Index

(Page numbers in italics indicate figures; page numbers followed by "t" indicate tables.)

```
Acetaminophen, 159t
Acetylcholine receptor blockade
 consequences of, 48t
 tricyclic antidepressants and, 67
Age, SSRI clearance rate and, 120t-121t, 124-125
Alcohol, antidepressant interaction with, 65 -66
Alfentanil, 159t
a-Adrenergic receptor blockade, 49t
Alprazolam
 CYP enzyme metabolism of, 159t
 drug interactions with, 190-192, 193t
Alprenolol, 158t
Amidarone, 159t
Amitriptyline
 CYP enzyme metabolism of, 158t-159t
 dopamine uptake and, 39t
 norepinephrine uptake and, 38t, 41
 polypharmacy of, 25t
 potency of, 27
 selectivity of, 41, 46t
 serotonin uptake and, 37t, 41
 side effects of, 70
Analgesic(s), 159t
Androstendione, 159t
Anesthetic(s), local, 159t
Anorexia
 imipramine and, 68t
 serotonin uptake blockade and, 48t
 SSRIs and, 82t, 86t, 87
Antiarrhythmic drug(s)
 CYP enzyme metabolism of, 158t-159t
 drug interactions with, 184
Antibiotic(s), 159t
Anticonvulsant drug(s), 159t
Antidepressant(s). See also specific drug, eg, Fluoxetine;
   specific type of drug, eg, Monoamine oxidase inhibitor(s).
 action mechanisms of, 16t
 CYP enzyme metabolism of, 158t-159t
 pharmacology of, 48t-49t
 prevalence of other drugs with, prevalence of, 162t
 side effects of, 48t-49t
 in vitro profile of, 53
```

Antiestrogen drug(s), 159t Antihistamine(s), 159t Antipsychotic drug(s), 158t-159t Anxiety amitriptyline and, 70 serotonin uptake blockade and, 48t sertraline and, 70 SSRIs and, 86t Astemizole CYP enzyme metabolism of, 159t drug interactions with, 153t Asthenia serotonin uptake blockade and, 48t SSRIs and, 86t
Barbiturate(s), 158t
Benzodiazepine(s)
CYP enzyme metabolism of, 159t
development of, 20
SSRI(s) interaction with, 66
Benzphetamine, 159t Benztropine, 25t
β-Blocker(s)
CYP enzyme metabolism of, 158t
drug interactions with, 184
Bupropion
fluoxetine interaction with, 150 seizure risk with, 149, 150
Burarolol, 158t
2 mai 10101, 1200
Caffeine, 158t
Calcium channel blocker(s), 159t
Carbamazepine
CYP enzyme metabolism of, 159t drug interactions with, 152t, 156, 192, 193t
Carcinogenesis, CYP enzyme 2D6 and, 138-140
Central depressant drug(s), histamine receptor blockade and,
48t
Chirality, 29-32
Cimetidine action mechanism of, 25t
drug interactions with, 152t
Cisapride, 159t
Citalopram. See also Desmethylcitalopram.
availability of, 18
brand names of, by country, 234t-236t
chirality of, 30-31

```
clearance of, age and gender and, 120t, 124-125
  CYP enzymes and, 176t-177t
   2D6 deficiency and, 165t
   2D6 functions and, 179t, 185, 186
   inhibition by, 170t-171t
   metabolism of, 158t
  development of, 16
  dopamine uptake and, 39t
 dosage of
   age and, plasma level and, 120t
   potency and, 50t, 51-52
  half-life of, 60t, 109t, 118t, 119
   cirrhosis and, 127t
  metabolism of, 110-111, 111t
  metabolites of, potency of, 57, 58t
  norepinephrine uptake and, 38t, 41
  pharmacokinetics of, 109t
   linear versus nonlinear, 117-119
  selectivity of, 41, 46t
  serotonin uptake and, 37t, 41
   dosage and, 50t, 51-52
  steady-state of, time to, 123
  structural formula of, 17
 in vitro profile of, 53
  washout of, 123
Citalopram enantiomer(s), 44t
Clarithromycin, 159t
Clomipramine. See also Desmethylclomipramine.
  action mechanisms of, 52, 54
  CYP enzyme metabolism of, 158t, 159t
  demethylation of, 55
   potency and, 56
  dopamine uptake and, 39t
  half-life of, 60t
  for major depression, 54
  norepinephrine uptake and, 38t, 41
  for obsessive-compulsive disorder, 54
  selectivity of, 46t
  side effects and, 54
  selectivity ratio of, 41
  serotonin uptake and, 37t, 41
  sodium channel inhibition by, 54
 in vitro profile of, 53
Clonazepam, 159t
Clonidine
  adrenergic blocker interaction with, 49t
  antidepressant interaction with, 49t
```

Clorpheniramine, action mechanism of, 25t Clozapine CYP enzyme metabolism of, 158t, 159t seizure risk with, 148, 149 Cocaine, 159t Codeine CYP enzyme metabolism of, 158t, 159t drug interactions with, 153t, 184 Constipation acetylcholine receptor blockade and, 48t amitriptline and, 70 imipramine and, 68, 68t sertraline and, 70 SSRIs and, 83t, 86t Cortisol, 159t Cyclosporine, 159t CYP enzyme(s) antidepressant demethylation and, 55-56 citalopram metabolism by, 110-111, 111t classification of, 132-133, 134t clozapine metabolism by, 150 deficiency of, 138-140 genetically determined, 160t discovery of, 13lt, 131-132, 133t drug clearance and, 140-141, 141-142, 143 drug metabolism by, 135, 136, 137 drug-drug interactions and, 143-144, 152t-153t fluoxamine metabolism by, 111t, 111-113 fluvoxamine metabolism by, 111t, 111-112 functions of, 136t, 138 genetics of, 134t, 137 inhibition constant and, 227-232 inhibition of consequences of, 163, 164t in vitro studies of, 167t, 167-169, 170t-171t in vivo studies of, 167t, 172, 173, 174-175 norfluoxetine inhibition of, 59 oxidative metabolism by, 111t, 113-114 reaction cycle of, 138 risperidone metabolism by, 111t, 114-115 SSRI inhibition of, 78, 98 steroidogenic, 133, 134t, 135, 136t tricyclic antidepressant metabolism by, 151 xenobiotic, 134t, 135, 136t, 175, 176t-177t, 178 CYP enzyme 1A2	drugs metabolized by, 158t effects of specific SSRIs on, 176t-177t, 178, 180-181 CYP enzyme 2C9/10 drugs metabolized by, 158t effects of specific SSRIs on, 176t-177t, 181-182, 193t CYP enzyme 2C19, effects of specific SSRIs on, 176t-177t, 182-183, 193t CYP enzyme 2D6 carcinogenesis and, 138-140 deficiency of, drug-induced, 163 dopamine uptake transporter pump and, 137 drugs metabolized by, 158t effects of specific SSRIs on, 176t-177t, 179t-180t, 184, 185, 186-187, 190, 230t myths concerning, 164, 166, 166t tricyclic antidepressant toxicity and, 100-101 CYP enzyme 3A3/4 drugs metabolized by, 159t effects of specific SSRIs on, 176t-177t, 190-192, 193t, 194 Cytochrome P450 enzyme(s). See CYP enzyme(s). Dapsone, 159t Debrisoquin, 158t Dehydroepiandrosterone 3-sulfate, 159t Depression, major clomipramine for, 54 prevalence of medical illnesses with, 162t SSRI(s) for, 75t tricyclic antidepressants for, 72 Desipramine action mechanism of, 25t CYP 2D6 functions and, 186, 188-189 dopamine uptake and, 39t drug interactions with, 173, 186, 188-189 norepinephrine uptake and, 38t, 41 selectivity of, 41, 46t serotonin uptake and, 37t, 41 Desmethylcitalopram CYP enzymes and inhibition by, 170t-171t metabolism of, 158t potency of, 58t, 60t Desmethylclomipramine clinical relevance of, 60t CYP enzyme metabolism of, 158t half-life of, 60t potency of, 44t, 58t
240	241

Clinical Pharmacology of SSRIs — Preskorn

selectivity of, 41	oxidase inhibitor(s), SSRI interaction with.
in vitro profile of, 53	clearance rate and, 145-146
Desmethylsertraline	CYP enzymes and, 143-144, 152t-153t
CYP enzymes and, 115	pharmacodynamic, 144-145, 145t
inhibition by, 170t-171t	pharmacokinetic, 145, 145t-146t, 150
pharmacokinetics of, 116-117	CYP enzymes and, 155-157, 156, 160
potency of, 58t	studies of, 173
Desmethylvenlafaxine, 159t	Drug monitoring. See Therapeutic drug monitoring.
Dexamethasone, 159t	Drug potency
Dextromethorphan	concentration and, 43, 47, 50t, 51-52
CYP enzyme metabolism of, 158t, 159t	determination of, 33-35, 35
drug interactions with, 152t	Dry mouth
Diabetes mellitus, depression prevalence with, 162t	acetylcholine receptor blockade and, 48t
Diarrhea	amitriptyline and, 70
amitriptyline and, 70	imipramine and, 68, 68t
imipramine and, 68t	sertraline and, 70
•	SSRIs and, 82t, 86t
serotonin uptake blockade and, 48t	
sertraline and, 70	Dyspepsia, SSRIs and, 82t
SSRIs and, 82t, 86t	Eigenletien gewesten CCDI for 01
Diazepam CVP	Ejaculation, premature, SSRIs for, 91
CYP enzyme metabolism of, 159t	Enantiomer. See also specific drug, eg, Citalopram
drug interactions with, 182-183	enantiomer(s).
Diltiazem, 159t	definition of, 29-30
Disopyramide, 159t	drug monitoring and, 30
drug interactions with, 152t	pharmacokinetics of, 30
Dizziness	Encainide, 158t
amitriptyline and, 70	Epilepsy, depression prevalence with, 162t
imipramine and, 68t	Erythromycin
sertraline and, 70	CYP enzyme metabolism of, 159t
SSRIs and, 48t, 82t, 86t	drug interactions with, 152t, 155
Docetaxel, 159t	Estradiol, 159t
Dopamine uptake	Ethosuximide, 159t
antidepressant potency and, 39t, 40	Ethylmorphine, 158t
drug selectivity and, 44t-45t	
SSRI metabolites and, 57, 58t, 60t	Fatigue
Drowsiness	amitriptyline and, 70
histamine receptor blockade and, 48t	imipramine and, 68t
imipramine and, 68t	sertraline and, 70
SSRIs and, 82t, 86t, 87	SSRIs and, 82t, 86t, 87
Drug development. See also specific drug, eg, Lithium,	Felodipine, 159t
development of.	Fenfluramine, 48t
criteria for, 19t	Flecainide, 158t
mechanism of action in, 18-19, 19t, 21	Fluoxetine. See also Norfluoxetine.
molecular targeting in, 21	availability of, 18
signal-to-noise ratio in, 24	benzodiazepine interaction with, 66
site of action in, 18-20, 19	brand names of, by country, 234t-236t
Drug interaction(s). See also specific drug, eg, Monoamine	bupropion interaction with, 150
1 5 5	Ţ Ţ

chirality of, 31	
clearance of, age and gender and, 120t, 124-125	
CYP enzymes and	
2C9/10 and, 193t	
2C19 and, 193t	
2D6 and, 179t-180t, 185, 186, 230t	
2D6 deficiency and, 163, 165t	
3A3/4 and, 193t	
inhibition by, 170t-171t	
metabolism of, 158t	
development of, 16	
dopamine uptake and, 39t	
dosage of	
age and, plasma level and, 120t	
efficacy and, 85	
potency and, 50t, 51-52	
drug interactions with, 152t, 181, 182-184, 188	
effects of, on specific CYP enzymes, 176t-177t	
efficacy of, acute, 92t, 93-95	
half-life of, 60t, 109t, 118t, 119-123	
cirrhosis and, 127t	
metabolism of, 111t, 111-113	
metabolites of, 116	
potency of, 57, 58t, 59	
norepinephrine uptake and, 38t, 41	
pharmacokinetics of, 109t	
linear versus nonlinear, 117-119	
relapse rate with, 92t, 97-98	
selectivity of, 41, 46t	
serotonin uptake and, 37t, 41	
dosage and, 50t, 51-52	
side effects of	
discontinuation rate from, 84	
incidence of, 82t-83t, 86t	
steady-state of, time to, 123	
structural formula of, 17	
in vitro profile of, 53	
washout of, 80, 123	
Fluoretine enantiomer(s), 45t	
Fluvoxamine	
availability of, 18	
benzodiazepine interaction with, 66	
brand names of, by country, 234t-236t	
clearance of, age and gender and, 120t, 124-125	
CYP enzymes and	
1A2 and, 178	
2C9/10 and, 193t	

```
2C19 and, 193t
   2D6 and, 179t, 185, 230t
   2D6 deficiency and, 165t
   3A3/4 and, 193t
   inhibition by, 170t-171t
  development of, 16
  dopamine uptake and, 39t
 dosage of
   age and, plasma level and, 120t
   potency and, 50t, 51-52
  drug interactions with, 152t, 155, 178-179, 182-183, 190-
  effects of, on specific CYP enzymes, 176t-177t
  efficacy of, acute, 92t, 93-94
  half-life of, 60t, 109t, 118t, 123
   cirrhosis and, 127t
  metabolism of, 111t, 111-112
  norepinephrine uptake and, 38t, 41
  for obsessive-compulsive disorder, 18
  pharmacokinetics of, 109t
   linear versus nonlinear, 117-119
  relapse rate with, 92t, 98-99
  selectivity of, 41, 46t
  serotonin uptake and, 37t, 41
   dosage and, 50t, 51-52
  side effects of, incidence of, 82t-83t, 86t
  steady-state of, time to, 123
  structural formula of, 17
  in vitro profile of, 53
  washout of, 123
  withdrawal from, 122-123
Gender, SSRI clearance rate and, 120t-121t, 124-125
Guanabenz, adrenergic blocker interaction with, 49t
Guanethidine, antidepressant interaction with, 48t
Guillain-Barré syndrome, as SSRI side effect, 16
Haloperidol, 158t
Headache
 imipramine and, 68t
 SSRIs and, 48t, 82t, 86t
Heart
  acetylcholine receptor blockade and, 48t
 SSRIs and, 83t
  tricyclic antidepressant effects on, 55, 67, 74
Heart disease
  depression prevalence with, 162t
```

SSRI metabolism and, 125, 128	Mexiletine, 158t
Hexobarbital, 158t	Midazolam, 159t
Histamine receptor blockade, 48t, 54	Migraine, SSRIs and, 48t
Hydroamphetamine, 158t	Minodipine, 159t
Hypertension drug(s), antidepressant interaction with, 48t-	Molecular targeting, in drug development, 21
49t,	Monoamine oxidase inhibitor(s)
66-67	action mechanisms of, 16t, 22, 23
Hypotension, adrenergic blockade and, 49t	development of, 20-21
	evolution of, 22
Imipramine	SSRI interaction with, 48t, 79-80, 144-145
CYP enzyme metabolism of, 158t, 159t	Muscarinic acetylcholine receptor blockade
dopamine uptake and, 39t	consequences of, 48t
norepinephrine uptake and, 38t, 41	tricyclic antidepressants and, 67
selectivity of, 41, 46t	Myocardial infarction, depression prevalence with, 162t
serotonin uptake and, 37t, 41	
side effects of, 68t, 69	Nausea
Immunosuppressant drug(s), 159t	amitriptyline and, 70
Inhibition constant, CYP enzyme effects and, 227-232	imipramine and, 68t
Insomnia	serotonin uptake blockade and, 48t
amitriptyline and, 70	sertraline and, 70
imipramine and, 68t	SSRIs and, 69, 82t, 86t
serotonin uptake blockade and, 48t	Nefazodone. See Phenylpiperazine (Nefazodone).
sertraline and, 70	Nervousness
SSRIs and, 82t	imipramine and, 68t
	SSRIs and, 82t, 86t, 87
Jitteriness, norepinephrine uptake blockade and, 48t	Neuroleptic drug(s), drug interactions with, 184
	Nicardipine, 159t
Ketoconazole, drug interactions with, 153t, 155	Nifedipine, 159t
	Niludipine, 159t
Lidocaine, 158t-159t	Nisoldipine, 159t
Lithium	Nitrendipine, 159t
development of, 20	Norepinephrine inhibitor(s), examples of, 16t
SSRI interaction with, 48t	Norepinephrine uptake
Liver disease, SSRI metabolism and, 125-126, 127t	antidepressant potency and, 38t, 40, 41
Loratadine, 159t	blockade of, consequences of, 48t
Lovastatin, 159t	drug selectivity and, 42, 44t-45t
	SSRI metabolites and, 57, 58t, 60t
Macrolide antibiotic(s), 159t	Norfluoxetine
Mechanism of action. See also specific drug, eg, Fluoxetine,	biogenic amine uptake and, 45t
action mechanism of.	chirality of, 31
definition of, 18-19, 19t	CYP 2D6 functions and, 180t
Memory impairment, acetylcholine receptor blockade and,	CYP enzyme inhibition by, 59, 170t-171t
48t	drug interactions with, 155, 184, 188, 190-192
Menstrual disorder, SSRIs and, 88t	half-life of, 60t, 119
Mephenytoin, 158t	cirrhosis and, 127t
Mephobarbital, 158t	pharmacokinetics of, 116
Metoprolol, 158t	potency of, 58t, 60t
•	1 / / / / / / / / / / / / / / / / / / /
246	

steady-state of, time to, 123	norepinephrine uptake and, 38t, 41
washout of, 123	pharmacokinetics of, 109t
Nortriptyline	linear versus nonlinear, 117-119
CYP enzyme metabolism of, 158t	renal disease and, 126, 127t
norepinephrine uptake and, 41	relapse rate with, 92t, 98-99
selectivity ratio of, 41	selectivity of, 41, 46t
serotonin uptake and, 41	serotonin uptake and, 37t, 41
	dosage and, 50t, 51-52
Obsessive-compulsive disorder	side effects of
fluvoxamine for, 18	discontinuation rate from, 84
SSRIs for, 91	incidence of, 82t-83t, 86t
Omeprazole, 159t	steady-state of, time to, 123
Opiate(s), 158t	structural formula of, 17
Oral contraceptive(s), drug interactions with, 152t	in vitro profile of, 53
Oxidative metabolism, 137, 139	washout of, 123
	withdrawal from, 122-123
Paclitaxel, 159t	Perhexiline, 158t
Pain, chronic, depression prevalence with, 162t	Perphenazine, 158t
Panic disorder, SSRIs for, 91	Pharmacokinetics, linear <i>versus</i> nonlinear, 117-119
Paracetamol, 158t	Phenformin, 158t
Parkinson's disease	Phenobarbital, drug interactions with, 152t
CYP enzyme 2D6 and, 138-140	Phenothiazine(s), development of, 20
depression prevalence with, 162t	Phenylpiperazine (Nefazodone)
Paroxetine	action mechanism of, 16t, 25t
brand names of, by country, 234t-236t	CYP enzyme metabolism of, 158t-159t
clearance of, age and gender and, 121t, 124-125	drug interactions with, 155
CYP enzymes and	Phenytoin
2C9/10 and, 193t	CYP enzyme metabolism of, 158t
	· · · · · · · · · · · · · · · · · · ·
2C19 and, 193t	drug interactions with, 152t, 156, 181, 193t
2D6 and, 179t, 185, 186-187, 228t	Potency, determination of, 33-35, 35
2D6 deficiency and, 163, 165t	Prazosin, 25t
3A3/4 and, 193t	Priapism, 49t
inhibition by, 170t-171t	Progesterone, 159t
metabolism of, 158t	Propafenone, 158t-159t
development of, 16	Propranolol
dopamine uptake and, 39t	CYP enzyme metabolism of, 158t
dosage of	drug interactions with, 152t
age and, plasma level and, 121t	Protein binding, concentration dependence of, 108
efficacy and, 85	
potency and, 50t, 51-52	Quinidine
drug interactions with, 152t-153t, 189, 190	action mechanism of, 25t
effects of, on specific CYP enzymes, 176t-177t	CYP enzyme metabolism of, 159t
efficacy of, acute, 92t, 93-95	drug interactions with, 152t
half-life of, 60t, 109t, 118t, 119, 122	
cirrhosis and, 127t	Renal disease
metabolism of, 111t, 113-114	depression prevalence with, 162t
metabolites of, 116	SSRI metabolism and, 125-126, 127t, 128

Respiratory disturbance, SSRIs and, 83t, 86t Rifampin, drug interactions with, 152t
Risperidone
antipsychotic efficacy of, dosage and, 146, 147
CYP enzyme metabolism of, 148, 158t
side effects of, 147, 148
Secobarbital, drug interactions with, 152t
Seizure
bupropion and, 149, 150
clozapine and, 148, 149
sodium channel blockade and, 49t
Selective serotonin reuptake inhibitor(s) (SSRIs). See SSRI(s)
Serotonin uptake
antidepressant potency and, 37t, 40, 41
blockade of, consequences of, 48t
citalopram enantiomers and, 44t
dosage, plasma level, potency and, 50t
drug selectivity and, 42, 44t-45t physiology of, 28-29
SSRI metabolites and, 57, 58t, 60t
Sertraline. See also <i>Desmethylsertraline</i> .
action mechanism of, 25t
brand names of, by country, 234t-236t
clearance of, age and gender and, 121t, 124-125
CYP enzymes and
2C9/10 and, 193t
2C19 and, 193t
2D6 and, 179t, 185, 187, 188-189, 230t
2D6 deficiency and, 165t
3A3/4 and, 193t
inhibition by, 170t-171t
metabolism of, 159t
development of, 16
dopamine uptake and, 39t
dosage of
age and, plasma level and, 121t
potency and, 50t, 51-52, 85
drug interactions with, 181, 182-183, 188-189, 190
effects of, on specific CYP enzymes, 176t-177t
efficacy of
acute, 92t, 93-96, 97
dosage and, 50t, 51-52
half-life of, 60t, 109t, 118t, 122 cirrhosis and, 127t
metabolism of, 111t, 114-115
metabolites of, 116-117
metaborites of, 110-11/

```
potency of, 57, 58t
 norepinephrine uptake and, 38t, 41
 pharmacokinetics of, 109t, 114-115
   linear versus nonlinear, 117-119
 relapse rate with, 92t, 98-99
 selectivity of, 41, 46t
 serotonin uptake and, 37t, 41
   dosage and, 50t, 51-52
 side effects of, 70
   discontinuation rate from, 84
   incidence of, 82t-83t, 86t
 steady-state of, time to, 123
 structural formula of, 17
 in vitro profile of, 53
 washout of, 123
Sexual dysfunction
 amitriptyline and, 70
 norepinephrine uptake blockade and, 48t
 serotonin uptake blockade and, 48t
 sertraline and, 70
 SSRIs and, 86t, 87, 88t-89t
Signal-to-noise ratio
 in drug development, 24
 enantiomeric form and, 30
Site of action
 concentration dependence of, 35
 definition of, 18-20, 19
Sodium channel blockade
 consequences of, 49t
 by tricyclic antidepressants, 54
Somnolence
 amitriptyline and, 70
 sertraline and, 70
Sparteine, 158t
SSRI(s). See also specific drug, eg, Fluoxetine.
 action mechanism of, 28
 action sites of, 23-24, 52
 advantages of, 28
 brand names of, by country, 234t-236t
 chirality of, 29-32
 clearance of
   age and gender and, 120t-121t, 124-125
   organ impairment and, 125-126, 127t, 128-129
  concentration-dependent effects of, 107-108, 108t
   active metabolites and, 115-117
   age and gender and, 120t-121t, 124-125
   antidepressant efficacy as, 50t, 101-105, 103
```

half-life as, 109t, 118t, 122-123, <i>123</i> metabolism as, 110-115
organ impairment and, 125-126, 127t, 128-129
pharmacokinetics as, 117-119
plasma level as, 120t-121t
protein binding as, 108
cost of, 72-73
current popularity of, 13
CYP enzymes and, 98
affinity for, 56
inhibition by, 78
metabolism of, 158t
development of, 16, 18, 23-24
discontinuation of, because of side effects, 84
dosage of
e
age and, 120t-121t
efficacy and, 85
plasma level and potency and, 50t, 51-52
drug interactions with, 77-80
efficacy of, 69, 71t, 72
acute, 91-98
concentration dependence of, 50t, 101-105, 103
on dopamine uptake, 39t, 40
dose and, 85
metabolites and, 60t
on norepinephrine uptake, 38t, 40
on serotonin uptake, 37t, 40
examples of, 15
half-lives of, 60t, 109t, 118t, 122-123, 123
cirrhosis and, 126
for major depression, 75t
metabolism of, 110-115
metabolites of, 57, 59, 115-117
action mechanisms of, 60t
clinical relevance of, 61-62
half-lives of, 60t
potency of, 57, 58t, 60t
monoamine oxidase inhibitor interaction with, 48t, 79-80,
144-145
for obsessive-compulsive disorder, 91
overdose of, 77-78
for panic disorder, 91
pharmacokinetics of, linear versus nonlinear, 117-119
physician comfort level with, 63
plasma level of, dose and age and, 120t-121t
for premature ejaculation, 91
protein binding of, 108

```
safety of, 64-67, 65t, 77-80
  selectivity of, 28-29, 46t
   biogenic amine uptake and, 42, 44t-46t, 48t-49t
   and effects on different neuroreceptors, 52, 53, 54-56
  side effects of, 65t, 67-69, 70
   determination of, 80
   discontinuation rate from, 84
   dose dependence of, 81, 87, 88t, 98
   incidence of, 81, 82t-83t, 86t
   sexual, 87, 88t-89t
  similarities in, 75-105
  steady-state of, time to, 123
  switching among, 98
  therapeutic monitoring of, 73-74, 99-105
  versus tricyclic antidepressants, differences in, 63-74
  washout of, 80, 123
  withdrawal from, 122-123
Steroid(s), 159t
Stroke, depression prevalence with, 162t
Sweating
 imipramine and, 68t
 SSRIs and, 83t, 86t
Sympathomimetic amine(s), antidepressant interaction with,
48t
Tachycardia
  acetylcholine receptor blockade and, 48t
 norepinephrine uptake blockade and, 48t
Tacrolimus, 159t
Tamoxifen, 159t
Terfenadine
 cardiac arrhythmias and, 155
  CYP enzyme metabolism of, 151, 155, 159t
  drug interactions with, 153t, 155, 190-191
Testosterone, 159t
Theophylline
 CYP enzyme metabolism of, 158t
 drug interactions with, 152t
Therapeutic drug monitoring
 to adjust dose upward, 101
  to avoid toxicity, 100-101
 decision making and, 104-105
  of enantiomer, 30
  fixed-dose studies as, 102
  lack of incentive for, 102
  of SSRIs, 73-74, 99-105
  of tricyclic antidepressants, 26, 73-74
```

Thioridazine, 158t
Timolol, 158t
Tolbutamide
CYP enzyme metabolism of, 158t
drug interactions with, 181, 193t
Trazodone, 158t
Tremor
amitriptyline and, 70
imipramine and, 68t
norepinephrine uptake blockade and, 48t
sertraline and, 70
SSRIs and, 82t, 86t
Triacetyloleandomycin, 159t
Triazolam, 159t
Tricyclic antidepressant(s). See also specific drug, eg,
Amitriptyline.
action mechanisms of, 16t, 22, 23-25, 150-151
alcohol interaction with, 65-66
antihistamine effects of, 65
antihypertensive drug interaction with, 48t-49t, 66-67
cardiac effects of, 55, 67, 74
clearance of, 24-25, 54-55, 151
cost of, 72-73
CYP enzyme metabolism of, 151, 158t
demethylation of, 55
potency and, 56
development of, 20t, 20-21
drug interactions with, 152t, 178-179, 184
evolution of, 22
for major depression, 72
monitoring intake of, 26
overdose of, 24, 65, 77
CYP enzyme 2D6 deficiency and, 100-101
symptoms of, 26, 151
pharmacokinetics of, 151
potency of, 69, 71t, 72
dopamine uptake and, 39t, 40
norepinephrine uptake and, 38t, 40
serotonin uptake and, 37t
response curves of, multiple concentrations and, 154
safety of, 64-67, 65t
selectivity of, 46t
biogenic amine uptake and, 42, 44t-46t, 48t-49t
side effects of, 25-26, 65t, 67-69, 68t, 70
clearance rate and, 54-55
sodium channel blockade by, 54
versus SSRIs, 63-74
•

therapeutic monitoring of, 73-74 Trimipramine, 158t Tryptophan, SSRI interaction with, 48t Tumor, terminal solid, depression prevalence with, 162t

Urinary frequency imipramine and, 68t SSRIs and, 83t, 86t Urinary retention acetylcholine receptor blockade and, 48t imipramine and, 68t SSRIs and, 83t

Valproate, drug interactions with, 156
Venlafaxine
action mechanism of, 16t
CYP enzyme metabolism of, 158t
Verapamil, 159t
Visual disturbance
acetylcholine receptor blockade and, 48t
amitriptyline and, 70
imipramine and, 68t
sertraline and, 70
SSRIs and, 82t
Vomiting, serotonin uptake blockade and, 48t

Warfarin
CYP enzyme metabolism of, 158t, 180-181
drug interactions with, 152t, 180-181
Weight gain, histamine receptor blockade and, 48t
Withdrawal syndrome, 122-123

Yohimbine, action mechanism of, 25t