Antidepressant medications: dosing and half-life information

Generic drug name	Proprietary drug name	Usual starting dose (mg)[a]	Usual daily dose (mg)	Available oral doses (mg)	Mean half-life, hours (active metabolites)[b]
Monoamine oxidase inhibitors					
Irreversible, nonselective monoamine oxidase inhibitors					
Isocarboxazid	Marplan	10	20–60	10	2
Phenelzine	Nardil	15	15–90	15	2
Tranylcypromine	Parnate	10	30–60	10	2
Transdermal monoamine oxidase inhibitors					
Transdermal selegiline	EMSAM	6	6	None Transdermal doses: 6 mg/24 hours 9 mg/24 hours 12 mg/24 hours	18–25
Reversible inhibitors of monoamine oxidase A					
Moclobemide[c]	Aurorix, Manerix	150	300–600	100, 150	2
Tricyclic antidepressants					
Tertiary-amine tricyclic antidepressants					
Amitriptyline	Elavil	25–50	100–300	10, 25, 50, 75, 100, 150	16 (27)
Clomipramine	Anafranil	25	100–250	25, 50, 75	32 (69)
Doxepin	Sinequan	25–50	100–300	10, 25, 50, 75, 100, 150, L	17
Imipramine	Tofranil	25–50	100–300	10, 25, 50, 75, 100, 125, 150	8 (17)
Trimipramine	Surmontil	25–50	100–300	25, 50, 100	24
Secondary-amine tricyclic antidepressants					

Desipramine	Norpramin	25–50	100–300	10, 25, 50, 75, 100, 150	17
Nortriptyline	Pamelor, Aventyl	25	50–150	10, 25, 50, 75, L	27
Protriptyline	Vivactil	10	15–60	5, 10	79
Tetracyclic antidepressants					
Amoxapine	Asendin	50	100–400	25, 50, 100, 150	8
Maprotiline	Ludiomil	50	100–225	25, 50, 75	43
Selective serotonin reuptake inhibitors					
Citalopram	Celexa	20	20–40[d]	10, 20, 40, L	35
Escitalopram	Lexapro	10	10–20	5, 10, 20, L	27–32
Fluoxetine	Prozac	20	20–60[d]	10, 20, 40, L	72 (216)
Fluoxetine Weekly	Prozac Weekly	90	NA	90	—
Fluvoxamine[e]	Luvox	50	50–300[d]	25, 50, 100	15
Paroxetine	Paxil	20	20–60[d]	10, 20, 30, 40, L	20
Paroxetine CR	Paxil CR	25	25–62.5	12.5, 25, 37.5	15–20
Sertraline	Zoloft	50	50–200[d]	25, 50, 100	26 (66)
Serotonin–norepinephrine reuptake inhibitors					
Duloxetine	Cymbalta	30	60–90	20, 30, 60	12
Venlafaxine	Effexor	37.5	75–225	25, 37.5, 50, 75, 100	5 (11)
Venlafaxine XR	Effexor XR	37.5	75–225	37.5, 75, 150	5 (11)
Serotonin modulators					
Nefazodone[e]	Serzone	50	150–300	100, 150, 200, 250	4
Trazodone	Desyrel	50	75–300	50, 100, 150, 300	7
Norepinephrine–serotonin modulators					
Mirtazapine	Remeron	15	15–45	7.5, 15, 30, 45, soltab	20

Norepinephrine–dopamine reuptake inhibitors					
Bupropion	Wellbutrin	150	300	75, 100	14
Bupropion SR	Wellbutrin SR	150	300	100, 150	21
Bupropion XL	Wellbutrin XL	300	300	100, 150	21

Note. L = liquid; NA = not applicable; CR = controlled release; XL or XR = extended release; soltab = orally disintegrating tablets; SR = sustained release.

aLower starting doses are recommended for elderly patients and patients with panic disorder, significant anxiety, or hepatic disease.

bMean half-lives of active metabolites are given in parentheses.

cNot available in the United States.

dDose varies with diagnosis. See text for specific guidelines.

eGeneric only.

Source. Dosing information from American Psychiatric Association 2000b. Half-life data from Physicians' Desk Reference 2005. Dosing and half-life information for transdermal selegiline system from EMSAM 2006.

Adapted from Marangell LB, Martinez JM: *Concise Guide to Psychopharmacology,* 2nd Edition. Arlington, VA, American Psychiatric Publishing, 2006, pp. 13–16. Used with permission.

Table 3–7. Norepinephrine (NE) and serotonin (5-HT) reuptake–blocking effects of the non-MAOI antidepressants

Antidepressant	Ne	5-HT
amitriptyline	+	++
amoxapine	++	+
bupropion	+/–	0
citalopram/escitalopram	0	+++
clomipramine	++	+++
desipramine	+++	+
doxepin	+	+
fluoxetine	0	+++

fluvoxamine	0	+++
imipramine	+	++
maprotiline	++	0
mirtazapine	+	–
nefazodone	0/+	+
nortriptyline	++	+
paroxetine	+[a]	+++
protriptyline	+++	+
sertraline	0	+++
trazodone	0	+
trimipramine	0	0
venlafaxine	+	++

Note. Data are approximations of relative activity from in vivo, in vitro, and clinical studies. Data on clomipramine include results on desmethylclomipramine on both active metabolites with pronounced effects on noradrenergic systems. In certain in vivo models, the tricyclic antidepressants (other than clomipramine) and trazodone have been reported not to block 5-HT uptake. MAOI = monoamine oxidase inhibitor. Strength of effect represented on a scale from 0 (no effect) to +++ (marked effect). +/– indicates marginal effect.

aEffect at high doses.

Table 3–8. Relative receptor-blocking effects of antidepressants

Antidepressant	**Ach**	**$_1$**	**H_1**	**5-HT_1**	**5-HT_2**
amitriptyline	+++	+++	++	+/–	+/–
amoxapine	+	++	+	+/–	+++
bupropion	0	0	0	0	0
citalopram/escitalopram	0	0	0	0	
clomipramine	+	++	+	0	+
desipramine	+	+	+	0	+/–
doxepin	++	+++	+++	+/–	+/–

fluoxetine	0	0	0	0	+/–
fluvoxamine	0	0	0	0	0
imipramine	++	+	+	0	+/–
maprotiline	+	+	++	0	+/–
mirtazapine	0	0	+++	+	+
nefazodone	0	+	0	+	++
nortriptyline	+	+	+	+/–	+
paroxetine	+	0	0	0	0
protriptyline	+++	+	+	0	+
sertraline	0	0	0	0	0
trazodone	0	++	+/–	+	++
trimipramine	++	++	+++	0	+/–
venlafaxine	0	0	0	0	0

Note. Data are approximations of relative activity from in vivo, in vitro, and clinical studies. ACh = muscarinic acetylcholine receptor; $_1$ = $_1$-adrenergic receptor; H_1 = histamine$_1$ receptor; 5-HT_1 = serotonin$_1$receptor; 5-HT_2 = serotonin$_2$ receptor. Strength of effect represented on scale from 0 (no effect) to +++ (marked effect). +/– indicates marginal effect.

Tricyclic antidepressants (TCAs): overview

Efficacy	Second- or third-line agents for MDD (FDA approved for all)
	Panic disorder
	OCD (FDA approved for clomipramine)
	Pain syndromes
	Migraine prophylaxis
	Enuresis (FDA approved for imipramine)
Side effects	Dry mouth, constipation, urinary retention, blurred vision, confusion

	Weight gain
	Sedation
	Sexual dysfunction
	Orthostasis
	Tachycardia
	Cardiac conduction abnormalities
Dosage and administration	Individualize with low hs dosing (25–50 mg) for imipramine and amitriptyline. Increase by 25–50 mg every 3–7 days to target dosage of 150–300 mg/day. (Nortriptyline should be started at 10–25 mg and increased, as needed, to a maximum dosage of 150 mg/day.) Monitor levels and ECGs after dose stabilized.
Safety in overdose	Lethal in overdose (induces arrhythmias).
	Lavage and monitor on a cardiac bed for QRS widening.
Discontinuation	Flulike and GI symptoms from cholinergic rebound. Reduce by 25–50 mg every 3 days.
Drug interactions	CNS depressants: sedation, ataxia Anticoagulants: warfarin levels Antipsychotics: TCA and antipsychotic levels Cimetidine: TCA levels Clonidine: hypertensive crisis (avoid) L-Dopa: TCAs absorption MAOIs: serotonin syndrome (avoid clomipramine; imipramine and amitriptyline may be used with close monitoring) Stimulants: TCA levels Oral contraceptives: TCA levels Quinidine: arrhythmias (avoid) SSRIs: TCA levels Sympathomimetics: arrhythmias, hypertension, tachycardia

Note. CNS = central nervous system; ECG = electrocardiogram; FDA = U.S. Food and Drug Administration; GI = gastrointestinal; MAOI = monoamine oxidase inhibitor; MDD = major depressive disorder; OCD = obsessive-compulsive disorder; SSRI = selective serotonin reuptake inhibitor.

Table 3–9. Common or troublesome side effects of tricyclic and tetracyclic drugs

Anticholinergic	Central nervous system
Dry mouth	Tremor
Constipation	Sedation
Blurred vision	Stimulation
Urinary hesitancy	Myoclonic twitches
Esophageal reflux	Seizure (maprotiline)
Cardiovascular	Extrapyramidal symptoms (amoxapine)
Orthostatic hypotension	Other
Palpitations	Perspiration
Conduction slowing	Weight gain
Hypertension	Sexual dysfunction
	Impotence

Partial list of cytochrome P450 (CYP) substrates and inhibitors

	CYP1A2	CYP2D6	CYP3A3/4
Substrates[a]	Aminophylline	Most antipsychotics	Acetaminophen
	Amitriptyline	Amphetamine	Alprazolam
	Caffeine	Codeine	Amiodarone
	Clozapine (in part)	Donepezil	Antiarrhythmics
	Cyclobenzaprine	Encainide	Calcium channel blockers
	Flutamide	Flecainide	Carbamazepine
	Imipramine	Galantamine	Cyclosporine
	Riluzole	Lipophilic -blockers	Donepezil
	Ramelteon	Mexiletine	Eszopiclone
	Theophylline	Oxycodone	Ethosuximide
		Tricyclic antidepressants[b]	Galantamine

		Tramadol	HMG-CoA reductase inhibitors
		Trazodone	Lamotrigine
		Type Ic antiarrhythmics	Lidocaine
		Venlafaxine	Midazolam
			Most antineoplastics
			Oral contraceptives
			Oxcarbazepine
			Phosphodiesterase inhibitors
			Pimozide
			Propafenone
			Protease inhibitors
			Quinidine
			Steroids
			Zaleplon
			Zolpidem
	CYP1A2	**CYP2D6**	**CYP3A3/4**
Inhibitors[c]	Cimetidine	Bupropion	Diltiazem
	Ciprofloxacin	Cimetidine	Fluvoxamine
	Enoxacin	Duloxetine	Grapefruit juice
	Flutamide	Fluoxetine	Imidazole antifungal agents
	Fluvoxamine	Paroxetine	Some macrolides
	Grapefruit juice	Quinidine	Nefazodone
	Ketoconazole	Ritonavir	Protease inhibitors
	Lomefloxacin	Sertraline	Verapamil
	Norfloxacin		

Note. HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A.

aMedications and substances metabolized by a given enzyme.

bThe 2D6 enzyme is the final common pathway for the metabolism of tricyclic antidepressants.

cMay increase levels of substrates.

Source. Callahan et al. 1996; Cozza et al. 2003; Greenblatt et al. 1998, 1999; Michalets 1998. Adapted from Marangell LB, Martinez JM: *Concise Guide to Psychopharmacology,* 2nd Edition. Arlington, VA, American Psychiatric Publishing, 2006. Used with permission.