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The **Black Book** of Psychotropic Dosing and Monitoring 2024

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Psychopharmacology BULLETIN

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DISCLOSURES

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The **Black Book** of Psychotropic Dosing and Monitoring 2024

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Introduction

The Black Book of Psychotropic Dosing and Monitoring

By Charles DeBattista, MD
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Since the last edition of the Black Book, several innovative agents have been approved or are poised to be approved in the coming year. These include novel antidepressants, the first muscarine agonist for the treatment of schizophrenia, the first psychedelic which may be approved for the treatment of PTSD (Post Traumatic Stress Disorder), and the first disease modifying drug for the treatment of Alzheimer's disease.

Three new antidepressants have come to the market in the past 18 months. The first of those, Auvelity, the combination of bupropion and dextromethorphan, takes advantage of a pharmacokinetic and pharmacodynamic synergism between the two drugs.[85] Dextromethorphan has several pharmacodynamic properties including actions on the NMDA receptor and the Sigma 1 receptor, adding to the indirect norepinephrine agonist properties of bupropion. How Dextromethorphan is rapidly metabolized via the CYP2D6 isoenzyme to dextrophan that may have mu opioid agonist properties. The combination with bupropion, a CYP2D6 inhibitor, inhibits the metabolism of dextromethorphan allowing for more consistent therapeutic levels. The combination of dextromethorphan 45 mg twice per day and bupropion SR 105 mg twice daily appears to be more effective than an equivalent dose of bupropion alone both in speeding up antidepressant response and achieving remission. However, it's not clear at this time how the combination would compare with a more typical dose of bupropion of 300–450 milligrams a day range. The

phase III program for Auvelity, showed that the drug was well tolerated with the most common side effects being dizziness, headache, and dry mouth.[86]

Another novel antidepressant agent approved in 2023 is zuranolone (Zurzuvae). Zuranolone is an oral analog of IV brexanalone, and like brexanolone, was approved for the treatment of post-partum depression.[83] The advantages of zuranolone over brexanalone are many. While brexanolone is a 60-hour intravenous infusion that must be administered in a health care facility, zuranolone is a once/day oral medication that is usually taken at home. Like brexanolone, and unlike most antidepressants, zuranolone has a short course of treatment, lasting just 14 days. Zuranolone's, as does brexanolone, is thought to act primarily as allosteric modulator of the GABA-a receptors. Despite only 14 days of treatment, zuranolone produced in depression in post-partum patients a clinically and significantly meaningful improvement at day 15 and continued to day 45 or 1 month past the end of treatment. Zuranolone is a schedule IV drug. The most common side effect in clinical trials was somnolence with 36% of participants reporting this side effect vs only 6% of those on placebo.[84] Other common side effects included dizziness, diarrhea and fatigue. While the FDA declined to approve zuranolone as monotherapy or as an adjunctive treatment to standard antidepressants in major depression itself, there are positive studies in non-post-partum major depression albeit with smaller effect sizes and less consistent duration of activity. It is likely that zuranolone will continue to be studied in other depressive syndromes such as depression with anxious distress.

The third "new" antidepressant approved late 2023 was gepirone (Exxua). Gepirone is not exactly a new or novel antidepressant and originally sought approval in the US about 20 years ago.[88] There had been two positive studies of gepirone during the original NDA application but also a number of failed, negative, or non-informative studies as well. Thus, the FDA declined to originally approve the drug. However, failed and negative trials are common with

antidepressants and after much internal debate, the FDA ultimately agreed to approve the drug based on the positive trials and a relatively favorable side effect profile. Gepirone, like buspirone, is a partial agonist of the 5HT1a receptor and a 5HT2 antagonist. As such, gepirone does not tend to be associated with sexual side effects, weight gain, or sedation. The most common side effects are dizziness, nausea, and insomnia which tend to improve in many patients over time.

Second generation antipsychotics (SGAs) continue to be the only class of agents [other than esketamine (Spravato)] approved in adjunctive treatment of resistant major depression. In addition to olanzapine (combined with fluoxetine; Symbyax), aripiprazole (Abilify), quetiapine (Seroquel), brexpiprazole (Rexulti), cariprazine (Vraylar) became the latest SGA to be approved in 2022.[90] Adjunctive cariprazine at 1.5 mg daily was significantly more effective than adjunctive placebo in patients with MDD who had failed to achieve an adequate response with an antidepressant alone after 6 weeks of treatment. Interestingly, a 3 mg dose of cariprazine was less consistently effective.[91] The major advantage of cariprazine over some of the other approved adjunctive SGA's is easy dosing, with the starting 1.5 mg dose being the optimal therapeutic dose for most people, and a lower metabolic side effect burden with most subjects having limited or no weight gain in short term trials. The most common side effect were akathisia/restlessness, fatigue, and nausea. Lumateperone (Caplyta) is also has positive phase III data in the adjunctive treatment of major depression and is expective file for approval in late 2024.

Another recent major development in psychopharmacology is the reemergence of psychedelics in the treatment of psychiatric disorders. The first of these is MDMA (phenethylamine 3,4-methylenedioxymethamphetamine) assisted psychotherapy for the treatment of PTSD. A New Drug Application (NDA) was accepted by the FDA for MDMA in the treatment of PTSD in late 2023.[87] Because the drug is being fast tracked as a "breakthrough" treatment by the FDA, it was expected to see approval in the summer of 2024. The phase II and III data for MDMA

assisted psychotherapy in the treatment of PTSD have been quite consistent and impressive. However, independent reviews have pointed to significant deficiencies in these studies including the bias introduced because of functional unblinding; virtually all patients in psychedelic studies can guess whether they got the active drug or placebo. The functional unblinding, the lack of standardization of adjunctive psychotherapy as well as the abuse potential of MDMA, may delay an FDA approval. The typical regimen in these trials included 3 preparatory psychotherapy sessions followed by once/month dosing sessions (lasting about 8 hours) and using doses of 120–160 mg in a split dose. There were typically 3 monthly dosing sessions, each followed by 3 integrative psychotherapy sessions to help subjects process and understand their experiences during the dosing sessions. In the most recent phase 3 trials, over 70% of subjects no longer met criteria for PTDS compared to 46% of those treated with psychotherapy and placebo alone.[89] The only approved medications for treating PTSD are two SSRIs, paroxetine and sertraline. These drugs effect only some dimensions of PTSD with only 20–30% achieving a remission level response with these drugs. Thus, MDMA assisted psychotherapy appears to achieve much higher levels of remission and response than has been true for the SSRIs. Since MDMA is not taken continuously, side effects from MDMA tend to be short lived. Side effects have included muscle tightness, nausea, diminished appetite, excessive sweating, feeling cold and dizziness among others. Since MDMA is currently a schedule I drug, it is likely that a rigorous Risk Evaluation Mitigation (REMs) program will be put in place and a limited number of centers and clinicians will be designated to perform MDMA assisted psychotherapy for PTSD. In addition to MDMA, psilocybin-assisted psychotherapy is in phase 3 trials for treating resistant depression but unlikely to be available before late 2025 at the earliest.

An argument can be made that there has not been a truly novel antipsychotic since the introduction of clozapine in the US in 1990. All first-generation antipsychotics have been dopamine 2 antagonists and second-generation drugs have involved some ratio of 5HT2 antagonism to

D2 blockade. In 2023, the FDA accepted the application of xenomaline/tropsium (KarXT) which may become the first muscarinic M1M4 agonist approved for the treatment of schizophrenia.[82,83] Tropsium is added as a muscarine antagonist to block the peripheral cholinergic effects of a muscarine agonist. Xenomaline/tropsium appears to be effective in treating both positive and negative symptoms of schizophrenia. In a phase 3 study of 407 patients with schizophrenia, xenomaline/tropsium at doses of xenomaline/50 mg/tropsium 20 mg twice daily up to 125 mg/30 mg twice daily was significantly more effective than placebo in treating both and negative symptoms over 5 weeks of treatment. As would be expected, the side effect profile of xenomaline/tropsium is very different that all currently available antipsychotics. There is no risk of EPS as it is not a dopamine antagonist, and xenomaline/tropsium is not associated with significant metabolic effects. The side effects are cholinergic in nature and include constipation, dry mouth, and nausea. A decision is expected in September of 2024.

The year 2023 also saw the approval of the first disease modifying drug in the treatment of Alzheimer's disease, lecanemab (Lequembi). While acetylcholinesterase inhibitors and memantine have been available for decades, these drugs modestly improve cognition in Alzheimer's disease patients and do not alter the progressive course of the illness. Lecanemab is an IV monoclonal antibody that targets the removal of beta-amyloid in the brain as well proto-fibrils that are also known to be toxic to neuronal tissue. When given early in the course of the illness, patients treated with Lecanemab showed 27% less decline on some measures of cognition and function than did patients treated with a placebo over 18 months (about 1 and a half years). It is not known whether treatment for longer than 18 months would show lesser or greater decline over time. However, there are simulation studies that suggest that Lecanemab may modestly reduce the number of patients who progress to severe Alzheimer's disease and require institutional care. The standard dose is 10 mg/kg given via IV over one hour every 2 weeks for 18 months. Lecanemab is typically administered in an infusion center so that side effects can

be monitored. The most serious side effects of Lecanemab are amyloid related imaging abnormalities (ARIA) that are associated with brain edema and microhemorrhages. ARIA can occur in up to 15% of patients. More common side effects are headache and nausea.

While it remains to be seen how useful these new agents will be in clinical practice, they do represent an approach to treating neuropsychiatric disorders that are a notable departure from the pharmacotherapy of the past half century. It seems likely that some patients who have not been able to respond to or tolerate traditional pharmacotherapy will find hope in these new medications.

Dosage Ranges

Table 1: PSYCHOTROPIC DRUG DOSAGE RANGES[11,20–28]

Generic	Brand Name	Dosage Range* (mg/day)
Alprazolam	Xanax	0.75–10
Amitriptyline	Elavil, Endep, Enovil	50–300
Amoxapine	Asendin	50–600
Armodafinil	Nuvigil	150–250
Asenapine	Saphris	5–10 mg BID sublingual
	Secuado	3.8–7.6 mg patch/24hr
Brexpiprazole	Rexulti	2–4
Bupropion	Wellbutrin, Wellbutrin SR, Zyban†	200–450 150–400 150–300
Bupropion/ dextromethorphan	(Auvelity)	105 mg/45 mg BID
Buspirone	BuSpar	15–60
Carbamazepine‡	Epitol, Tegretol	400–1,600
Cariprazine	Vraylar	3–6
Chlordiazepoxide§	Librium, Libritabs, Mitran	15–100
Chlorpromazine‖	Ormazine, Thorazine	30–800
Citalopram	Celexa	20–60
Clomipramine	Anafranil	25–250
Clonazepam**	Klonopin	0.50–4
Clorazepate§	ClorazeCaps, ClorazeTabs, Gen-XENE, Tranxene	15–60
Clozapine	Clozaril	12.5–900
Desipramine	Norpramin, Pertofrane	25–300
Desvenlafaxine	Pristiq	50–100
Diazepam	Valium, Valrelease, Zetran	4–40
Doxepin	Adapin, Sinequan	25–300
Droperidol	Inapsine	2.5–15
Duloxetine	Cymbalta	40–120
Eszopiclone	Lunesta	1–3
Fluoxetine	Prozac, Sarafem	20–80
Fluphenazine	Permitil, Prolixin	1–40
Flurazepam	Dalmane	15–30
Fluvoxamine	Luvox	50–300
Gabapentin	Neurontin	300–3,600
Galantamine	Reminyl	16–32
Gepirone	(Exxua)	54.5–72.6 mg
Halazepam	Paxipam	60–160
Haloperidol	Haldol	1–100
Iloperidone	Fanapt	6–12 mg BID
Imipramine	Janimine, Tofranil	50–300
Isocarboxazid	Marplan	20–60
Lamotrigine	Lamictal	25–400
Lemborexant	Dayvigo	5
Levomilnacipran	Fetzima	40–120
Lisdexamfetamine	Vivance	30–70
Lithium	Cibalith-S, Eskalith, Lithane, Lithobid, Lithonate, Lithotabs	600–1,800
Lorazepam	Ativan	1–10
Loxapine	Loxitane	20–250
Lumataperone	Caplyta	42
Lurasidone	Latuda	40–160

Generic	Brand Name	Dosage Range* (mg/day)
Maprotiline	Ludiomil	25–225
Methylphenidate HCl	Concerta	18–54
	Ritalin, Ritalin-SR	10–60
Mirtazapine	Remeron	15–45
Modafinil	Provigil	100–400
Nefazodone	Serzone	200–600
Nortriptyline	Aventyl, Pamelor	75–150
Olanzapine	Zyprexa	5–20
Oxazepam	Serax	30–120
Oxcarbazepine	Trileptal	600–1,200
Paroxetine††	Paxil	20–60
Perphenazine	Trilafon	12–64
Phenelzine	Nardil	15–90
Pimozide	Orap	1–10
Prazepam	Centrax	30–60
Protriptyline	Vivactil	15–60
Quazepam	Doral	7.5–15
Quetiapine	Seroquel	50–750
Risperidone	Risperdal	2–16
Rivastigmine	Exelon	6–12
Sertraline	Zoloft	50–200
Suvorexant	Belsomra	10–20
Temazepam	Restoril	15–30
Thioridazine	Mellaril	20–800
Thiothixene	Navane	6–60
Tiagabine	Gabitril	4–32
Topiramate	Topamax	50–400
Tranylcypromine	Parnate	30–60
Trazodone	Desyrel	150–600
Triazolam	Halcion	0.125–0.5
Trifluoperazine	Stelazine	2–40
Trimipramine	Surmontil	50–300
Valproic Acid/ Divalproex	Depakene, Depakote	750–4,200
Venlafaxine‡‡	Effexor,	75–375
	Effexor XR***	75–225
Vilazodone	Viibryd	30–40 mg
Vortioxetine	Trintillex	10–20
Zaleplon	Sonata	5–20
Ziprasidone	Geodon	40–160
Zolpidem	Ambien	5–10
Zuranolone	(Zurzuvae)	25–50 mg Postpartum Depression

*Recommended dosages may vary by indication. Dosage ranges include starting doses that may not represent effective dosages. Some drugs may be contraindicated or may require lower doses in pediatric, geriatric, or debilitated patients. Consult the prescribing information of individual drugs for more detailed information.

†Zyban is indicated as an aid to smoking cessation.

‡Although carbamazepine is not approved by the FDA for psychiatric indications, the authors view it as one of the most important agents available for the treatment of bipolar disorder. This view is supported in the medical literature.

§For alcohol detoxification and withdrawal, doses of up to 300 mg of chlordiazepoxide and 90 mg of clorazepate may be warranted.

‖Labeling suggests that higher doses in severe cases may be appropriate, up to 2,000 mg/day, but little therapeutic gain is achieved by >1,000 mg/day for extended periods. Intramuscular doses may be necessary.

**Starting dosage of clonazepam should not be >1.5 mg/day for PD but doses up to 20 mg/day are approved for seizure disorders.

††Dosage range for paroxetine adjusted for OCD and PD.

‡‡Recommended starting dose is 75 mg/day.

***37.5 mg/day for 4–7 days is an initial dosing option.

Antidepressants

Table 2: MOOD DISORDERS: ANTIDEPRESSANTS[10,11,21–24,26,27,29–35]

Drug	Typical Starting Dosage (mg)	Typical Dosage Range* (mg/day)
Amitriptyline (Elavil, Endep, Enovil)	25 TID or 50 QHS	50–300
Amoxapine (Asendin)	50 BID/TID	50–600
Brexanalone (Zulresso)	30 mcg/kg/hr IV	30–90 mcg/kg/hr × 60 hrs
Bupropion (Wellbutrin)	100 BID	200–450‡
Bupropion SR (Wellbutrin SR)	150 QAM	150–400‡
Bupropion XL (Wellbutrin XL)	150 QD	300–450 QD
Bupropion SR (Zyban)	150 QD	150–300‡
Bupropion/ dextromethorphan (Auvelity)	105 mg/45 daily	105 mg/45 mg BID
Citalopram (Celexa)	20	20–60
Clomipramine (Anafranil)	25–100 QD in divided doses within first 2 weeks	25–250
Desipramine (Norpramin, Pertofrane)	25 TID	100–300
Desvenlafaxine (Pristiq)	50 mg	50–100 mg
Doxepin (Sinequan)	25 TID	75–300
Duloxetine (Cymbalta)	20	40–120
Esketamine intransal (Spravato)	56 mg Intranal	56–84
Fluoxetine (Prozac, Sarafem)	20 QD	20–80
Fluvoxamine (Luvox)	50 QD	50–300
Gepirone (Exxua)	18.2 mg QD	72.6 mg QD
Imipramine (Janimine, Tofranil)	25 TID	75–300
Maprotiline (Ludiomil)	25 TID	75–225
Isocarboxazid (Marplan)	10	20–60
Levomilnacipran (Fetzima)	20	40–120
Milnacipran (Savella)	12.5 mg	50–100 mg BID
Mirtazapine (Remeron)	15 QHS	15–45
Nefazodone (Serzone)	100 BID	200–600
Nortriptyline (Aventyl, Pamelor)	25 TID/QD	75–150
Paroxetine (Paxil)**	20 QAM	10–60
Phenelzine (Nardil)	15 TID	15–90
Protriptyline (Vivactil)	5 TID	15–60
Sertraline (Zoloft)	50 QAM	50–200
Tranylcypromine (Parnate)	Individualized	30–60

	FDA Indication(s)	Proposed Therapeutic Plasma Concentration (ng/mL)
	Depression	120–250[†]
	Depression, psychotic depression	—
	Post Partum Depression	—
	Depression	<100[†]
	Depression	
	Depression	
	Smoking cessation	
	Depression	—
	OCD	100–250
	Depression	115–180[§]
	Depression, anxiety	
	Depression, anxiety, psychotic depressive disorders with associated anxiety	70–250[†]
	Depression, anxiety, neuropathic pain, chronic pain	—
	Depression, Suicidality in Depression	—
	Depression, OCD, bulimia nervosa, PMDD	—
	OCD	—
	Depression, childhood enuresis	200–250[†,§]
	Depression	—
	Depression	—
	Depression	
	Fibromyalgia	
	Depression	—
	Depression	—
	Depression	50–150[§]
	Depression, OCD, PD, social anxiety disorder, GAD	—
	Depression, atypical depression	—
	Depression	70–250
	Depression, OCD, PD, PTSD	—
	Depression, depression without melancholia	—

Table 2: MOOD DISORDERS: ANTIDEPRESSANTS[10,11,21–24,26,27,29–35] *(CONT'D)*

Drug	Typical Starting Dosage (mg)	Typical Dosage Range* (mg/day)
Trazodone (Desyrel)	50 TID	150–600
Trimipramine (Surmontil)	25 TID	50–300
Venlafaxine (Effexor)	37.5 BID	75–375
Venlafaxine ER (Effexor XR)††	37.5–75 QD	75–225
Vilazodone (Vybryd)	10 mg	20–40 mg
Vortioxetine (Trintillex)	10 mg	10–20
Zuranolone (Zurzuvae)	25 mg qhs	50 mg s

*In geriatric patients, the appropriate dosage is widely variable, but in general it is one half the young adult dosage range for TCAs and for compounds with significant cardiovascular toxicity.
†Parent and metabolite.
‡Not >150 mg/dose. Zyban is indicated as an aid to smoking cessation.
§Therapeutic drug monitoring is well established.
**Dosage range for paroxetine adjusted for OCD and PD.
††37.5 mg/day for 4–7 days is an initial dosing option.
FDA=Food and Drug Administration; OCD=obsessive-compulsive disorder; PMDD=premenstrual dysphoric disorder; PD=panic disorder; GAD=generalized anxiety disorder; PTSD=posttraumatic stress disorder.

Table 3: PHARMACOKINETIC COMPARISON OF SELECTED ANTIDEPRESSANTS[10,11,36,37]

	Sertraline	Fluoxetine
Half-life (hours)	26	48–72
Metabolite activity	20–30% activity	Equal
Metabolite half-life (hours)	62–104	96–384
Steady state (days)	7–10	28–35
Dose-proportional plasma levels	Yes	No
Protein binding (%)	98	94.5
Dose reduction in elderly	No	Yes
	EscitaLopram	**VenLafaxine**
Half-life (hours)	27–33	3–7
Metabolite activity	Low activity	Equal
Metabolite half-life (hours)	—	9–13
Steady state (days)	7–10	3
Dose-proportional plasma levels	Yes	Yes
Protein binding (%)	56	27–30
Dose reduction in elderly	No	No

	FDA Indication(s)	Proposed Therapeutic Plasma Concentration (ng/mL)
	Depression	—
	Depression	—
	Depression	—
	Depression, GAD	—
	Depression	—
	Depression	—
	Postpartum Depression	—

Paroxetine	Esketamine		Fluvoxamine
21 (mean)	7–12		15.6
Inactive	Low activity		Questionable
—	1–1.3		14–16
~10	NA		7
No	No		No
93–95	45		80
Yes	No		Yes
CLomipramine	**Amitriptyline**	**Bupropion**	**Mirtazapine**
19–37	9–46	14	20–40
Equal	Equal	4 variably active	10% activity
54–77	16–88	8–24	20–40
7–14	4–10	Variable	3–4
No	Yes	Yes	Yes
97	90–97	80	85
Yes	Yes	Yes	No

Table 4: CENTRAL NERVOUS SYSTEM NEUROTRANSMITTERS: SELECTED ANTIDEPRESSANT EFFECTS[10,11,36,38]

	Serotonin	Norepinephrine	Dopamine	GABAa
Amitriptyline	++++	++++	0	0
Amoxapine	+++	+++	0	0
Bupropion	0/+	+*	++	0
Citalopram	++++	0	0	0
Desipramine	+	++++	0/+	0
Doxepin	+++	+	0	0
Fluoxetine	++++	0	0/+	0
Fluvoxamine	++++	0	0/+	0
Gepirone	+++	0	0	0
Imipramine	+++	++	0/+	0
Lithium	0/++§	0	0	0
Maprotiline	0	++++	0	0
Mirtazapine	+++*	++†	0	0
Nortriptyline	++	+++	0	0
Paroxetine	++++	0/+	0/+	0
Protriptyline	+	++++	0	0
Sertraline	++++	0	0/+	0
Trazodone	++‡	0	0	0
Trimipramine	++	++	0	0
Venlafaxine	++++	+++	0/+	0
Vortioxetine	****	0	0	0
Zuranolone	0	0	0	++

++++=high; +++=moderate; ++=low; +=very low; 0=none.
*5-HT_2 and 5-HT_3 antagonist.
†$\alpha_2$presynaptic antagonist.
‡5-HT_2 antagonist.
§Acutely increases; chronically stabilizes.

Table 5: SUBSTRATES, INHIBITORS, AND INDUCERS OF SOME IMPORTANT CYTOCHROME P450 (CYP) ISOFORMS[10,39–43]

CYP % *of all CYP**	Substrates	
CYPIA2	3° amine TCAs	Olanzapine
13	(N-demethylation)	Phenacetin
	Acetaminophen	Propranolol
	Caffeine	Tacrine
	Clozapine (major)	Theophylline
	Methadone	
CYP2C9	Celecoxib	NSAIDs
20	Fluvastatin	Phenytoin (major)
(for all 2C)	Glipizide	Rosiglitazone
	Irbesartan	S-warfarin
	Losartan	Tolbutamide
CYP2CI9†	3° amine TCAs	Mephobarbital
20	(N-demethylation)	Moclobemide
(for all 2C)	Citalopram (partly)	Nelfinavir
	Diazepam (partly)	Omeprazole
	(N-demethylation)	(5-hydroxylation)
	Hexobarbital	Phenytoin (minor)
	Indomethacin	R-warfarin
	Lansoprazole	S-mephenytoin

	Inhibitors		Inducers
	Cimetidine	Mibefradil	Char-grilled meat
	Fluoroquinolines (ciprofloxacin, norfloxacin)	Moclobemide	Omeprazole
		Naringenin	Tobacco
	Fluvoxamine	Ticlopidine	
	Amiodarone	Fluvoxamine	Phenytoin
	D-propoxyphene	Miconazole	Rifampin
	Disulfiram	Phenylbutazone	Secobarbital
	Fluconazole	Sulphaphenazole	
	Fluvastatin	Zafirlukast	
	Cimetidine	Ketoconazole	Rifampin
	Felbamate	Moclobemide	
	Fluoxetine	Omeprazole	
	Fluvoxamine	Phenytoin	
	Imipramine	Tranylcypromine	

Table 5: SUBSTRATES, INHIBITORS, AND INDUCERS OF SOME IMPORTANT CYTOCHROME P450 (CYP) ISOFORMS[10,39–43] *(CONT'D)*

CYP % *of all CYP**	**Substrates**	
CYP2D6†	2° and 3° amine TCAs	Hydrocodone
2	(2, 8, 10-hydroxylation)	Mexiletine
	Alprenolol	Mirtazepine (partly)
	Amphetamine	Nortriptyline
	Beta blockers	Oxycodone
	Carvedilol	Paroxetine
	Clozapine (minor)	Perphenazine
	Codeine (hydroxylation,	Propafenone (IC
	O-demethylation)	antiarrhythmics)
	D-fenfluramine	Risperidone
	Desipramine	Tamoxifen
	Dextromethorphan	Thioridazine
	(O-demethylation)	Timolol
	Donezepil (partly)	Tramdol
	Fluoxetine (partly)	Trazodone
	Fluphenazine	
	Haloperidol (reduction)	
CYP2EI	Acetaminophen	Isoflurane
7	Chlorzoxazone	Methoxyflurane
	Ethanol	Sevoflurane
	Halothane	
CYP3A4	3° amine TCAs	Lidocaine
30	(N-demethylation)	Loratadine
(for all 3A)	Acetaminophen	Lovastatin
	Alfentanil	Midazolam
	Alprazolam	Mirtazapine (partly)
	Amiodarone	Nefazodone
	Androgens	Nifedipine
	Atorvastatin	Nimodipine
	Buspirone	Nisoldipine
	Carbamazepine	Nitrendipine
	Cerivastatin	Omeprazole (sulfonation)
	Citalopram (partly)	Propafenone
	Codeine (demethylation)	
	Cyclophosphamide	Protease inhibitors
	Cyclosporine	(HMG-CoA reductase
	Dexamethasone	inhibitors)
	Diazepam (partly)	Quetiapine
	(hydroxylation and	Quinidine
	N-demethylation)	Sertraline
	Diltiazem	Sildenafil

	Inhibitors		Inducers
	Amiodarone	Hydroxybupropion	
	Bupropion	Methadone	
	Celecoxib	Moclobemide	
	Cimetidine	Paroxetine	
	Fluoxetine	Perphenazine	
	Fluphenazine	Quinidine	
	Fluvoxamine (weak)	Ritonavir	
	Haloperidol	Sertraline (weak)	
		Thioridazine	
	Diethyldithio-carbamate (Disulfiram metabolite)		Ethanol
			Isoniazid
	Amiodarone	Ketoconazole	Barbiturates
	Cimetidine	(azole antifungals)	Carbamazepine
	Clarithromycin	Mibefradil	Dexamethasone
	Dexamethasone	Naringenin (grapefruit)	Phénobarbital
	Diltiazem	Nefazodone	Phenytoin
	Erythromycin	Nelfinavir	Pioglitazone
	Fluconazole	Ritonavir	Rifampin
	Fluoxetine	Saquinavir	St. John's wort
	Fluvoxamine	Sertraline (weak)	
	Gestodene	Troleandomycin (macrolides)	
	Indinavir (protease inhibitors)	Verapamil	
	Itraconazole		

Table 5: SUBSTRATES, INHIBITORS, AND INDUCERS OF SOME IMPORTANT CYTOCHROME P450 (CYP) ISOFORMS[10,39–43] *(CONT'D)*

CYP % *of all CYP**	Substrates	
	Disopyramide	Simvastatin
	Donepezil (partly)	Sufentanil
	Erythromycin	Tacrolimus
	(macrolides)	Tamoxifen
	Estrogens (steroids)	Tiagabine
	Ethosuximide	Triazolam
	Felodipine	Verapamil
	Fentanyl	Vinblastine
	Ifosfamide	Vincristine
		Ziprasidone
		Zuranolone

†Clinically significant human polymorphism reported.
CYP 450=cytochrome P450; TCAs=tricyclic antidepressants; NSAIDS=nonsteroidal anti-inflammatory drugs.
CYP=cytochrome P450; TCAs=tricyclic antidepressants.

Table 6: EXAMPLES OF DRUGS* THAT MIGHT INTERACT WITH AN ANTIDEPRESSANT[12]

CYP 1A2	CYP 2C19	CYP 2C9
Acetaminophen	Barbiturates	Diclofenac
Caffeine	Citalopram	Ibuprofen
Clozapine	Diazepam	Naproxen
Haloperidol	Mephenytoin	Omeprazole
Olanzapine	Moclobemide	Phenytoin
Phenacetin	Propranolol	Piroxicam
Phenothiazines	3° TCAs	S-Warfarin
R-warfarin (minor)		Tolbutamide
Tacrine		
3° TCAs		
Theophylline		
Thiothixene		

*Drug can be a substrate and/or an inhibitor of a given enzyme system.
†Inhibitor at 2D6, not a substrate.
††Loratadine not contraindicated.
CYP=cytochrome P450; TCA=tricyclic antidepressant.

	Inhibitors	Inducers

CYP 2D6	CYP 3A4
Amphetamines	Androgens
Chlorpheniramine	Benzodiazepines (alprazolam,
Codeine/hydrocodone	triazolam, clonazepam, diazepam)
Desipramine other 2° TCAs	Calcium channel blockers
Dextromethorphan	Carbamazepine
Fiecainide/encainide	Corticosteroids
Haloperidol (minor)	Cyclosporine
Phenothiazines	Dapsone
Propranolol, timolol, metoprolol	Estrogens
Reduced haloperidol	HMG-CoA reductase inhibitors
Risperidone	Ketoconazole, itraconazole
Quinidine†	Macrolide antibiotics
Tamoxifen	Nonsedating antihistamines††
Tramadol	Paclitaxel
	Quinidine
	Tamoxifen
	Zolpidem

Table 7: EXAMPLES OF DRUG INTERACTIONS[10,11,39,42–48]

Drug	Interaction	Mechanism
TCA Interactions		
Alcohol	sedation, ataxia	CNS depression synergism
Calcium channel blockers	TCA levels	Inhibit oxidation of TCAs
Carbamazepine	TCA levels	Hepatic enzyme induction
Clmetidine	TCA levels	Inhibit TCA metabolism
Clonidine	Antagonize antihypertensive effects	Norepinephrine reuptake
Estrogen	TCA levels	Inhibit oxidation of TCAs
Guanethidine	Reverse antihypertensive effects	Block norepinephrine reuptake
Haloperidol/ phenothiazines	antipsychotic levels	CYP 2D6 inhibition
Methadone	TCA levels	Inhibit TCA metabolism
MAOIs	Serotonin syndrome	Serotonin synergism
Quinidine	TCA levels, arrhyth mia	Inhibit CYP 2D6
SSRIs	TCA levels	Inhibit various CYP systems
Stimulants	TCA levels	Inhibit TCA metabolism
SSRI Interactions		
Cyproheptadine	Reverse antidepressant effect	Serotonin antagonism
Dextromethorphan	Serotonin syndrome	Serotonin synergism
Hallucinogens	LSD flashbacks	5-HT_2 agonism
MAOIs	Serotonin syndrome	Serotonin synergism
TCAs	TCA toxicity	Inhibit various CYP systems
Tryptophan	Serotonin syndrome	Serotonin synergism
Theophlline	Theophylline toxicity	Inhibit theophylline metabolism (fluvoxamine)
Warfarin	warfarin levels	Inhibit CYP 2C
MAOI Interactions		
Barbiturates	sedation	Inhibit barbiturate metabolism
Hypoglycemics	effects of hypoglycemics	MAOIs lower blood sugar
Meperidine	Serotonin syndrome	Serotonin synergism
SSRIs	Serotonin syndrome	Serotonin synergism
Succinylcholine	Prolonged apnea in surgery	Decreased cholinesterase levels
Sympathomimetics	Hypertensive crisis	indirect pressor effect
TCAs	Serotonin syndrome	Serotonin synergism
Tyramine (dietary)	Hypertensive crisis	indirect pressor effects
Zuranolone Barbiturate	decrease Zuranolone levels	CYP 2A4 induction

Drug	Interaction	Mechanism
Phenytoin	decrease Zuranolone levels	CYP 2A4 induction
St. John's Wort	decrease Zuranolone levels	CYP 2A4 induction
Glucocorticoids	decrease Zuranolone levels	CYP 2A4 induction
CNS Depressants	Excessive Sedation	CNS synergism
Venlafaxine Interactions		
Clmetidine	venlafaxine levels	CYP P450 inhibition
Haloperidol	haloperidol levels Haloperidol elimination half-life unchanged	Unknown
MAOIs	Serotonin syndrome	Serotonin synergism
SSRIs	Potential venlafaxine levels	2D6 inhibition
	Serotonin syndrome	Serotonin synergism
Nefazodone Interactions		
Glucocorticoids	steroid	Inhibit 3A4

TCA=tricyclic antidepressant; =increased; CNS=central nervous system; =decreased; CYP=cytochrome P450; MAOIs=monoamine oxidase inhibitors. =incr eased; TCAs=tricyclic antidepressants; CYP=cytochrome P450; SSRIs=selective serotonin reuptake inhibitors; LSD=lysergic acid diethylamide; MAOIs=monoamine oxidase inhibitors.

Antidepressant Monitoring

Table 8: TCA MONITORING[10,11]

Baseline	At Therapeutic dose steady state	Annually or PRN
	(Steady state at 5 x half life (t1/2) of drug)	
EKG, HR, BP (with orthostasis)	EKG, HR, BP with orthostasis	EKG, BP, HR
	Serum levels	Serum levels
Serum Level Monitoring	10–14 hour after last dose for once daily dosing 4–6 hours after last dose of split dosing	

TCA	Therapeutic Serum level (µ/L)	Toxic Level (µ/L)
Amitriptyline	120–250	>500
Desipramine	115–250	>500
Nortriptyline	50–150	>300
Imipramine	180–350	>500

Table 9: INTRANASAL ESKETAMINE BP/HR MONITORING[1,10,11]

Esketamine may cause increases in BP and Heart rate.

For baseline BP >140/90 the risks of an increase in BP should be weighed against potential benefit. Food and drink discouraged for 2 hours prior to drug to reduce nausea/vomiting.

Prior to Administration	40 minutes	120 minutes
BP and HR	BP and HR	BP and HR

BP should be stable or reducing to baseline to discharge home. Patients should not drive to or from visits and should abstain from driving until the following day.

(PDR 2020)

Table 10: BREXANALONE IV MONITORING[2,3,11]

Brexanalone is associated with a risk of excessive sedation and loss of consciousness in some patients.

Before Administration

Counsel the patient on signs and symptoms of excessive sedation, loss of consciousness, and the importance of immediately reporting to a healthcare provider any signs and symptoms of excessive sedation using the Patient Information Guide. Provide a copy of the material to the patient.

During treatment, every 2 hours:

- Assess the patient's health status for signs and symptoms pf excessive sedation and loss of consciousness.

During treatment:

- Assess the patient's oxygen saturation using continuous pulse oximetry.

After treatment discontinuation, prior to discharge:

- Assess the patient's level of sedation

After treatment discontinuation, within 3 business days of completion date:

- Report excessive sedation or loss of consciousness to the REMS Program using the Excessive Sedation and Loss of Consciousness Adverse Event Form

Mood Stabilizers

Table 11: MOOD STABILIZERS[10,11,49,54]

	Lithium*
	(Cibalith-S, Eskalith, Lithane, Lithobid, Lithonate, Lithotabs)
Serum plasma levels	0.6–1.2 mEq/L (acute)
Usual adult daily dosage	600–1,800 mg
Onset of action	5–14 days
Protein binding	Not bound to plasma proteins
$t_{1/2}$	24 hours (average) with age and/or with decreased renal function
Metabolic pathway(s)	Not metabolized, primarily excreted unchanged in urine
Route(s) of elimination	Renal
Common drug interactions	lithium serum concentrations (fluoxetine,† ACE inhibitors, diuretics, NSAIDs) lithium serum concentrations (acetazolamide, osmotic diuretics, theophylline, urinary alkalinizers) Antipsychotics may increase lithium neurotoxicity
Common adverse effects	Nausea, vomiting, diarrhea, polyuria, polydipsia, tremor, hypothyroidism
Indication(s)	Manic episodes of bipolar disorder, bipolar disorder maintenance

=decreased; =increased; CYP=cytochrome P450; ACE=angiotensin-converting enzyme; NSAIDs=nonsteroidal anti-inflammatory drugs; CNS=central nervous system; GI=gastrointestinal.

*Women taking a mood stabilizing agent should be given a pregnancy test at baseline and then as clinically indicated.

†Both increases and decreases have been reported and lithium levels should be monitored when used together.

‡Carbamazepine may decrease the efficacy of oral contraceptives through enzyme induction.

Valproic Acid*	Carbamazepine*,‡
(Depakene, Depakote)	(Carbitrol, Tegretol)
50–100 (µ/mL)	4–12 (µg/mL)
750–4,200 mg	400–1,600 mg
5–15 days	3–15 days
90% concentration dependent with high concentration (variable due to saturation)	76%
6–16 hours (average) with age and/or decreased hepatic function	Initial range 26–65 hours; with repeated dosing, 12–17 hours
Hepatic (glucuronidation, mitochondrial boxidation, microsomal oxidation)	Hepatic: CYP 3A, 2D6
Glucuronidation, renal	Renal (72%), fecal (28%)
Interacts with drugs that are hepatically metabolized; enzyme inducers can decrease concentrations of valproic acid; valproic acid can increase	Induces metabolism of CYP 3A4-dependent drugs; decreases phenobarbital, phenytoin, sex steroids, haloperidol, valproic acid, calcium channel blockers, etc.
phenobarbital by impairment of nonrenal clearance (severe CNS depression)	(see Table 6). Valproate increases 10, 11 epoxide metabolite of carbamazepine.
GI distress, diplopia, sedation, tremor, edema, weight gain, alopecia, and thrombocytopenia	Dizziness, drowsiness, ataxia, and weight gain
Bipolar disorder, acute mania (and seizure disorders)	Partial complex seizures

Table 12: BASELINE AND ROUTINE MONITORING PARAMETERS FOR MOOD STABILIZERS[10,11,15–17,50,53,54]

Laboratory Parameters	Lithium*
Serum plasma concentrations	Weekly × 4 weeks, then monthly × 3 months, then every 3 months or as clinically indicated
Complete blood count	Baseline, monthly × 3 months, then as clinically indicated
Blood chemistries	Baseline, then every 12 months or as clinically indicated (eg, serum creatinine, renal function, and electrolytes)
ECG (in patients 45 years or with preexisting cardiac disease)	Baseline, then every 12 months or as clinically indicated
Urinalysis	Baseline, then as clinically indicated
PT/PTT	—
Thyroid function tests (T3 ,T4,TSH, FTI)	Baseiine, then every 12 months

*Women taking a mood stabilizing agent should be given a pregnancy test at baseline and then as clinically indicated.
†Although carbamazepine is not approved by the FDA for psychiatric indications, the authors view it as one of the most important agents available for the treatment of bipolar disorder. This view is supported in the medical literature.
‡Carbamazepine may decrease the efficacy of oral contraceptives through enzyme induction.
ECG=electrocardiogram; PT/PTT=prthrombin time;
TSH=thyroid stimulaing hormone; FTI=free thyroid index;
FDA=Food and Drug Administration.

Carbamazepi ne*,†,‡	VaLproic Acid*
2 weeks after initiation, then every 3 months or as clinically indicated	2 weeks after initiation, then every 3 months or as clinically indicated
Baseline, then monthly × 3 months, then as clinically indicated	Baseline, then monthly × 6 months, then every 6 months or as clinically indicated (include differential and platelets)
Baseline, then annually as indicated	Baseline, monthly then × 6 months, then every 6 months or as clinically indicated (eg, hepatic and renal function)
Baseline, then every 12 months	Baseline, then as clinically indicated
Baseline, then as clinically indicated	Baseline, then every 6 months or as clinically indicated
—	Baseline, then every 6 months or as clinically indicated
Baseline, then every 12 months	—

Anxiolytics/Hypnotics

Table 13: BENZODIAZEPINE ANXIOLYTICS*[10,11,21,34,35]

	Approved Oral Adult Dosage Range (mg/day)	Approximate Equivalent Dosages (mg/day)	Half-life of Parent Drug (hrs)
Alprazolam†,‡ (Xanax)	General: 0.75–4.0 Panic disorder: 1–10	0.5	6.3–26.9
Chlordiazepoxide†,‖ (Librium, Libritabs, Mitran)	15–100	10	24–48
Clonazepam†,‡ (Klonopin)	1.5–20	0.25	18–50
Clorazepate†,‖ (ClorazeCaps, ClorazeTabs, Gen-XENE, Tranxene)	15–60	7.5	Prodrug
Diazepam† (Valium, Valrelease, Zetran)	4–40	5	20–80
Lorazepam† (Ativan)	1–10	1	12
Oxazepam† (Serax)	30–120	15	5.7–10.9
Prazepam† (Centrax)	20–60	10	Prodrug

*Adverse events commonly seen with the benzodiazepines include drowsiness, ataxia, confusion, fatigue, anterograde amnesia, light-headedness, and dizziness.
†Single doses provide sedation and calming; chronic dosing reduces symptoms of generalized anxiety disorder.
‡Clonazepam and alprazolam are FDA approved for PD.
‖For alcohol detoxification and withdrawal, doses of up to 300 mg of chlordiazepoxide and 90 mg of clorazepate may be warranted.
D=relatively contraindicated; FDA = Food and Drug Administration; PD=panic disorder.

Peak Plasma Level t_{max}(hrs)	Half-life for Major Active Metabolites (hrs)	Metabolic Pathway	Pregnancy Risk Category
1–2	None	Oxidation	D
Several hours	Desmethyl-chlordiazepoxide (18) Demoxepam (14–95) Desmethyldiazepam (30–200) Oxazepam (3–21)	N-dealkylation	D (not FDA specified)
1–2	None	Reduction, hydroxylation, oxidation	D (not FDA specified)
1–2	Oxazepam (3–21) Desmethyldiazepam (30–200)	Oxidation, hydroxylation, conjugation	D (not FDA specified)
0.5–2	Desmethyldiazepam (30–200) 3-Hydroxydiazepam (5–20) Oxazepam (3–21)	Oxidation, hydroxylation, demethylation	D (not FDA specified)
2	None	Conjugation	D
3	None	Conjugation	D (not FDA specified)
6	—	Oxidation	D (not FDA specified)

Table 14: NONBENZODIAZEPINE ANXIOLYTICS[10,11,56–58]

Drug	Brand Name	Dosage (mg)	Indications
Buspirone*	BuSpar	5–20 mg TID or 15–30 mg BID	GAD
Hydroxyzine†	Vistaril, Atarax	50–100 mg QD	Anxiety, tension

*Adverse events commonly seen with buspirone include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.
†Second-agent.
GAD=generalized anxiety disorder.

Table 15: BENZODIAZEPINE DRUG INTERACTIONS[10,11,42,43]

Drug	Interaction	Mechanism
Antacids	absorption and benzodiazepine levels	gastric pH
Carbamazepine	benzodiazepine levels	CYP induction
Cimetidine	benzodiazepine levels	CYP inhibition
Digoxin	digoxin levels	Unknown
Erythromycin	alprazolam levels	3A4 inhibition
Ethanol	sedation/respiratory depression	CNS depression synergism
Nefazodone	alprazolam, triazolam levels	3A4 inhibition
Opioids	sedation, respiratory depression	CNS additive
SSRIs	diazepam, alprazolam levels	2D6 and 3A4 inhibition
Valproic acid	benzodiazepine levels	metabolism

=decreased; CYP=cytochrome P450; =increased; CNS=central nervous system; SSRIs=selective serotonin reuptake inhibitors.

Table 16: HYPNOTIC AGENTS[10,11,21–34]

	Dally Adult Dosage (mg/day)	Time to Peak Plasma Level (hours)
Benzodiazepines		
Estazolam (ProSom)	0.5–2	0.5–6
Flurazepam (Dalmane)	15–30	0.5–1 4.7–100†
Quazepam (Doral)	7.5–15	2 73†
Temazepam (Restoril)	7.5–30	1.2–1.6
Triazolam (Halcion)	0.125–0.5	2
Nonbenzodiazepines		
Chloral hydrate (Noctec, Aquachloral Supprettes)	500–2,000	0.5–12†
Zaleplon (Sonata)	5–20	1
Zolpidem (Ambien)	5–10	1.6

†Values given for active metabolite.

$t_{1/2}$ (hours)	Metabolic Pathway	Pharmacokinetic Parameters Active Metabolites	Protein Binding (%)
10–24	Oxidation	None	93
2.3 36–120†	Oxidation, N-dealkylation	N-desalkylflurazepam, hydroxyethylflurazepam, flurazepam aldehyde	97
39 36–120†	Oxidation	N-desalkylflurazepam, 2-oxoquazepam	>95
3.5–18.4	Conjugation	None	96
1.5–5.5	Conjugation	None	89
8–11†	Oxidation, reduction	Trichloroethanol	35–41†
1	Oxidation	5-oxo-zaleplon	92
2.6 1.4–4.5	Oxidation, hydroxylation	None	92.5

Antipsychotics

Table 17: FIRST GENERATION ANTIPSYCHOTIC DOSAGES AND ADVERSE EFFECTS[10,11,21,22,25]

	Class	Traditional Equivalents
Chlorpromazine[†] (Ormazine, Thorazine)	Aliphatic phenothiazine	100
Thioridazine (Mellaril)	Piperidine phenothiazine	100
Mesoridazine (Serentil)	Piperidine phenothiazine	50
Fluphenazine (Permitil, Prolixin)	Piperazine phenothiazine	2
Perphenazine (Trilafon)	Piperazine phenothiazine	8
Trifluoperazine (Stelazine)	Piperazine phenothiazine	5
Thiothixene (Navane)	Thioxanthene	4
Haloperidol (Haldol)	Butyrophenone	2
Loxapine (Loxitane)	Dibenzoxazepine	10
Molindone (Moban)	Dihydroindolone	10
Pimozide (Orap)	Piperidine	—
Droperidol (Inapsine)	Butyrophenone	—

	Adverse Effects[‡]	
	Extrapyramidal	**Sedation**
Chlorpromazine	++	+++
Thioridazine	+	+++
Mesoridazine	+	+++
Fluphenazine	++++	++
Perphenazine	+++	++
Trifluoperazine	+++	++
Thiothixene	+++	++
Haloperidol	++++	+
Loxapine	+++	++
Molindone	+++	++
Pimozide	+++	+
Droperidol	++++	+++

[*]In elderly patients, doses should be lowered and tailored to the patient.
[†]Labeling suggests higher doses may be appropriate, noting intramuscular doses up to 2,000 mg (using >1,000 mg only in severe cases).
[‡]Severity: ++++=extremely high; +++=high; ++=moderate; +=low.

Dosage* Range (mg/day) PO	Usual Maximum Dosage for Organic Mental Syndrome (mg/day)	Usual Dosage for Patients >65 Years of Age (mg/day)*
30–800	400	400
20–800	200	200
30–400	—	—
1–40	10	10
12–64	16	16
2–40	20	20
6–60	15	15
1–100	15	15
20–250	60	60
15–225	55	55
1–10	—	—
2.5–15	—	—

Adverse Effects‡	
Anticholinergic	**Orthostatic Hypotension**
+++	+++
++++	+++
++++	++
++	++
++	++
++	++
++	++
+	+
++	++
++	++
+	+
+	++

Table 18: SECOND GENERATION ANTIPSYCHOTIC DOSAGES AND ADVERSE EFFECTS[10,11,13,14,28,59–62]

	Starting Dose
Aripiprazole (Abilify)	2–5
Asenapine (Saphris, Secuado)	10–20
Brexpiprazole (Rexulti)	0.5–1
Cariprazine (Vraylar)	1.5
Clozapine (Clozaril)	12.5–25
Ileoperidone (Fanapt)	1–2
Lumateperone (Caplyta)	42
Lurasidone (Latuda)	20–40
Olanzapine (Zyprexa)	5–10
Pimavanserin (Nuplazid)	17
Quetiapine (Seroquel)	25–50
Risperidone (Risperdal)	0.5–1
Ziprasidone (Geodon)	20–40

	Adverse Effects†	
	Extrapyramidal	**Sedation**
Aripiprazole	++	+
Asenapine	+	++
Brexpiprazole	++	+
Cariprazine	++	+
Clozapine	0	++++
Ileoperidone	+	+
Lumateperone	0/+	++
Lurasidone	+	++
Olanzapine	+	++++
Risperidone	+++§	++
Quetiapine	0/+	++/++
Ziprasidone	++	++

*In elderly patients, doses should be lowered and tailored to the patient.
†Severity: ++++=extremely high; +++=high; ++=moderate; +=low; 0=none.
‡Tolerance develops; slow dose titration is necessary.
§Dose-dependent extrapyramidal effects.
N/A=not available.

Dosage* Range (mg/day) PO	Recommended Dosage for Patients >65 Years of AGE mg/day*
10–30	2–15
10–20	5–20
2–3	1–2
3–6	1.5–3
300–900	25–100
12–24	6–12
42	42
60–120	20–60
5–20	5–10
17–34	10–17
50–750	Slower rate of dose titration, lower target dose
2–16	0.5 to start
40–160	Slow rate of dose titration, lower target dose

	Adverse Effects†	
Weight Gain	Anticholinergic	Orthostatic Hypotension
++	+	+
+	+	+++
+	+	+
+	+	+
++++	++++	++++‡
++	++	++
0/+	0	0/+
+	+	+
++++	++	+
+	+	++‡
+++	++	++
+/0	+	++

Table 19: PHARMACOKINETIC PARAMETERS AND DOSING OF DEPOT AND LONG ACTING ANTIPSYCHOTICS*[10,11,63,64]

First Generation Antipsychotics

Drug	Starting Dosage	Maintenance Dosage
Haloperidol decanoate	20 × oral haloperidol 100–450 mg/28 days	10–15 × oral haloperidol 50–300 mg/28 days
Fluphenazine decanoate	1.2 × oral fluphenazine 12.5–75 mg/7–14 days	Based on starting dose and clinical response
Fluphenazine enanthate	12.5–100 mg/7–21 days	Based on starting dose and clinical response

Second Generation Long Acting Injectable Antipsychotics

Drug	Starting Dose
Aripiprazole (Abilify Maintena)	400 mg/monthly
Aripiprzole Lauroxil (Aristada)	441 mg/monthly
Paliperidone	
Invega Sustenna	234 mg on day 1, and 156 mg 1 week later
Invega Trinza	273 mg
Invega Hafyera	1092–1560 mg
Risperidone Consta	25 mg for 2 weeks
Olanzapine Relprevv	150 mg for 2 weeks

*Patients maintained for 1 year or longer demonstrated a very long time to wash out drug (terminal observed half-life exceeding 60 days).
N/A=not available.

Table 20: ANTIPARKINSONIAN AGENTS[10,11,23,65,67]

Drug	Approximate Dose Equivalent (mg)	Dosage Range (mg/day)	Dose Forms
Antimuscarinics			
Benztropine (Cogentin)	1	1–8	T, I
Biperiden (Akineton)	2	2–8	T, I
Ethopropazine (Parsidol)	50	50–600	T
Orphenadrine (Various)	50	50–250	T
Procyclidine (Kemadrin)	2	7.5–20	T
Trihexyphenidyl (Artane)	2	2–15	T, C-SR, L
Antihistaminic			
Diphenhydramine (Various)	50	50–400	C,T, L, I
Dopamine Agonists			
Amantadine (Symadine, Symmetrel)	N/A	100–400	C, L
Ropinirole (Requip)	N/A	0.75–24*	T
Pramipexole (Mirapex)	N/A	1.5–4.5*	T

*Maintenance dose for Parkinson's disease.
T=tablet; I=injection; C=capsule; SR=sustained release; L=liquid solution, elixir, or suspension; N/A=not available.

t_{max} (days)	$t_{1/2}$ Single Dose (days)	$t_{1/2}$ Multiple Dose (days)	Time to Steady State (weeks)
4–11	21	21	12
0.3–2	6–10	14	4–8
2–3	3.5–4	N/A	3

Maintenance Dosage	$T_{1/2}$	Steady State
300–400 mg/monthly	30–46 days	4 months
441–882 mg/month. Or 882 mg/every 6 weeks or 1064 mg/every 8 weeks	29–35 days	4 months
39 mg to 234 mg (average maintenance dose 117 mg)/monthly	25–49 days	4–5 months
273–829/ every three months	84–95 days	12–15 Months
180 days	180 days	18 Months
25–50 mg/every 2 weeks	3–6 day	4 weeks
150–300 mg/every 2 weeks or 405 mg/every 4 weeks	30 days	3 months

Table 21: ANTIPSYCHOTIC DRUG INTERACTIONS[10,11,42–60,67]

Interacting Medication	Mechanism	Clinical Effect
Drug interactions assessed to have major severity		
Anticholinergics	Pharmacodynamic effects Additive anticholinergic effect	Decreased antipsychotic effect
Barbiturates	Phenobarbital induces antipsychotic metabolism	Decreased antipsychotic concentrations
Beta-blockers	Synergistic pharmacologic effect; antipsychotic inhibits metabolism of propranolol; antipsychotic increases plasma concentrations	Severe hypotension
Carbamazepine	Induces antipsychotic metabolism	Up to 50% reduction in antipsychotic concentrations

Table 21: ANTIPSYCHOTIC DRUG INTERACTIONS[10,11,42–60,67] *(CONT'D)*

Interacting Medication	Mechanism	Clinical Effect
Charcoal	Reduces GI absorption of antipsychotic and absorbs drug during enterohepatic circulation	May reduce antipsychotic effect or cause toxicity when used during overdose or for GI disturbances
Cigarette smoking	Induction of microsomal enzymes	Reduced plasma concentrations of antipsychotic agents
Epinephrine, norepinephrine	Antipsychotic antagonizes pressor effect	Hypotension
Ethanol	Additive CNS depression	Impaired psychomotor skills
Fluvoxamine	Fluvoxamine inhibits metabolism of haloperidol and clozapine	Increased concentrations of haloperidol and clozapine
Guanethidine	Antipsychotic antagonizes guanethidine neuronal uptake	Impaired antihypertensive effect
Lithium	Unknown	Rare reports of neurotoxicity
Meperidine	Additive CNS depression	Hypotension and sedation
Amphetamines, anorexiants	Decrease pharmacologic effect of amphetamine; drug-disease state interaction	Diminished weight-loss effect; amphetamines may exacerbate psychosis; treatment-refractory patients may improve
ACE inhibitors	Additive hypotensive effect	Hypotension, postural intolerance
Antacids containing aluminum	Insoluble complex in GI tract formed	Possible reduced antipsychotic effect
Antidepressants (antidepressant, nonspecific)	Decreases metabolism of antidepressant through competitive inhibition	Increased antidepressant concentration
Benzodiazepines	Increases pharmacologic effect of benzodiazepine	Respiratory depression, stupor, hypotension
Bromocriptine	Antipsychotic antagonizes dopamine receptor stimulation	Increased prolactin
Caffeinated beverages	Form precipitate with antipsychotic solutions	Possible diminished antipsychotic effect
Cimetidine	Reduces antipsychotic absorption and inhibits clearance	Increased or decreased antipsychotic effect

Interacting Medication	Mechanism	Clinical Effect
Clonidine	Antipsychotic potentiates α-2-adrenergic hypotensive effect	Hypotension
Disulfiram	Impairs antipsychotic metabolism	Increased antipsychotic concentrations
Methyldopa	Unknown	Blood pressure elevations
Phenytoin	Induction of antipsychotic metabolism; increases phenytoin metabolism	Decreased antipsychotic concentrations; decreased phenytoin levels
SSRIs	Impair antipsychotic metabolism; pharmacodynamic interaction	Sudden onset of extrapyramidal symptoms
Valproic acid	Antipsychotic inhibits valproic acid metabolism	Increased valproic acid half-life and levels

ACE=angiotensin-converting enzyme; GI=gastrointestinal; CNS=central nervous system; SSRIs=selective serotonin reuptake inhibitors.

Table 22: ACUTE NEUROLOGIC SIDE EFFECTS OF ANTIPSYCHOTIC MEDICATIONS[10,11,60,67,68]

Reaction	Clinical Features	Approximate Onset	Treatment
Acute dystonia	Spasm of tongue, throat, face, jaw, eyes, neck, or back muscles	<1 week	Injectable benztropine or diphenhydramine, followed by oral anticholinergics or benzodiazepines
Akathisia	Motor restlessness, inability to stay still	<1 week–2 weeks	If possible, reduce dose of antipsychotic; add beta-blockers, benzodiazepines, or anticholinergics
Pseudoparkinsonism	Bradykinesia, rigidity, resting tremor, rabbit syndrome, sialorrhea, flat affect	~1 week	Add anticholinergics or amantadine; diphenhydramine and lorazepam may also be effective

Table 23: PHARMACOKINETIC PARAMETERS OF SELECTED ORAL ANTIPSYCHOTICS[10,11,21,22,60,65–69]

	Bioavailability (%)	Protein Binding (%)	vd (L/kg)*
Chlorpromazine	10–33	90–95	7–20
Clozapine	—	95	4–66
Haloperidol	40–70	92	10–35
Fluphenazine	10–50	90–95	—
Olanzapine	–60	93	10–20
Perphenazine	25	—	10–35
Quetiapine	100	83	6–14
Risperidone	70	90	—
Thioridazine	25–33	99	—
Thiothixene	50	90–95	—

*Range given includes mean +/– standard deviation.
†Data inconclusive regarding therapeutic range for these drugs.
‡Optimal concentration for response not emcompassing neuroleptic threshold (3–5 ng/mL).
§Trough concentration, predose.
**Peak concentration 2–3 hours postdose.

Table 24: APA/ADA RECOMMENDATIONS FOR PATIENTS WHO ARE TAKING ANTIPSYCHOTICS*

Prior to starting an antipsychotic
Screen for personal of family history of diabetes, high blood pressure, heart disease, high cholesterol
Weight and height (BMI •25)
Waist circumference (>40 inches in males, 35 inches in females)
Blood pressure >130/85
Fasting glucose >110
Fasting cholesterol (HDL <40, total >200)
Fasting triglyceride levels (>175)
Reassess weight at weeks 4, 8, 12 and quarterly thereafter. Weight gain >5% consider switching antipsychotics.
Reassess glucose, lipids and blood pressure 3 months after starting the antipsychotic. Thereafter, check BP annually or as needed. Lipids checked at 5 year intervals or as needed.
Assessing EPS symptoms (place after table 19) Extrapyramidal symptoms may be checked at every visit or every 6 months.

*Diabetes Care 2004; 27(2): 596–601.

Plasma $t_{1/2}$ (hours)	Active Metabolites	Therapeutic plasma concentration (ng/ml)
8–35	7-hydroxy	100–300†
4–66	Desmethyl	350
12–36	Reduced haloperidol	3.0–30 5–12‡
14–24	Hydroxy	0.2–3
21–54	—	9–20†
8–21	None known	—
–6	7-hydroxy 7-hydroxy-N-dealkylated	—
3–20	9-hydroxy	—
9–30	Mesoridazine, sulphoridazine	200–800†
34	None known	1.0–5.0*§ 10–30***

Table 25: VMAT INHIBITORS FOR THE TREATMENT OF TARDIVE DYSKINESIA[4,5,10,11]

VMAT2 Inhibitor	Starting dose	Therapeutic Dose
Valbenazine (Ingrezza)	40 mg	40–80 mg
Deutetrabenzaine (Austedo)	6 mg bid	12–24 mg bid

ADA/APA Monitoring protocol for patients on Second Generation Antipsychotics (SGA)s

	Baseline	4 weeks	8 weeks
Personal/family history	X		
Weight (BMI)	X	X	X
Waist circumference	X		
Blood pressure	X		
Fasting plasma glucose	X		
Fasting lipid profile	X		

Table 26: CLOZAPINE MONITORING BY ACUTE NEUTROPHIL COUNT (ANC) LEVEL FOR THE GENERAL POPULATION. (FOR PATIENTS WITH BENIGN ETHNIC NEUTROPENIA, PLEASE SEE CLOZAPINE REMS)

ANC Level	Recommendation
Normal Range for a New Patient (ANC ≥1500/μL)	• Initiate treatment • If treatment interrupted: – <30 days, continue monitoring as before – ≥30 days, monitor as if new patient (Patient interrupted treatment for any reason other than low ANC)
Mild Neutropenia (1000 to 1499/μL)*	• Continue treatment
Moderate Neutropenia (500 to 999/μL)*	• Hematology consultation • Suspend treatment for suspected clozapine induced neutropenia • Resume treatment once ANC normalizes to ≥1000/μL
Severe Neutropenia (less than 500/μL)*	• Hematology consultation • Suspend treatment for suspected clozapine induced neutropenia • Consider discontinuing unless the benefits clearly outweigh the risks

*Confirm all initial reports of ANC less than 1500/μL (ANC < 1000/μL for BEN patients) with a repeat ANC measurement within 24 hours.
Source: Adapted from *Clozapine and the Risk of Neutropenia: An Overview for Healthcare Providers, 2014* (www.clozapinerems.com).

12 weeks	Quarterly	Annually	Every 5 years
		X	
X	X		
		X	
X		X	
X		X	
X			X

ANC Frequency
• Weekly from initiation to 6 months • Every 2 weeks from 6 to 12 months • Monthly after 12 months
• Three times weekly until ANC ≥1500/μL • Once ANC ≥1500/μL, return to patient's last normal range ANC monitoring interval
• Daily until ANC ≥1000/μL, then • Three times weekly until ANC ≥1500/μL • Once ANC ≥1500/μL, check ANC weekly for 4 weeks, then monthly as appropriate
• Daily until ANC ≥1000/μL • Three times weekly until ANC ≥1500/μL • If patient is restarted on clozapine, monitor as a new patient or as needed

Psychostimulants/Alzheimer's

Table 27: ANOREXIANTS[10,11,45–52,70–72]

Agent	dosage range (mg/day)	Indication
Amphetamine (Biphetamine)	5–40	Obesity
Naltrexone + Bupropion 8/90 mg (Contrave)	1–2 tablets BID	Obesity
Methamphetamine (Desoxyn)	10–15	Obesity
Orlistat (Xenical)	120 TID with meals	Obesity
Phendimetrazine (various)	70–105	Obesity
Phentermine (Adipex-P, various)	18.75–37.5	Obesity
Phentermine + Topiramate 3.75/23 mg (Qsmia)	1–2 tablets Daily	Obesity

Table 28: PSYCHOSTIMULANTS[10,11,73]

Agent	Dosage Range (mg/day)	Indication
Dextroamphetamine (Dexedrine)	5–40 5–60	ADHD Narcolepsy
Dextroamphetamine + amphetamine (Adderall)	5–40 5–60	ADHD Narcolepsy
Methamphetamine (Desoxyn)	5–25*	ADHD
Methylphenidate (Ritalin, Ritalin LA, Aptenso XR)	10–40 10–60	ADHD Narcolepsy
Methylphenidate HCl (Concerta)	18–54	ADHD
Modafinil (Provigil)	200–400	Narcolepsy, idiopathic hypersomnia
Armodafinil (Nuvigil)	150–250	
Lisdexamfetamine (Vyvanse)	30–70	ADHD, Binge Eating

ADHD=attention-deficit/hyperactivity disorder. *20–25 mg is effective dosage range; can be titrated up from 5 mg.

Table 29: DRUGS FOR ALZHEIMER'S DISEASE[10,11,19,21,74,78] (CHOLINESTERASE INHIBITORS)

Drug	Dosage	Peak Plasma	Elimination Half-life
Donepezil (Aricept)	5–10 mg/day	3–4 hours	70 hours
Galantamine (Reminyl)	16–32 mg/day	1 hour	7 hours
Lecanemab (Lequembi)	Single 10 mg/kg IV	2 hrs	5–7 days
Rivastigmine (Exelon)	6–12 mg/day	1.4–2.6 hours	1.5–3 hours

CYP=cytochrome P450.

Steady State	Protein Binding	Metabolism
15 days	96%	2D6, 3A3/4
–	18%	2D6, 3A4
6 wks	unknown	Proteolytic Enzymes
24–48 days	40%	Not CYP dependent

Table 30: ADVERSE EFFECTS OF CHOLINESTERASE INHIBITORS[10,11,18,20,74–77,79,80]

Symptom	Donepezil	Galantamine
GI		
Nausea, vomiting	+	++++
Weight loss	+	+
LFTs rise	–	–
CNS		
Insomnia	+/–	+
Fatigue	+/–	+
Depression	+/–	+
Miscellaneous		
Syncope	+/–	+
Increased urination	+/–	+
Rhinitis	+/–	+

++++=high; +++=moderate; ++=low; +=very low; –=none. GI=gastrointestinal; LFTs=liver function tests; CNS=central nervous system.

Rivastigmine	Tacrine
++	+++
++ (dose dependent)	+
–	+++
+/–	+
+/–	+/–
+/–	+/–
+	+/–
+/–	+/–
–	–

Rating Scales

The Quick Inventory of Depressive Symptomatology (16-Item) (Self-Report) (QIDS-SR$_{16}$)[6]

Name or ID: _____ **Date:** _____

CHECK THE ONE RESPONSE TO EACH ITEM THAT BEST DESCRIBES YOU FOR THE PAST SEVEN DAYS.

During the past seven days...

1. Falling Asleep:

☐ 0 I never take longer than 30 minutes to fall asleep.

☐ 1 I take at least 30 minutes to fall asleep, less than half the time.

☐ 2 I take at least 30 minutes to fall asleep, more than half the time.

☐ 3 I take more than 60 minutes to fall asleep, more than half the time.

2. Sleep During the Night

☐ 0 I do not wake up at night.

☐ 1 I have a restless, light sleep with a few brief awakenings each night.

☐ 2 I wake up at least once a night, but I go back to sleep easily.

☐ 3 I awaken more than once a night and stay awake for 20 minutes or more, more than half the time.

3. Waking Up Too Early:

☐ 0 Most of the time, I awaken no more than 30 minutes before I need to get up.

☐ 1 More than half the time, I awaken more than 30 minutes before I need to get up.

☐ 2 I almost always awaken at least one hour or so before I need to, but I go back to sleep eventually.

☐ 3 I awaken at least one hour before I need to, and can't go back to sleep.

4. Sleeping Too Much:

☐ 0 I sleep no longer than 7–8 hours/night, without napping during the day.

☐ 1 I sleep no longer than 10 hours in a 24-hour period including naps.

☐ 2 I sleep no longer than 12 hours in a 24-hour period including naps.

☐ 3 I sleep longer than 12 hours in a 24-hour period including naps.

During the past seven days...

5. Feeling Sad:

☐ 0 I do not feel sad.

☐ 1 I feel sad less than half the time.

☐ 2 I feel sad more than half the time.

☐ 3 I feel sad nearly all of the time.

Please complete either 6 or 7 (not both)

6. Decreased Appetite:

☐ 0 There is no change in my usual appetite.

☐ 1 I eat somewhat less often or lesser amounts of food than usual.

☐ 2 I eat much less than usual and only with personal effort.

☐ 3 I rarely eat within a 24-hour period, and only with extreme personal effort or when others persuade me to eat.

- OR -

7. Increased Appetite:

☐ 0 There is no change from my usual appetite.

☐ 1 I feel a need to eat more frequently than usual.

☐ 2 I regularly eat more often and/or greater amounts of food than usual.

☐ 3 I feel driven to overeat both at mealtime and between meals.

Please complete either 8 or 9 (not both)

8. Decreased Weight (Within the Last Two Weeks):

☐ 0 I have not had a change in my weight.

☐ 1 I feel as if I have had a slight weight loss.

☐ 2 I have lost 2 pounds or more.

☐ 3 I have lost 5 pounds or more.

- OR -

9. Increased Weight (Within the Last Two Weeks):

☐ 0 I have not had a change in my weight.

☐ 1 I feel as if I have had a slight weight gain.

☐ 2 I have gained 2 pounds or more.

☐ 3 I have gained 5 pounds or more.

The Quick Inventory of Depressive Symptomatology (16-Item) (Self-Report) (QIDS-SR$_{16}$)[6]

During the past seven days...

10. Concentration / Decision Making:

☐ 0 There is no change in my usual capacity to concentrate or make decisions.

☐ 1 I occasionally feel indecisive or find that my attention wanders.

☐ 2 Most of the time, I struggle to focus my attention or to make decisions.

☐ 3 I cannot concentrate well enough to read or cannot make even minor decisions.

11. View of Myself:

☐ 0 I see myself as equally worthwhile and deserving as other people.

☐ 1 I am more self-blaming than usual.

☐ 2 I largely believe that I cause problems for others.

☐ 3 I think almost constantly about major and minor defects in myself.

12. Thoughts of Death or Suicide:

☐ 0 I do not think of suicide or death.

☐ 1 I feel that life is empty or wonder if it's worth living.

☐ 2 I think of suicide or death several times a week for several minutes.

☐ 3 I think of suicide or death several times a day in some detail, or I have made specific plans for suicide or have actually tried to take my life.

13. General Interest

☐ 0 There is no change from usual in how interested I am in other people or activities.

☐ 1 I notice that I am less interested in people or activities.

☐ 2 I find I have interest in only one or two of my formerly pursued activities.

☐ 3 I have virtually no interest in formerly pursued activities.

During the past seven days...

14. Energy Level:

☐ 0 There is no change in my usual level of energy.

☐ 1 I get tired more easily than usual.

☐ 2 I have to make a big effort to start or finish my usual daily activities (for example, shopping, homework, cooking, or going to work).

☐ 3 I really cannot carry out most of my usual daily activities because I just don't have the energy.

15. Feeling Slowed Down:

☐ 0 I think, speak, and move at my usual rate of speed.

☐ 1 I find that my thinking is slowed down or my voice sounds dull or flat.

☐ 2 It takes me several seconds to respond to most questions and I'm sure my thinking is slowed.

☐ 3 I am often unable to respond to questions without extreme effort.

16. Feeling Restless:

☐ 0 I do not feel restless.

☐ 1 I'm often fidgety, wringing my hands, or need to shift how I am sitting.

☐ 2 I have impulses to move about and am quite restless.

☐ 3 At times, I am unable to stay seated and need to pace around.

Patient Health Questionnaire (PHQ-9)[10]

Patient Name: _____ **Date:** _____

		Not at all	Several days	More than half the days	Nearly every day
1.	Over the *last 2 weeks*, how often have you been bothered by any of the following problems?				
	a. Little interest or pleasure in doing things	☐	☐	☐	☐
	b. Feeling down, depressed, or hopeless	☐	☐	☐	☐
	c. Trouble falling/staying asleep, sleeping too much	☐	☐	☐	☐
	d. Feeling tired or having little energy	☐	☐	☐	☐
	e. Poor appetite or overeating	☐	☐	☐	☐
	f. Feeling bad about yourself or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
	g. Trouble concentrating on things, such as reading the newspaper or watching television.	☐	☐	☐	☐
	h. Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual.	☐	☐	☐	☐
	i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐
2.	If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all ☐	Somewhat difficult ☐	Very difficult ☐	Extremely difficult ☐

PHQ-9* Questionnaire for Depression Scoring and Interpretation Guide

For physician use only

Scoring:

Count the number (#) of boxes checked in a column. Multiply that number by the value indicated below, then add the subtotal to produce a total score. The possible range is 0-27. Use the table below to interpret the PHQ-9 score.

Not at all (#) _____ × 0 = _____

Several days (#) _____ × 1 = _____

More than half the days (#) _____ × 2 = _____

Nearly every day (#) _____ × 3 = _____

Total score: _____

Interpreting PHQ-9 Scores			Actions Based on PH9 Score
		Score	Action
Minimal depression	0–4	< 4	The score suggests the patient may not need depression treatment
Mild depression	5–9		
Moderate depression	10–14	> 5–14	Physician uses clinical judgment about treatment, based on patient's duration of symptoms and functional impairment
Moderately severe depression	15–19		
Severe depression	20–27	> 15	Warrants treatment for depression, using antidepressant, psychotherapy and/or a combination of treatment.

*PHQ-9 is described in more detail at the McArthur Institute on Depression & Primary Care website www.depression-primarycare.org/clinicians/toolkits/materials/forms/phq9/

CLIENT NAME: _____ DATE: _____

CLIENT ID#: _____ MD: _____

BRIEF PSYCHIATRIC RATING SCALE (BPRS)[7]

Please enter the score for the term which best describes the patient's condition.

0 = not assessed, 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe

1. SOMATIC CONCERN Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not. **SCORE** ☐	**5. GUILT FEELINGS** Over-concern or remorse for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report with appropriate affect; do not infer guilt feelings from depression, anxiety or neurotic defenses. **SCORE** ☐
2. ANXIETY Worry, fear, or over-concern for present or future. Rate solely on the basis of verbal report of patient's own subjective experiences. Do not infer anxiety from physical signs or from neurotic defense mechanisms. **SCORE** ☐	**6. TENSION** Physical and motor manifestations of tension "nervousness", and heightened activation level. Tension should be rated solely on the basis of physical signs and motor behavior and not on the basis of subjective experiences of tension reported by the patient. **SCORE** ☐
3 EMOTIONAL WITHDRAWAL Deficiency in relating to the interviewer and to the interviewer situation. Rate only the degree to which the patient gives the impression of failing to be in emotional contact with other people in the interview situation. **SCORE** ☐	**7. MANNERISMS AND POSTURING** Unusual and unnatural motor benavior, the type of motor behavior which causes certain mental patients to stand out in a crowd of normal people. Rate only abnormality of movements; do not rate simple heightened motor activity here. **SCORE** ☐
4. CONCEPTUAL DISORGANIZATION Degree to which the thought processes are confused, disconnected, or disorganized. Rate on the basis of integration of the verbal products of the patient; do not rate on the basis of patient's subjective impression of his own level of functioning. **SCORE** ☐	**8. GRANDIOSITY** Exaggerated self-opinion, conviction of unusual ability or powers. Rate only on the basis of patient's statements about himself or self-in-relation-to-others, not on the basis of his demeanor in the interview situation. **SCORE** ☐

9. DEPRESSIVE MOOD Despondency in mood, sadness. Rate only degree of despondency; do not rate on the basis of inferences concerning depression based upon general retardation and somatic complaints. **SCORE** ☐	**14. UNCOOPERATIVENESS** Evidence of resistance, unfriendliness, resentment, and lack of readiness to cooperate with the interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation; do not rate on basis of reported resentment or uncooperativeness outside the interview situation. **SCORE** ☐
10. HOSTILITY Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others; do not infer hostility from neurotic defenses, anxiety, nor somatic complaints. (*Rate attitude toward interviewer under "uncooperativeness"*). **SCORE** ☐	**15. UNUSUAL THOUGHT CONTENT** Unusual, odd, strange or bizarre thought content. Rate here the degree of unusualness, not the degree of disorganization of thought processes. **SCORE** ☐
11. SUSPICIOUSNESS Brief (*delusional or otherwise*) that others have now, or have had in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions which are currently held whether they concern past or present circumstances. **SCORE** ☐	**16. BLUNTED AFFECT** Reduced emotional tone, apparent lack of normal feeling or involvement. **SCORE** ☐
12. HALLUCINATORY BEHAVIOR Perceptions without normal external stimulus correspondence. Rate only those experiences which are reported to have occurred within the last week and which are described as distinctly different from the thought and imagery processes of normal people. **SCORE** ☐	**17. EXCITEMENT** Heightened emotional tone, agitation, increased reactivity. **SCORE** ☐
13. MOTOR RETARDATION Reduction in energy level evidenced in slowed movements. Rate on the basis of observed behavior of the patient only; do not rate on the basis of patient's subjective impression of own energy level. **SCORE** ☐	**18. DISORIENTATION** Confusion or lack of proper association for person, place or time. **SCORE** ☐

Abnormal Involuntary Movement Scale (AIMS)[8]

Instructions: Complete the examination procedure before making ratings. Circle score for each item.

Patient Name:	Date:	None	Minimal, may be extreme normal	Mild	Moderate	Severe
Facial and Oral Movements						
1. Muscles of Facial Expression e.g., movements of forehead, eyebrows, periorbital area, cheeks; Include frowning, blinking, smiling, grimacing		0	1	2	3	4
2. Lips and Perioral Area e.g., puckering, pouting, smacking		0	1	2	3	4
3. Jaw e.g., biting, clenching, chewing, mouth opening, lateral movement		0	1	2	3	4
4. Tongue Rate only increases in movement both in and out of mouth, NOT inability to sustain movement		0	1	2	3	4
Extremity Movements						
5. Upper (arms, wrists, hands, fingers) Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).		0	1	2	3	4
6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot		0	1	2	3	4
Trunk Movements						
7. Neck, shoulders, hips e.g., rocking, twisting, squirming, pelvic gyrations		0	1	2	3	4
Global Judgments						
8. Severity of abnormal movements		0	1	2	3	4
9. Incapacitation due to abnormal movements		0	1	2	3	4
10. Patient's awareness of abnormal movements (rate only patient's report) 0 = not aware; 1 = aware, no distress; 2 = aware, mild distress; 3 = aware, moderate distress; 4 = aware, severe distress		0	1	2	3	4
Dental Status						
11. Current problems with teeth and/or dentures?		No	Yes			

Notes:

AIMS Examination Procedure

Either before or after completing the Examination Procedure, observe the patient unobtrusively, at rest (e.g., in the waiting room)

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask the patient whether there is anything in his/her mouth (i.e., gum, candy, etc.) And if there is, remove it.
2. Ask patient about the current condition of his/her teeth. Do teeth bother patient now?
3. Ask the patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position).
5. Ask patient to sit with hands hanging unsupported. If male, between legs; if female and wearing a dress, hanging over knees. (Observe hands or other body areas).
6. Ask patient to open mouth. (Observe tongue at rest within mouth). Do this twice.
7. Ask patient to protrude tongue. (Observe abnormalities of tongue movement). Do this twice.
8. Ask patient to tap thumb, with each finger as rapidly as possible for 10 to 15 seconds; first with right hand, then with left hand. (Observe facial and leg movements).
9. Flex and extend patient's left and right arms (one at a time).
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included).
11. Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth).
12. Have patient walk a few paces, turn, and walk back to chair. (Observe hands and gait). Do this twice.

Guy W: ECDEU Assessment Manual for Psychopharmacology - Revised (DHEW Publ No ADM 76-338), US Department of Health, Education and Welfare; 1976.

Generalized Anxiety Disorder 7-item (GAD-7) scale[9]

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
Add the score for each column	+	+	+	
Total Score *(add your column scores)* =				

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all _____

Somewhat difficult_____

Very difficult _____

Extremely difficult _____

Scoring

Scores of 5, 10, and 15 are taken as the cut-off points for mild, moderate and severe anxiety, respectively. When used as a screening tool, further evaluation is recommended when the score is 10 or greater.

Using the threshold score of 10, the GAD-7 has a sensitivity of 89% and a specificity of 82% for GAD. It is moderately good at screening three other common anxiety disorders—panic disorder (sensitivity 74%, specificity 81%), social anxiety disorder (sensitivity 72%, specificity 80%) and post-traumatic stress disorder (sensitivity 66%, specificity 81%).

Source: Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder. *Arch Inern Med.* 2006;166:1092–1097.

YOUNG MANIA RATING SCALE (YMRS)[81]

GUIDE FOR SCORING ITEMS

The purpose of each item is to rate the severity of that abnormality in the patient. When several keys are given for a particular grade of severity, the presence of only one is required to qualify for that rating.

The keys provided are guides. One can ignore the keys if that is necessary to indicate severity, although this should be the exception rather than the rule.

Scoring between the points given (whole or half points) is possible and encouraged after experience with the scale is acquired. This is particularly useful when severity of a particular item in a patient does not follow the progression indicated by the keys.

Specify **one** of the reasons listed below by putting the appropriate number in adjacent box.

1. ELEVATED MOOD

☐

0 - Absent

1 - Mildly or possibly increased on questioning

2 - Definite subjective elevation; optimistic, self-confident; cheerful; appropriate to content

3 - Elevated, inappropriate to content; humorous

4 - Euphoric; inappropriate laughter; singing

2. INCREASED MOTOR ACTIVITY ENERGY

☐

0 - Absent

1 - Subjectively increased

2 - Animated; gestures increased

3 - Excessive energy; hyperactive at times; restless (can be calmed)

4 - Motor excitement; continuous hyperactivity (cannot be calmed)

3. SEXUAL INTEREST

☐

0 - Normal; not increased

1 - Mildly or possibly increased

2 - Definite subjective increase on questioning

3 - Spontaneous sexual content; elaborates on sexual matters; hypersexual by self-report

4 - Overt sexual acts (toward patients, staff, or interviewer)

4. SLEEP

☐

0 - Reports no decrease in sleep

1 - Sleeping less than normal amount by up to one hour

2 - Sleeping less than normal by more than one hour

3 - Reports decreased need for sleep

4 - Denies need for sleep

5. IRRITABILITY

☐

0 - Absent

2 - Subjectively increased

4 - Irritable at times during interview; recent episodes of anger or annoyance on ward

6 - Frequently irritable during interview; short, curt throughout

8 - Hostile, uncooperative; interview impossible

6. SPEECH (Rate and Amount)

0 - No increase
2 - Feels talkative
4 - Increased rate or amount at times, verbose at times
6 - Push; consistently increased rate and amount; difficult to interrupt
8 - Pressured; uninterruptible, continuous speech

7. LANGUAGE - THOUGHT DISORDER

0 - Absent
1 - Circumstantial; mild distractibility; quick thoughts
2 - Distractible; loses goal of thought; change topics frequently; racing thoughts
3 - Flight of ideas; tangentiality; difficult to follow; rhyming, echolalia
4 - Incoherent; communication impossible

8. CONTENT

0 - Normal
2 - Questionable plans, new interests
4 - Special project(s); hyperreligious
6 - Grandiose or paranoid ideas; ideas of reference
8 - Delusions; hallucinations

9. DISRUPTIVE - AGGRESSIVE BEHAVIOR

0 - Absent, cooperative
2 - Sarcastic; loud at times, guarded
4 - Demanding; threats on ward
6 - Threatens interviewer; shouting; interview difficult
8 - Assaultive; destructive; interview impossible

10. APPEARANCE

0 - Appropriate dress and grooming
1 - Minimally unkempt
2 - Poorly groomed; moderately dishevelled; overdressed
3 - Dishevelled; partly clothed; garish make-up
4 - Completely unkempt; decorated; bizarre garb

11. INSIGHT

0 - Present; admits illness; agrees with need for treatment
1 - Possibly ill
2 - Admits behavior change, but denies illness
3 - Admits possible change in behavior, but denies illness
4 - Denies any behavior change

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