

ANTIDEPRESSANT	Usual Adult Dose	Usual Initial Dose	Anticholinergic Effect	Sedative Effect
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Tricyclic Tertiary Amines

Amitriptyline (Elavil®, Endep®)	150-200	50-100	+++++	+++++
Imipramine (Tofranil®)	150-200	50-100	+++	+++
Trimipramine (Surmontil®)	150-200	50-100	++++	++++
Doxepin (Adapin®, Sinequan®) ¹	150-250	50-100	++++	++++
Clomipramine (Anafranil®) ²	150-250	50-100	++++	+++

Tricyclic Secondary Amines

Desipramine (Norpramin®)	150-250	50-100	+	+
Protriptyline (Vivactil®)	30-60	15-30	++++	+
Nortriptyline (Aventyl®, Pamelor®)	75-100	20-40	+++	++

Tricyclic Dibenzoxazepine

Amoxapine (Asendin®) ³	200-400	100-150	++	++
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Tetracyclic

Maprotiline (Ludiomil®)	150-225	50-100	+++	++++
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Triazolopyridine Derivative

Trazodone (Desyrel®)	250-400	100-150	-/+	++++
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Monoamine Oxidase Inhibitor

Phenelzine (Nardil®)	15-90	15	++	+
Isocarboxazid (Marplan®)	20-60	20	++	+++
Tranlycypromine (Parnate®)	30-60	30	++	+++
Selegiline (EMSAM®)	6-12 ⁸	6	+	-

Phenylpropylamine

Fluoxetine (Prozac®) ^{4, 5, 9}	20-60	20	-	-
Fluoxetine (Prozac® Weekly)	90	90	-	-

Naphthalenamine

Sertraline (Zoloft®) ⁴	50-200	50	+	+
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Phenylpiperidine

Paroxetine (Paxil®) ^{4, 7}	20-50	20	+	+/++
Paroxetine (Paxil CR®)	25-75	25	+	+/++

Aralkylketone

Fluvoxamine (Luvox®)	100-300	50	+	+
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Bicyclic Phthalane

Citalopram (Celexa®) ⁴	20-40	20	-/+	-/+
Escitalopram (Lexapro®) ⁴	10-20	10	-/+	-/+

Monocyclic Aminoketone

Bupropion (Wellbutrin®, Zyban®)	300-450	100-150	-	-
Bupropion (Wellbutrin SR®)	150-300	150	-	-
Bupropion (Wellbutrin-XL®)	300	150	-	-

Phenethylamine

Venlafaxine (Effexor®)	75-375	75	++	++
Venlafaxine (Effexor-XR®)	75-225	37.5-75	++	++

Phenylpiperazine

Nefazodone (Serzone®) ⁶	100-600	100	++	++
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Piperazinoazepine

Mirtazapine (Remeron®)	15-45	15	+/++	+/+++
Mirtazapine (Remeron SolTab®)	15-45	15	+/++	+/+++

Thiophenepropanamine

Duloxetine (Cymbalta®)	60-120	60	++	++
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1. Zonalon®/Prudoxin® 5% as topical antipruritic (dermatology)

2. Clomicalm® for canine SAD (veterinary)

3. ~15% metabolized to loxapine (Loxitane®)

4. Available in liquid formulation (mg/mL)

5. Marketed as Sarafem® for PMDD

6. Brand name manufacturing DC'd on 06/14/04

7. Marketed as Pexeva®

8. mg/24 hr. patch

9. Reconcile® for canine SAD

ANTIDEPRESSANT OVERVIEW

The chart presented in this article provides an overview of some aspects of the 26 currently available antidepressants in the United States.

The chart* gives five columns. The first column provides the generic and chemical names of the medications. The second column lists the usual or typical adult dose. The third column lists the usual or typical initial/starting dose. The fourth column lists how drying (anticholinergic) the medication is on a scale of zero to five with zero being a dash and five being five plus signs. Similar ratings are listed in the fifth and final column, which indicates how sedating the medications are likely to be, symptoms of which would be feeling tired, drowsy, or fatigued.

This chart is targeted to an adult population and the dosages ranges listed are not necessarily applicable to pediatric, adolescent, or geriatric populations. Doses for these age groups are often $\frac{1}{2}$ to $\frac{1}{3}$ of adult doses. It should also be noted that the final two columns (having to do with anticholinergic and sedative effects) are this author's subjective opinion and is a rough guess based on a combination of clinical experience, review of literature, supervision, and psychiatric consultation. The fact that the second and third columns indicate "usual" adult dose and "usual" initial dose reflect the fact that there may be situations where the usual adult dose is much lower or higher than listed as well as acknowledging that the usual initial dose might be much less than what is listed. Some patients will get a therapeutic response on seemingly sub-therapeutic doses while other patients will not get a therapeutic response without supra-therapeutic doses. In addition, one cannot presume that because a certain drug is primarily sedating for most people that for another individual it might be activating. Conversely because a drug might be more activating for the majority of patients it might be unexpectedly sedating for another individual. This would not be able to be predicted, however, in advance. The top six yellow blocks essentially list (with the exception of EMSAM[®]) the older antidepressants, which are in relative non-use. For the most part, these medications have been relegated to the "Smithsonian Institute of Psychopharmacology." The older tricyclics tend to be found more in the regimens of patients who are being treated for pain syndromes because of the analgesic properties of these medications. Clomipramine (Anafranil[®]) is occasionally used in treatment refractory OCD that has not responded to adequate trials of two or three SSRIs. Trazodone (Desyrel[®]), although rarely used as an antidepressant because of problems with priapism, is probably one of the more widely used hypnotics in the United States, although this is clearly an off-label use of the medication. Because it is non-anticholinergic but sedating, non-habituating, and not a CNS depressant, low doses of the drug (25-100mg) are used by many people as a sleeping aid so as to avoid the marketed approved hypnotics which are addicting, CNS depressants, and can cause state-dependent learning. One situation in which the tricyclics (TCAs) might be used is in severe treatment-resistant major depression, which has inadequately or poorly responded to several trials of newer antidepressants. Two additional problems with the heterocyclic antidepressants are their cardiotoxicity and lethality in overdose. With the exception of the last medication listed the rest of the chart summarizes the newer antidepressants. With Lexapro we now have six SSRIs although Lexapro[®] is simply (supposedly?) a "new and improved Celexa." The other six newer antidepressants that are non-SSRIs include bupropion, venlafaxine, nefazodone, mirtazapine, duloxetine, and selegiline.

Alternate names of some of the medications include the following:

- ▶ fluoxetine is also marketed as Sarafem[®] for pre-menstrual dysphoric disorder (PMDD)
- ▶ bupropion is also marketed as Zyban[®] for smoking cessation
- ▶ doxepin is also marketed as Zonalon[®] or Prudoxin[®] a topical cream used in the field of dermatology for pruritis
- ▶ clomipramine is also marketed as Clomicalm[®] for canine separation anxiety disorder in the veterinary medicine field; fluoxetine was also recently approved for the same indication as Reconcile[®].

Newer additions of previously marketed agents include:

- ▶ Prozac Weekly[®] which is a single 90mg tablet given once-a-week
- ▶ Wellbutrin SR[®] and XL[®], sustained release versions of Wellbutrin[®] to reduce the number of times per day it needs to be taken
- ▶ Effexor XR[®], an extended release version of Effexor[®] to reduce the number of times that it needs to be taken per day
- ▶ Remeron SolTab[®], an orally disintegrating tablet version of Remeron[®]
- ▶ Paxil CR[®], a controlled-release formulation of Paxil[®]
- ▶ Lexapro[®], the single isomer formulation of Celexa[®]

It should be noted that the newer formulations of the above medications have nothing to do with improved efficacy but are simply designed to help with ease of administration, increased compliance, and potentially reduced side-effects.

The most recent medications approved antidepressant in the U.S. market were duloxetine and selegiline. Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI), which is marketed as Cymbalta[®]. This is the second SNRI on the market and, therefore, is a competitor to venlafaxine, which is the only other currently marketed SNRI. This will not represent any additional efficacy advantages. Selegiline (EMSAM[®]) is an MAO-B antidepressant version of the old Parkinson's drug. It is a transdermal patch formulation.

Two of the five non-SSRIs have been falling out-of-favor with prescribers. Serzone[®] has seen a rapid decline in sales due to problems with liver toxicity world-wide, toxicity that has been serious enough to result in at least 25 fatalities. It is only available as generic nefazodone currently. Remeron[®] has been associated with dramatic and serious weight gain and is also rapidly declining in sales in this author's area for that reason. Neither of these issues have to do with lesser efficacy in general or the possibility of preferential efficacy for certain individuals. Even though it has not been withdrawn by the FDA, the manufacturer of the parent compound decided to discontinue making the drug in June, 2004. Generic formulations of Serzone[®] (nefazodone) can still be obtained from any number of generics manufacturers without loss of efficacy (i.e. presumed bioequivalence).

For individuals who have difficulties swallowing pills/tablets or who may only need very low doses of the medication for a therapeutic response, some of the newer medications are available in liquid formulation. Please refer to Figure 1. which summarizes this issue.

ORAL SUPENSION/LIQUID FORMULATION						
	<i>Prozac[®]</i> <i>(fluoxetine)</i>	<i>Zoloft[®]</i> <i>(sertraline)</i>	<i>Paxil[®]</i> <i>(paroxetine)</i>	<i>Luvox[®]</i> <i>(fluvoxamine)</i>	<i>Celexa[®]</i> <i>(citalopram)</i>	<i>Lexapro[®]</i> <i>(escitalopram)</i>
YES/NO	Yes	Yes	Yes	No	Yes	Yes
% alcohol	0.23%*	12%**	0%	---	0%	0%
mg/ml	20mg/5ml	20mg/ml	10mg/5ml	---	10mg/5ml	5mg/5ml
oz bottle	120ml (4 oz)	60ml (2 oz)	250ml(8.3 oz)	---	120ML (4 oz)	240ml (8 oz)
Flavor	mint	---	Orange	---	peppermint	peppermint
Scent	mint	menthol	Citrus	---	mint	Mint
Color	clear	clear	Orange	---	clear	clear

*"inert" amount (i.e. inactive ingredient)

**contraindicated if taking disulfiram (Antabuse[®])

Although it is beyond the scope of this brief article to address the issue of which antidepressant should be chosen as a first-line agent, it can simply be stated that the current state-of-the-art is that it cannot be determined for any individual patient which antidepressant might work best for them in advance. Some of the factors, however, that play into making a decision as to which agent to begin with include the following:

- ▶ Previous history of response or non-response to a particular agent or class
- ▶ Known family history of response or non-response to a particular agent or class
- ▶ Cost
- ▶ Known side-effect profile
- ▶ Co-morbidity
- ▶ Concurrent medical conditions
- ▶ Concurrent substance abuse
- ▶ Concurrent psychotropic or non-psychotropic medication
- ▶ Concurrent use of herbal/organic products
- ▶ P450 (drug-drug interaction) profile
- ▶ Limited formulary by “mangled care”
- ▶ Past history of compliance/non-compliance
- ▶ Previous history of suicide attempts (therapeutic index of antidepressant consideration)

In summary, this chart is simply designed to give the practitioner a brief overview of the current antidepressant market and to provide some general guidelines as to dosing and anticipated side-effects. The current in-the-pipeline antidepressants do not appear to convey any greater efficacy, lower cost, or shorter latency of onset of action than the currently available antidepressants and we can only hope that through research the next generation of antidepressants might include one that has a consistently greater efficacy with fewer side-effects, with a more rapid onset of action, and with fewer drug-drug interactions. The next antidepressant likely to get approval is the single isomer of venlafaxine (desvenlafaxine) to be marketed as Pristiq®.

To date, we do not have such a drug and with most prescribers the goal is to find the medication that achieves the greatest efficacy at the lowest dose with the fewest side-effects. It should be noted, however, that most patients who indicated that they have “tried” an antidepressant have not really had an adequate trial based on an adequate dose for an adequate duration of time. Most patients have either had expected or unexpected side-effects and did not continue with the drug to see if those side-effects might “level off” or go away and/or never really push the drug to levels that would have potentially achieved euthymia or therapeutic efficacy.

It should also be kept in mind that all antidepressants should be used with great caution in any patient with known or latent bipolarity in light of their potential to induce cycling (hypomania/mania).

I trust this brief overview will be helpful to clinicians in their clinical consultation and collaborative psychopharmacologic efforts and trust that this will be effectively integrated into the recommendations of each clinician's State Board of Psychology recommendations regarding collaborative/Level II practice.

*Column Ratings	— = 0
	-/+ = 0.5 or ½
	+ = 1
	++ = 2
	+++ = 3
	++++ = 4
	+++++ = 5