazepam	87	1.9	26	63	Enzyme-limited	>99% Hepatic <1% Renal Mainly nitroreduction	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \uparrow$	None	

Drug	*Protein Binding (%)*	*Volume of Distribution (V_d) (liter/kg)*	*Half-life ($t_{1/2}$) (h)*	*Clearance (Cl) (ml/min)*	*Class*	*Hepatic/Renal Elimination*	*Effect of Liver Disease on Drug Disposition*	*Adjustment of Dose*
Oxazepam	90	1.6	6.0	140	Enzyme-limited, binding-sensitive	>99% Hepatic <1% Renal Extensive glucuronidation	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \rightarrow$. Neither AVH nor cirrhosis alters disposition significantly	None
Pentobarbital	65	1.0	30	30	Enzyme-limited, binding-sensitive	99% Hepatic <1% Renal	No data; expect $Cl \downarrow$, $t_{1/2} \uparrow$	Single dose, no change; chronic, lower dose
Primidone	19	0.86	17	41	—	60% Hepatic 40% Renal (in children)	$t_{1/2} \rightarrow$; V_d slight $\uparrow$; Cl slight $\uparrow$ in hepatitis	None
Temazepam	98	1.2	14	80	—	>98% Hepatic <2% Renal Mainly glucuronidation	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \rightarrow$	None
Others								
Alfentanil	90	0.28	1.5	200	Flow/enzyme-sensitive	99% Hepatic 1% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$; $f_p \uparrow$ (dose-dependent)	Decrease dose
Atracurium	—	0.16	0.33	385		Hofmann elimination; autometabolism	$t_{1/2} \rightarrow$; $V_d \uparrow$; $Cl \rightarrow$; long $t_{1/2}$ of metabolite	Decrease dose if long-term use
Caffeine	31	0.54	6.0	63	Enzyme-limited, binding-insensitive	95% Hepatic 5% Renal	$t_{1/2} \uparrow$ slightly; $V_d \rightarrow$; $Cl \downarrow$ 40%; $f_p \uparrow$; large therapeutic ratio	None
Chlormethiazole	64	0.12	7.0	1100	Flow-limited; vitamin B substitute	>99% Hepatic <1% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; $Cl \downarrow$ 28%; $f_p \uparrow$	Probably not necessary
Cimetidine	20	1.1	2.3	550	—	40% Hepatic 60% Renal	$t_{1/2} \rightarrow$; $V_d \uparrow$ or $\downarrow$ or $\rightarrow$; $Cl \rightarrow$ or $\downarrow$; f_p changes assumed unimportant. Drug associated with increased incidence of mental confusion in cirrhotics	Decrease dose in severe liver disease
Clofibrate (CPIB)	95	0.15	18.0	8	Enzyme-limited, binding-sensitive	90% Hepatic <10% Renal Glucuronidation of metabolite	$t_{1/2} \rightarrow$; $V_d \uparrow$ slightly; $Cl \rightarrow$; $f_p \uparrow$. AVH does not alter Cl; cirrhosis does have an effect on $Cl_{int} \downarrow$ 50%	Decrease dose in cirrhosis by 50%
Diphenhydramine	78	6.5	9.5	696	Flow-limited	>98% Hepatic <2% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$; free $Cl \downarrow$; total $Cl \rightarrow$; $f_p \uparrow$	Decrease dose
Doxacurium	30	0.22	1.5	190	—	>90% Renal	Negligible unless renal function decreased	None
Famotidine	17	1.1	3.3	430	—	70% Renal (unchanged) 30% Hepatic	Negligible unless renal function decreased	None
Fentanyl	80	3.5	4.0	750	—	92% Hepatic 8% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$	None

Drug	*Protein Binding (%)*	*Volume of Distribution (V_d) (liter/kg)*	*Half-life ($t_{1/2}$) (h)*	*Clearance (Cl) (ml/min)*	*Class*	*Hepatic/Renal Elimination*	*Effect of Liver Disease on Drug Disposition*	*Adjustment of Dose*
Omeprazole	95	0.35	0.75	550	Flow-limited	>90% Hepatic	$t_{1/2}$, Cl,	None
Ranitidine	15	1.5	2.3	600	—	30% Hepatic 70% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$ or $\downarrow$	None
Sulfisoxazole	92	0.15	6.6	20	Enzyme-limited, binding-sensitive	50% Hepatic 50% Renal Acetylation	$t_{1/2} \rightarrow$; $V_d \uparrow$; $Cl \uparrow$; $f_p \uparrow$	None
Theophylline	52	0.5	8.0	45	Enzyme-limited, binding-sensitive	91% Hepatic 9% Renal	$t_{1/2} \uparrow$; $V_d \rightarrow$ cirrhosis, $\uparrow$ hepatitis and cholestasis; $Cl \downarrow$ 55%; $f_p \uparrow$. Low therapeutic index caution	Decrease dose by 50%
Thiopental	85	2.3	9.0	275	Enzyme-limited	>99% Hepatic <1% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \uparrow$	Uncertain; may need to decrease dose
Tolbutamide	98	0.15	5.0	20.0	Enzyme-limited, binding-sensitive	95% Hepatic 5% Renal	$t_{1/2}$ slightly $\uparrow$ or $\rightarrow$; $V_d \rightarrow$; $Cl \uparrow$; $f_p \uparrow$. AVH has been reported to increase rate of elimination	None; probably not used in liver disease
Warfarin	99	0.20	23	8.0	Enzyme-limited, binding-sensitive	99% Hepatic 1% Renal	$t_{1/2} \rightarrow$; $V_d \rightarrow$; $Cl \rightarrow$; $f_p \rightarrow$. AVH no effect, but may be related to extent of liver damage	None; probably not used in liver disease

[a] GI, gastrointestinal; AVH, acute viral hepatitis; LD, liver disease.