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Medication Fact Book *for* Psychiatric Practice

FIFTH EDITION

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FIFTH EDITION

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Published by Carlat Publishing, LLC

PO Box 626, Newburyport, MA 01950

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Introduction

HOW TO USE THIS BOOK

Medication information is presented in three ways in this book.

Fact sheets: In-depth information for select medications, somatic treatments, and side effects. There are 148 fact sheets in this book. The medication fact sheets don't cover all psychiatric medications, but we have included most of the commonly prescribed and newer medications.

Quick-scan medication tables: These are most often located at the beginning of each therapeutic category and list the very basics: generic and brand names, strengths available, starting doses, and target doses. These tables contain most of the commonly prescribed psychiatric medications.

Treatment algorithms: These are quick-reference decision trees to serve as a memory aid and to help in clinical decision making. They don't cover every medical nuance but serve as general overviews.

CHANGES AND ADDITIONS TO THE FIFTH EDITION

Medication fact sheets have been updated to reflect availability of newer strengths and formulations, as well as generics. New clinical data have been incorporated into the previous edition's fact sheets. Many categories of medications have been expanded to include a larger number of medications: 17 new fact sheets and 7 appendices with 6 new tables are included in this edition. Also, in this edition we've introduced algorithms within many of the chapters. These added flowcharts offer guidelines for treating conditions such as adult ADHD, depression, psychosis, anxiety, dementia, insomnia, bipolar mania, alcohol use disorder, and opioid use disorder. We've also added sections on medications for treating restless legs and using somatic therapies like bright light therapy, electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and vagus nerve stimulation (VNS).

CATEGORIES OF MEDICATIONS

We did our best to categorize medications rationally. However, in some cases a medication can fall into more than one category. In such cases, we categorized the medication with the types of disorders for which it is most often used. If you're having trouble finding a medication in a particular chapter, look in the index to find its page number.

MORE ON THE MEDICATION FACT SHEETS

The goal of these fact sheets is to provide need-to-know information that can be easily and quickly absorbed during a busy day of seeing patients. Our main criterion is that all the information should fit on a single page. Please refer to the *PDR (Physicians' Desk Reference)* when you need more in-depth information.

For the most part, each fact sheet contains the following information:

- Both the brand and generic names.
- **A [G] or (G) denotes generic availability.**
- FDA-approved indications.
- Off-label uses. We list the more common off-label uses, based on both the medical literature and our own clinical experience. Just because we list a potential use does not imply that we endorse a medication as being particularly effective for that use. We are simply alerting you to the fact that there is some evidence for efficacy.
- Dosage forms, along with available strengths.
- Dosage guidance. We provide recommendations on how to dose medications; these are derived from a variety of sources, including package inserts, clinical trials, and common clinical practice. In other words, don't be surprised when our dosing instructions are at odds with what you find in the *PDR*.
- Lab monitoring recommendations. We include the usual routine monitoring measures for each medication. Of course, you may need to think beyond the "routine" if the clinical picture warrants it.
- Cost information. Pricing information for a 1-month supply of a common dosing regimen was obtained from the website GoodRx (www.goodrx.com), accessed in July 2019. These are the prices a patient would have to pay if he or she had no insurance (GoodRx also offers coupons to purchase certain medications at reduced prices). Because of wide variations in price depending on the pharmacy, we list price categories rather than the price in dollars. The categories are:
  - $: Inexpensive: <$50/month
  - $$: Moderately expensive: $50–$100/month
  - $$$: Expensive: $100–$200/month

Hypnotics

GENERAL PRESCRIBING TIPS

The preferred way to treat insomnia is to treat the underlying cause, as opposed to reflexively writing scripts for hypnotics. There are plenty of reasons for our patients to lose sleep, including depression and anxiety, stressful life circumstances, and medication side effects. A common scenario, for example, is the patient who presents with major depression with insomnia as one of the depressive symptoms. In this case, we recommend either prescribing an antidepressant alone, or an antidepressant plus a 2-week prescription for a hypnotic. In most cases, the antidepressant will have kicked in around the 2-week point, and your patient will no longer need the hypnotic.

In addition to treating the underlying disorder, get into the habit of discussing sleep hygiene techniques with your patients. The key elements of sleep hygiene are:

- Avoid or reduce the use of substances that interfere with sleep, such as nicotine, caffeine, and alcohol.
- Get more exercise.
- Make the bedroom more conducive to sleep—eg, keep the lighting dim, reduce screen time, get comfortable sheets, and reserve the bed for sleeping and sex.
- Practice basic sleep restriction, which means reducing the time in bed to sleep time only.
- Do some relaxation exercises, such as deep breathing, meditation, or progressive muscle relaxation.

Another non-pharmacological intervention is cognitive behavioral therapy for insomnia (CBT-I), which is generally more effective than medications, especially for those with chronic insomnia. CBT-I decreases insomnia by about 50% and, unlike medications, 50%–70% of patients maintain their clinical gains after it is discontinued. Unfortunately, it may be challenging to find a local therapist who is skilled in the techniques involved. If you are interested in becoming trained yourself, check out www.med.upenn.edu/cbti/cont_ed.html and www.med.upenn.edu/cbti.

Assuming that you and your patient have resigned yourselves to a hypnotic, there's a pretty long menu of reasonable offerings. The options below are not listed in any particular order, because we don't really have any specific recommendations one way or another. We tend to pick and choose among them, which often requires trials of more than one before hitting on the sleep ambrosia for a particular patient.

- **"Z-drugs"** (eszopiclone, zaleplon, zolpidem) bind selectively to specific subunits of the GABA receptors that induce sleep, but they don't have the same relaxation effects of benzos and are probably somewhat less addictive. Zolpidem 5 mg–10 mg has become an old standard. For patients who wake up in the middle of the night, use zaleplon instead because of its very short duration of action.
- **Antihistamines** (diphenhydramine and doxylamine) are over-the-counter agents that induce sedation by blocking histamine H1 receptors. Start with diphenhydramine 25 mg QHS and increase to 50 mg if needed. The older the patient, the less appropriate this option, as antihistamines can cause confusion when used chronically. While this can occur with anyone, it's more common in the elderly.
- **Benzodiazepines.** While we are aware of the dangers of tolerance, some patients take a small dose of one of the benzos every night and seem to suffer no ill effects, and there is often no dosage creep over many years or even decades.
- **Ramelteon** is a melatonin agonist.
- **Suvorexant** is in a new class of agents called **dual orexin (OX1 and OX2) receptor antagonists,** or DORAs for short.
- **Doxepin** (Silenor) was approved by the FDA for use as a hypnotic. It is an old drug in new clothing—a tricyclic antidepressant being used for its antihistamine properties. Because it is expensive, we suggest using a low dose of generic doxepin to achieve the same effects as Silenor. This may entail prescribing the liquid version in order to get to doses in the 3 mg range.
- **Trazodone,** another antidepressant, is commonly used for insomnia at a dose of 25 mg–50 mg QHS. You can find the fact sheet for trazodone in the Antidepressants chapter.
- **Mirtazapine** is a sedating antidepressant, and is quite effective for insomnia but causes weight gain.
- **Quetiapine** is the classic sedating antipsychotic, which is commonly prescribed at 25 mg and is quite popular as a non-addictive alternative for substance users.

Potential Side Effects of Most Hypnotics

Although taken by millions, hypnotics are a high-risk class of medications, especially for the elderly, who are at greater risk for confusion, memory problems, and gait disturbances (sometimes leading to falls). Therefore, try to avoid hypnotics in the elderly, and when you do use them, use the lowest effective dose for the shortest duration of time possible.

Certain precautions apply to most hypnotics, and we'll list them below to minimize repetition in the fact sheets:

- **Daytime grogginess or hangover effect:** Most likely to occur with antihistamines or with longer-acting benzodiazepines or extended release zolpidem.
- **Anterograde amnesia:** Most likely to occur with benzodiazepines and Z-drugs. Among benzos, triazolam (Halcion) has a particularly bad rep. Just avoid triazolam—there's no need to prescribe it given the wealth of alternatives.
- **CNS depression:** Hypnotics may impair physical or mental abilities and alertness; advise patients to use caution when performing tasks that require alertness (eg, driving).
- **Respiratory depression:** Benzodiazepines in particular may depress respiration; avoid in patients at risk, including those with COPD or sleep apnea, or those taking other depressants such as opiates. In fact, the FDA issued a black box warning about the dangers of combining benzodiazepines with opiates due to a concerning incidence of serious side effects with the combination, including profound sedation, respiratory depression, coma, and death (see the Anxiolytics chapter introduction for more details on this warning).
- **Paradoxical reactions,** including hyperactive or aggressive behavior, have been reported, and are particularly seen with benzodiazepines; younger patients, elderly, and those with head injury or organic brain syndromes are at greatest risk.
- **Tolerance** to sedating effects of benzodiazepines generally occurs after several weeks of continuous use (one-third of patients will experience tolerance after 4 weeks of use). Tolerance to anxiolytic effects occurs more slowly, and to anti-seizure effects very little or not at all. Psychological and physical dependence occurs with prolonged use.
- **Discontinuation syndrome:** Withdrawal effects occur with most hypnotics and include rebound insomnia, agitation, anxiety, and malaise. Discontinuation syndromes from benzodiazepines are most severe with longer-term use, higher doses, and shorter-acting agents; in severe cases, discontinuation may include seizures. Hypnotics should not be abruptly discontinued; doses should be tapered gradually.
- **Recreational use and abuse** may occur with many hypnotics, particularly the benzodiazepines. Avoid or minimize use in patients who have addiction risk or when abuse is suspected.
- **Complex sleep-related behaviors** such as sleep-driving, sleep-eating, sleep-texting, and sleep-sex have been reported. Although this can occur when using benzodiazepines or Z-drugs alone and at usual therapeutic doses, they often occur with high-dose use or in combination with other CNS depressants, including alcohol. Typically, these events occur when the individual is not fully awake, and often there will be no memory of the behavior. In 2019, the FDA added a black box warning specifying that these behaviors can lead to injury and death, and recommended that we not prescribe them to anyone who has experienced complex sleep-related behaviors in the past.

TREATMENT ALGORITHM: Insomnia

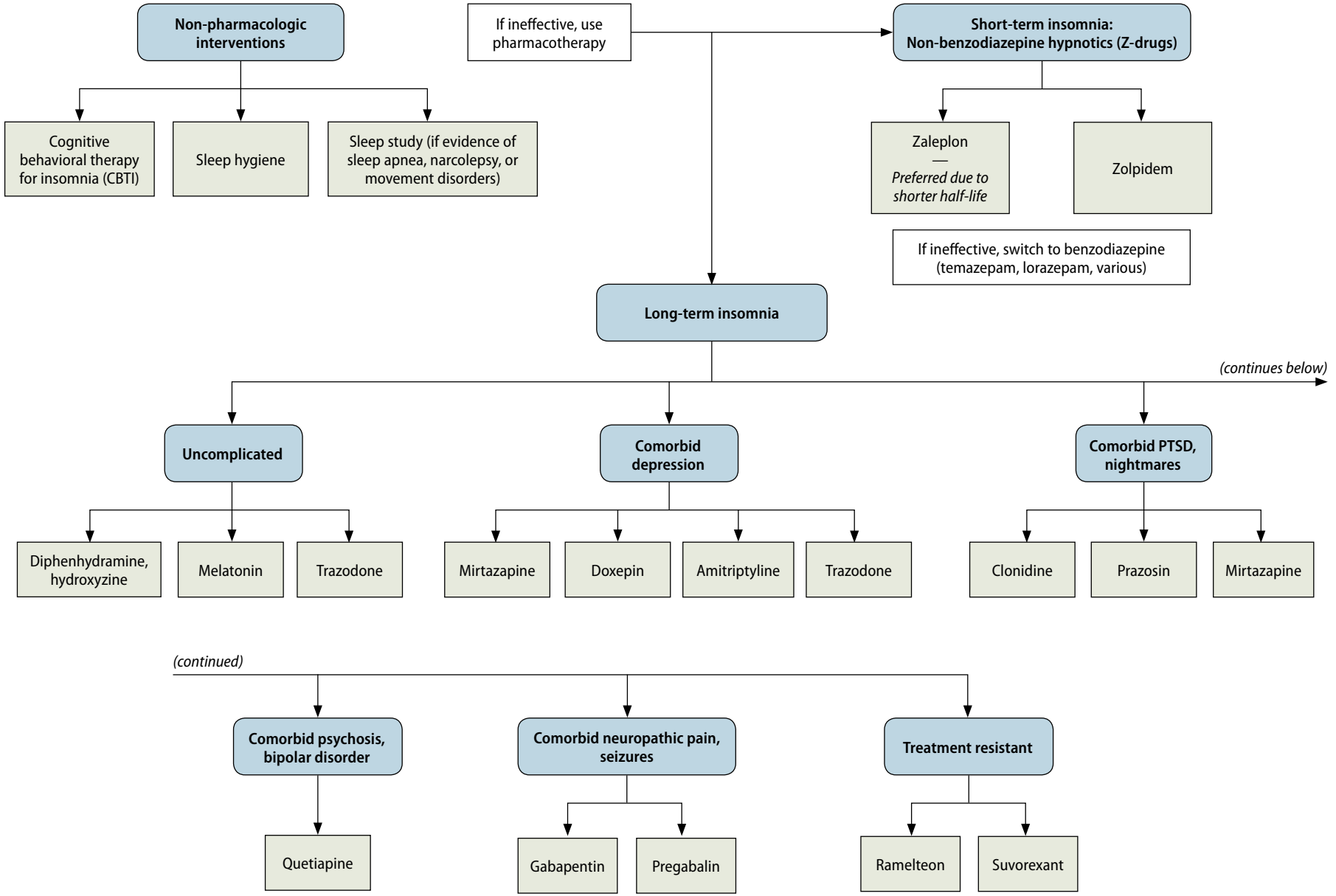

TABLE 12: Hypnotics

Generic Name (Brand Name) Year FDA Approved *[G] denotes generic availability*	Relevant FDA Indication(s)	Available Strengths (mg except where noted)	Usual Dosage Range for Insomnia (starting–max) (mg at HS)[1]	Onset of Action[2]	Half-Life (hours)	Duration of Action (hours)[2]
Clonazepam [G] (Klonopin, Klonopin Wafers[3]) 1975	Panic disorder Insomnia (off-label use)	Tablet: 0.5, 1, 2 ODT: 0.125, 0.25, 0.5, 1, 2	0.25 to 1	1 hr	20–80	4–8
Diphenhydramine [G] (Benadryl, others) 1946 Available OTC and Rx	Insomnia (adults and children 12+ years)	Capsule: 25, 50 Tablet: 25 Liquid: 12.5 mg/mL	25–50	1 hr	3.5–9	4–6
Doxepin [G] (Silenor) 2010/1969 Generic not available in 3 mg, 6 mg	Insomnia (sleep maintenance)	Tablet: 3, 6 Capsules: 10, 25, 50, 75, 100, 150 Liquid: 10 mg/mL	6	1 hr	15	4–6
Doxylamine [G] (Unisom, others) 1978 Available OTC and Rx	Nighttime sleep aid	Tablet: 25	25–50	1 hr	10	4–6
Eszopiclone [G] (Lunesta) 2004	Insomnia (sleep onset and sleep maintenance)	Tablet: 1, 2, 3	1–3	30 min	6	6–8
Flurazepam [G] (Dalmane[3]) 1970	Insomnia (short-term)	Capsule: 15, 30	15–30	30–60 min	40–100	7–8
Lorazepam [G] (Ativan) 1977	GAD Insomnia (off-label use)	Tablet: 0.5, 1, 2 Liquid: 2 mg/mL	1–4	30–60 min	10–20	4–6
Ramelteon (Rozerem) 2005	Insomnia (sleep onset)	Tablet: 8	8	30 min	1–2.6	Unknown
Suvorexant (Belsomra) 2014	Insomnia (sleep onset and sleep maintenance)	Tablet: 5, 10, 15, 20	10–20	30–60 min	12	6–8

[1]For approximate benzodiazepine dose equivalencies, refer to Table 10.1

[2]Onset and duration vary from person to person, dose to dose, and preparation to preparation

[3]Brand discontinued; available as generic only

Generic Name (Brand Name) Year FDA Approved *[G] denotes generic availability*	Relevant FDA Indication(s)	Available Strengths (mg except where noted)	Usual Dosage Range for Insomnia (starting–max) (mg at HS)[1]	Onset of Action[2]	Half-Life (hours)	Duration of Action (hours)[2]
Temazepam [G] (Restoril) 1981	Insomnia (short-term)	Capsule: 7.5, 15, 22.5, 30	15–30	30–60 min	9–18	4–6
Trazodone [G] (Desyrel[3], Oleptro[3]) 1981/2010	Depression Insomnia (off-label use)	Tablet: 50, 100, 150, 300 ER tablet: 150, 300	25 to 50–200	1 hr	7–10	Unknown
Triazolam [G] (Halcion) 1982	Insomnia (short-term)	Tablet: 0.125, 0.25	0.25–0.5	15–30 min	1.5–5.5	Unknown
Zaleplon [G] (Sonata) 1999	Insomnia (short-term, sleep onset)	Capsule: 5, 10	10–20	30 min	1	4
Zolpidem [G] (Ambien, Ambien CR, Edluar, Zolpimist) 1992 Generic not available for Zolpimist or Edluar SL	Insomnia (IR: short-term, sleep onset; CR: sleep onset and maintenance)	Tablet: 5, 10 ER tablet: 6.25, 12.5 SL tablet: 5, 10 Oral spray: 5 mg/spray	10, 12.5 CR (5, 6.25 in women)	30 min	2.5–3	6–8
Zolpidem low dose [G] (Intermezzo) 2011	Difficulty falling asleep after middle-of-the-night awakening	SL tablet: 1.75, 3.5	1.75 women; 3.5 men	30 min	2.5	4

[1]For approximate benzodiazepine dose equivalencies, refer to Table 10.1

[2]Onset and duration vary from person to person, dose to dose, and preparation to preparation

[3]Brand discontinued; available as generic only

ANTIHISTAMINES (Diphenhydramine, Doxylamine) Fact Sheet [G]

Bottom Line:
Antihistamines can be very effective sleep aids for many patients, although some patients may experience too much grogginess ("hangover") in the morning. Good first-line agents due to low risk of drug tolerance, dependence, or abuse, but exercise caution in the elderly, who may not tolerate peripheral effects.

FDA Indications:
Insomnia (adults, children 12–17 years); allergies; motion sickness; **antiparkinsonism**.

Off-Label Uses:
EPS; nausea and vomiting (morning sickness).

Dosage Forms:
- **Tablets, chewable tablets, caplets, capsules, and oral solutions, varies by brand:** 25 mg, 50 mg.
- **Common brand names:**
  - **Diphenhydramine:** Benadryl, Compoz, Nytol, Simply Sleep, Sleep-Eze, Sominex, Unisom SleepGels, Unisom SleepMelts, and generic.
  - **Doxylamine:** NyQuil, Unisom SleepTabs, and generic.

Dosage Guidance:
Insomnia: Start 25 mg, 30 minutes before bedtime. The dose required to induce sleep can be as low as 6.25 mg, but usual dose is 25 mg. Some patients may require 50 mg at bedtime.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Dry mouth, ataxia, urinary retention, constipation, drowsiness, memory problems.
- Serious but rare: Blurred vision, tachycardia.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Histamine H1 antagonist.
- Metabolized by liver, primarily CYP2D6; t ½: for diphenhydramine, 3.5–9 hours; for doxylamine, 10 hours (12–15 in elderly).
- Avoid use with other antihistamines or anticholinergics (additive effects).

Clinical Pearls:
- These antihistamines non-selectively antagonize central and peripheral histamine H1 receptors. They also have secondary anticholinergic effects, which can cause side effects including dry mouth and urinary retention, as well as cognitive impairment in susceptible populations.
- Be aware that anticholinergic drugs are often used to treat or prevent extrapyramidal symptoms in patients taking antipsychotics; diphenhydramine is often chosen and dosed at night to take advantage of its sedative effect.

Fun Fact:
The name NyQuil is a portmanteau of "night" and "tranquil."

DOXEPIN (Silenor) Fact Sheet [G]

Bottom Line:

Silenor/doxepin may be a good agent to put in your arsenal, particularly for those patients in whom you want to avoid benzodiazepines or Z-drugs. Clinically and pharmacologically, Silenor at 3 mg–6 mg/nightly differs very little from 10 mg/nightly of the generic doxepin, available at a fraction of the price. There appears to be no good reason to use the much more expensive branded product; stick to the low-dose generic.

FDA Indications:

Insomnia (sleep maintenance). Generic doxepin (at higher doses) approved for **depression**, **anxiety disorders**.

Off-Label Uses:

Headache; neuropathic pain; fibromyalgia; anxiety disorders.

Dosage Forms:

- **Tablets (Silenor):** 3 mg, 6 mg.
- **Capsules (G):** 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg.
- **Oral concentrate (G):** 10 mg/mL.

Dosage Guidance:

Insomnia:

- Silenor: Start 6 mg QHS (this is the starting, target, and max dose), taken within 30 minutes of bedtime. Use 3 mg/day in elderly. Avoid meals within 3 hours of taking Silenor.
- Doxepin: Start 10 mg capsule, or achieve a lower dose by using the oral concentrate or by opening the 10 mg capsule, dissolving it in a cup of juice, and drinking a portion of the juice.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: Generic: $; Silenor: $$$$

Side Effects:

- Most common: Somnolence, nausea, dry mouth, constipation.
- Serious but rare: Orthostasis (more likely at higher doses).

Mechanism, Pharmacokinetics, and Drug Interactions:

- Tricyclic antidepressant with norepinephrine and serotonin reuptake inhibition and histamine H1 antagonism.
- Metabolized primarily through CYP2C19 and 2D6 (also 1A2 and 2C9 to lesser extent); t ½: 15 hours.
- Clinically significant drug interactions not likely at the low doses used for hypnotic effects.

Clinical Pearls:

- Silenor is a branded version of generic doxepin, but available in lower doses.
- Taking within 3 hours of eating delays therapeutic effect by up to 3 hours. For faster onset and to minimize next-day effects, don't take within 3 hours of a meal.

Fun Fact:

Somaxon Pharmaceuticals, the original but fledgling manufacturer of Silenor, was acquired by Pernix, which hopes to eventually pursue over-the-counter approval.

ESZOPICLONE (Lunesta) Fact Sheet [G]

Bottom Line:
Like other Z-drugs, eszopiclone is an effective sedative with less potential for dependence than the benzodiazepines. Dosing is simple and, apart from the bitter aftertaste, its rapid onset and long duration of action make it well accepted among patients. As with all sedatives/hypnotics, nightly use should be discouraged.

FDA Indications:
Insomnia (sleep onset and sleep maintenance).

Off-Label Uses:
None.

Dosage Forms:
Tablets (G): 1 mg, 2 mg, 3 mg.

Dosage Guidance:
Start 1 mg QHS; may ↑ to max 3 mg QHS. Use lower doses in elderly (max 2 mg QHS). Take immediately before falling asleep and with at least 7–8 hours before planned awakening time. Avoid administering with a high-fat meal (delays onset of effect).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Somnolence, headache, unpleasant taste, dizziness, dry mouth.
- Serious but rare: Anaphylaxis, complex sleep-related behavior (sleep-driving, cooking, eating, phone calls).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Selective GABA-A alpha-1 subunit agonist.
- Metabolized primarily through CYP3A4 and 2E1; t ½: 6 hours (9 hours in elderly).
- Avoid concomitant use with other CNS depressants, including alcohol (additive effects). Potent CYP3A4 inhibitors (eg, fluvoxamine, erythromycin) may increase effects of eszopiclone significantly, whereas CYP3A4 inducers (eg, carbamazepine) may decrease eszopiclone levels; adjust eszopiclone dosing.

Clinical Pearls:
- Schedule IV controlled substance.
- Non-benzodiazepine in structure, but binds to the GABA-benzodiazepine receptor complex like benzodiazepines do; selective for the alpha receptor subtype (causing hypnotic effects but none of the other pharmacologic effects of benzodiazepines); one of the Z-drugs. Eszopiclone is the S-enantiomer of zopiclone (a hypnotic agent available in other countries).
- Unlike benzodiazepines, eszopiclone does not disrupt sleep architecture (stages).
- Taking after a large, high-fat meal will delay its onset of action (by about an hour). Because of its rapid onset of action, eszopiclone should be taken immediately before bedtime or once difficulty falling asleep has occurred.
- Higher doses increase next-day impairment of driving and alertness.

Fun Fact:
Sepracor, the manufacturer, tried to get Lunesta approved in Europe under the brand name Lunivia, but the European agency determined that eszopiclone was too similar to the already-marketed zopiclone to qualify as a patentable product. Sepracor, realizing that it might encounter future generic competition, withdrew its application.

FLURAZEPAM (Dalmane) Fact Sheet [G]

Bottom Line:
Flurazepam is not our first choice of benzodiazepines for insomnia—it has active metabolites and a very long half-life. Go with either temazepam or lorazepam instead.

FDA Indications:
Insomnia (short term).

Off-Label Uses:
Anxiety disorders; acute mania or psychosis; catatonia.

Dosage Forms:
Capsules (G): 15 mg, 30 mg.

Dosage Guidance:
Start 15 mg QHS. Max 30 mg nightly. Use lower doses in elderly.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Somnolence, dizziness, weakness, ataxia.
- Serious but rare: Anterograde amnesia, increased fall risk, paradoxical reaction (irritability, agitation), respiratory depression (avoid in patients with sleep apnea).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Binds to benzodiazepine receptors to enhance GABA effects.
- Metabolized primarily through CYP3A4; t ½: 40–100 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). Avoid use with potent 3A4 inhibitors (eg, erythromycin, ketoconazole, fluvoxamine) as they may increase flurazepam levels significantly, whereas CYP3A4 inducers (eg, carbamazepine) may decrease flurazepam levels; adjust flurazepam dosing.

Clinical Pearls:
- Schedule IV controlled substance.
- Flurazepam is less favored than temazepam because of active metabolites, long half-life, potential for accumulation, and next-day grogginess.
- Tolerance to sedative effect may develop within 2–4 weeks of use, and benzodiazepines affect sleep architecture; thus, long-term use is discouraged.

Fun Fact:
Advertising for Dalmane in the 1970s featured a nightgown-clad woman trapped inside a giant eyeball sphere, trying to get out. The tagline: "One less concern for your patient with insomnia."

RAMELTEON (Rozerem) Fact Sheet

Bottom Line:
A good alternative to benzodiazepines and Z-drugs for patients at risk for drug abuse or dependence. Compared to other hypnotics, ramelteon poses a lower risk for respiratory depression and hangover effect (morning grogginess). A good agent to have in your bag of tricks, but consider the possibility of rare hormonal effects. Also consider that over-the-counter melatonin (which ramelteon mimics) may do the same job at a lower price.

FDA Indications:
Insomnia (sleep onset).

Off-Label Uses:
Jet lag; shift-work sleep disorder.

Dosage Forms:
Tablets: 8 mg.

Dosage Guidance:
Start, target, and maximum dose 8 mg QHS, 30 minutes before bedtime. Avoid administering with high-fat meal (delays therapeutic effect by 45 minutes).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $$$$

Side Effects:
- Most common: Headache, somnolence, fatigue, dizziness, nausea.
- Serious but rare: Anaphylaxis, angioedema, complex sleep-related behavior (sleep-driving, cooking, eating, phone calls), increased prolactin, abnormal cortisol or testosterone levels.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Melatonin-1 and melatonin-2 receptor agonist.
- Metabolized primarily through CYP1A2 (major), and to a lesser extent CYP2C9 and 3A4; t ½: 1–2.6 hours.
- Avoid concomitant use with CNS depressants (additive effects). Exercise caution in patients taking potent CYP1A2 inhibitors (eg, fluvoxamine), which could increase ramelteon's effects.

Clinical Pearls:
- Because ramelteon's mechanism of action relates to melatonin receptors and regulation of circadian rhythms, it does not cause patients to "feel" sedated. Often patients say that it doesn't start working for several days—however, clinical trials have shown efficacy from the first night of use. It's good to warn patients about this ahead of time, or they may conclude it's ineffective after a single night and stop using it.
- No evidence of abuse potential or physical dependence.
- Hormonal alterations occur very rarely and usually with high-dose (16 mg in one study) and longer-term use (6–12 months). If unexplained amenorrhea, galactorrhea, decreased libido, or fertility problems occur, consider evaluating patient's prolactin or testosterone levels.

Fun Fact:
Another melatonin agonist, agomelatine, has been studied as an antidepressant, partly because circadian rhythms are disrupted in depression. It is approved overseas, but the manufacturer scrapped its development in the US.

SUVOREXANT (Belsomra) Fact Sheet

Bottom Line:
Other than a new mechanism of action, there's not much about suvorexant to recommend. There's no reason to expect it to work any better than the other hypnotics already on the market, and it has the same abuse liability. We're concerned that next-day impairment is a potential side effect at the highest approved dose of 20 mg, particularly since sleepless patients may decide on their own to take even higher doses. It's not a first-line hypnotic.

FDA Indications:
Insomnia (sleep onset and sleep maintenance).

Off-Label Uses:
None.

Dosage Forms:
Tablets: 5 mg, 10 mg, 15 mg, 20 mg.

Dosage Guidance:
Start 10 mg QHS, 30 minutes before bedtime and with at least 7 hours remaining before planned awakening time. If tolerated but not effective, may increase to max 20 mg QHS. For more rapid onset, patients should wait at least an hour after a meal before taking it. Avoid administering within an hour of a high-fat meal (delays therapeutic effect by about 1.5 hours).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $$$$

Side Effects:
- Most common: Somnolence, headache, abnormal dreams, dry mouth.
- Serious but rare: Impaired alertness and motor coordination, including impaired driving; sleep paralysis (inability to speak or move for up to a few minutes during the sleep-wake transition), hypnagogic/hypnopompic hallucinations (including vivid and disturbing perceptions), and cataplexy-like symptoms (leg weakness for seconds up to a few minutes both in the nighttime and the daytime) reported, especially at higher doses.

Mechanism, Pharmacokinetics, and Drug Interactions:
- "DORA" or dual orexin (OX1 and OX2) receptor antagonist.
- Metabolized primarily through CYP3A4, with minor contribution from 2C19; t ½: 12 hours.
- Caution with CYP3A4 inhibitors and inducers; suvorexant dose adjustment recommended. Caution with alcohol and other CNS depressants.

Clinical Pearls:
- Schedule IV controlled substance. One study found that drug abusers "liked" suvorexant as much as Ambien.
- Suvorexant has a unique mechanism of action. Unlike other hypnotics, it does not act by stimulating GABA or melatonin receptors or by blocking histamine. Instead, suvorexant blocks orexin receptors (orexins are neurotransmitters that promote wakefulness).
- Risk of next-day impairment increases with dose; caution patients taking 20 mg against next-day driving and other activities requiring mental alertness.

Fun Fact:
Merck expected to gain FDA approval for suvorexant in summer 2013. However, the FDA expressed concerns about safety with the 30 mg–40 mg dosing range Merck was proposing and denied approval. It was finally approved in August 2014 at lower doses.

TEMAZEPAM (Restoril) Fact Sheet [G]

Bottom Line:
We consider temazepam (and lorazepam) to be first-line agents for insomnia if a benzodiazepine is appropriate for use.

FDA Indications:
Insomnia (short term).

Off-Label Uses:
Anxiety disorders; acute mania or psychosis; catatonia.

Dosage Forms:
Capsules (G): 7.5 mg, 15 mg, 22.5 mg, 30 mg.

Dosage Guidance:
Start 15 mg QHS. Max 30 mg nightly. Use lower doses in elderly.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: 15 mg, 30 mg: $; 7.5 mg, 22.5 mg: $$

Side Effects:
- Most common: Somnolence, dizziness, weakness, ataxia.
- Serious but rare: Anterograde amnesia, increased fall risk, paradoxical reaction (irritability, agitation), respiratory depression (avoid in patients with sleep apnea).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Binds to benzodiazepine receptors to enhance GABA effects.
- Metabolized primarily through liver but no CYP450 involvement; t ½: 9–18 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). No risk for CYP450 drug interactions.

Clinical Pearls:
- Schedule IV controlled substance.
- Temazepam has long been a favored hypnotic for the elderly because of the lack of active metabolites, its short half-life, and absence of drug interactions.
- If abruptly discontinued, withdrawal symptoms are usually seen on the first day and last for 5–7 days in patients taking this type of short-intermediate half-life benzodiazepine.
- Tolerance to sedative effect may develop within 2–4 weeks of use, and benzodiazepines affect sleep architecture; thus, long-term use is discouraged.

Fun Fact:
The US Air Force uses temazepam as one of the approved "no-go pills" to help aviators and special duty personnel sleep in support of mission readiness; "ground tests" are required prior to authorization being issued to use the medication in an operational situation.

TRIAZOLAM (Halcion) Fact Sheet [G]

Bottom Line:
There are far better benzodiazepines (lorazepam, temazepam) to use for insomnia in appropriate patients. We cannot recommend using triazolam; some experts have even suggested that it be banned from the US market given the higher likelihood for adverse effects (anterograde amnesia, psychiatric disturbances).

FDA Indications:
Insomnia (short term).

Off-Label Uses:
Anxiety disorders; acute mania or psychosis; catatonia.

Dosage Forms:
Tablets (G): 0.125 mg, 0.25 mg.

Dosage Guidance:
Start 0.25 mg QHS; max 0.5 mg QHS. Take immediately before bedtime. Use lower doses in elderly.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Drowsiness, headache, dizziness, ataxia.
- Serious but rare: Anterograde amnesia, increased fall risk, paradoxical reaction (irritability, agitation); respiratory depression (avoid in patients with sleep apnea).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Binds to benzodiazepine receptors to enhance GABA effects.
- Metabolized primarily through CYP3A4; t ½: 1.5–5.5 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). Avoid use with potent 3A4 inhibitors (eg, erythromycin, ketoconazole, fluvoxamine) as they may increase triazolam levels significantly, whereas CYP3A4 inducers (eg, carbamazepine) may decrease triazolam levels; adjust triazolam dosing.

Clinical Pearls:
- Schedule IV controlled substance.
- Rapid onset of effect; best to take when already in bed.
- Due to its short half-life, triazolam is not effective for patients who suffer from frequent awakenings or early wakening; mostly useful for sleep onset.
- Rebound insomnia and other withdrawal symptoms are more likely and more severe with a short-acting benzodiazepine such as triazolam.
- Tolerance to sedative effect may develop within 2–4 weeks of use, and benzodiazepines affect sleep architecture; thus, long-term use is discouraged.
- May induce more anterograde amnesia than other benzodiazepines; concomitant use of alcohol or use of higher dose (0.5 mg) increases risk.
- Due to studies that suggest the frequency of severe psychiatric disturbances is higher with triazolam compared to other benzodiazepines, the United Kingdom and Brazil have banned it.

Not-So-Fun Fact:
Serial killer Jeffrey Dahmer used triazolam to sedate his victims.

ZALEPLON (Sonata) Fact Sheet [G]

Bottom Line:
Great for inducing sleep, but not great for sleep maintenance throughout the night. Zaleplon is the only sleeping pill that can be taken at 3 or 4 a.m. without causing functional impairment when the patient gets out of bed at 7 or 8 a.m., although patients should always use caution the next day.

FDA Indications:
Insomnia (short term, sleep onset).

Off-Label Uses:
None.

Dosage Forms:
Capsules (G): 5 mg, 10 mg.

Dosage Guidance:
Start 10 mg QHS, which is the usual dose for most adults. Max 20 mg QHS in those who tolerate but don't benefit from the usual 10 mg dose. Avoid administering with a high-fat meal (delays onset of effect by 2 hours). Use lower doses in elderly.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $

Side Effects:
- Most common: Somnolence, dizziness, headache.
- Serious but rare: Anaphylaxis, complex sleep-related behavior (sleep-driving, cooking, eating, phone calls).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Selective GABA-A alpha-1 subunit agonist.
- Metabolized primarily through aldehyde oxidase and also CYP3A4; t ½: 1 hour.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). Potent CYP3A4 inhibitors (eg, fluvoxamine, erythromycin) may increase effects of zaleplon significantly, whereas CYP3A4 inducers (eg, carbamazepine) may decrease zaleplon levels; adjust zaleplon dosing.

Clinical Pearls:
- Schedule IV controlled substance.
- Patients should take it immediately before going to bed or once they are in bed to minimize amnesic episodes.
- Because of zaleplon's very short half-life, it rarely causes next-day impairment.
- Unlike benzodiazepines, zaleplon does not disrupt normal sleep stages.
- Most useful for sleep initiation disorders; does not substantially increase total sleep time or decrease number of awakenings.
- Classified as a Schedule IV drug, but at therapeutic doses, abuse potential is somewhat less than benzodiazepines. However, abuse potential at high doses (2.5–7.5 times recommended dose) is similar to that of benzodiazepines.
- Fewer withdrawal effects than with benzodiazepines, but abrupt discontinuation, particularly from higher doses, can cause withdrawal symptoms (mostly rebound insomnia).

Fun Fact:
The name "Sonata" calls to mind the classical music composition featuring 3 or 4 movements, much like the phases of sleep.

ZOLPIDEM (Ambien, Edluar, Intermezzo, Zolpimist) Fact Sheet [G]

Bottom Line:
Good hypnotic that can also help with sleep maintenance, particularly in the ER formulation. The "new" lower-dose sublingual version (Intermezzo) is simply a patent extender, and we find it difficult to justify the higher cost (use generic zaleplon instead for middle-of-the-night awakening).

FDA Indications:
Insomnia (IR: Short term, sleep onset; CR: Sleep onset and maintenance; Intermezzo: Difficulty falling asleep after middle-of-the-night awakening).

Off-Label Uses:
None.

Dosing:
- **Tablets (G):** 5 mg, 10 mg.
- **ER tablets (G):** 6.25 mg, 12.5 mg.
- **SL tablets (Edluar):** 5 mg, 10 mg.
- **SL tablets (Intermezzo, [G]):** 1.75 mg, 3.5 mg.
- **Oral spray (Zolpimist):** 5 mg/spray.

Dosage Guidance:
- Start 10 mg QHS (5 mg in women). ER: Start 12.5 mg QHS (6.25 mg in women). Take immediately before bed, with at least 7–8 hours remaining before planned awakening time. Dose may be increased to max 10 mg (or 12.5 mg ER) QHS if no daytime grogginess. Higher doses may lead to greater abuse potential. Use lower doses in elderly.
- Lower doses of 1.75 mg (women), 3.5 mg (men) SL QHS can be used with ≥4 hours remaining before wake time.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: IR, ER: $; Intermezzo, Zolpimist: $$; Edluar: $$$$

Side Effects:
- Most common: Headache, somnolence, dizziness, diarrhea.
- Serious but rare: Complex sleep-related behavior (sleep-driving, cooking, eating, phone calls).

Mechanism, Pharmacokinetics, and Drug Interactions:
- Selective GABA-A alpha-1 subunit agonist.
- Metabolized primarily through CYP3A4; t ½: 2.5–3 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). Potent CYP3A4 inhibitors may increase effects of zolpidem, whereas CYP3A4 inducers (eg, carbamazepine) may decrease zolpidem levels; adjust zolpidem dosing.

Clinical Pearls:
- Schedule IV controlled substance.
- Unlike benzodiazepines, zolpidem does not disrupt normal sleep stages.
- At therapeutic doses, abuse potential is somewhat less than with benzodiazepines.
- Less withdrawal effects than with benzodiazepines, but abrupt discontinuation, particularly from higher doses, can cause withdrawal symptoms (mostly rebound insomnia).
- CR formulation: The dual layer allows some medication to be released immediately, with the rest released gradually, resulting in higher levels through the night.

Fun Fact:
Bioavail Labs received FDA approval for an orally disintegrating tablet form of zolpidem called Tovalt in 2007. It has since been discontinued due to poor sales.

APPENDIX D: LAB MONITORING FOR PSYCHIATRIC MEDICATIONS

This is a short and sweet table listing the medications that most psychiatrists would agree require lab monitoring. Our recommendations are quite abbreviated, and we haven't spelled out whether you should order labs before or after starting the medications, nor how you should do follow-up monitoring. There's just too much variation in practice for us to give authoritative detailed guidelines. These medications are mainly here to jog your memory, so you don't forget to at least consider what type of monitoring to do.

APPENDIX D TABLE: Recommended Laboratory Tests for Psychiatric Medications

Medications	Recommended Laboratory Tests
Acamprosate	BUN/creatinine if renal impairment is suspected
Amantadine	BUN/creatinine if renal impairment is suspected
Antipsychotics—second generation, primarily clozapine, olanzapine, quetiapine, paliperidone, risperidone[1]	Fasting glucose and lipids
Atomoxetine	LFTs
Carbamazepine	CBZ level, complete blood count (CBC), sodium, LFTs, pregnancy test, HLA-B*1502 in Asians[2]
Chlorpromazine	ECG if cardiac disease
Citalopram	ECG if cardiac disease, dose ≥40 mg/day
Clozapine	Fasting glucose and lipids, CBC
Desvenlafaxine	Periodic BP
Deutetrabenazine	ECG if cardiac disease
Disulfiram	LFTs if liver disease is suspected
Duloxetine	LFTs if liver disease is suspected[3]
Gabapentin	BUN/creatinine if renal impairment is suspected
Levomilnacipran	Periodic BP/pulse rate
Lithium	Li level, TSH, BUN/creatinine[4], pregnancy test, ECG if cardiac disease
Methadone	ECG if cardiac disease
Mirtazapine	Lipids
Naltrexone	LFTs if liver disease is suspected
Oxcarbazepine	Sodium, HLA-B*1502 in Asians[2]
Paliperidone	Prolactin if symptoms, fasting glucose and lipids
Pregabalin	BUN/creatinine if renal impairment is suspected
Risperidone	Prolactin if symptoms, fasting glucose and lipids
SSRIs	Sodium in elderly if fatigue, dizziness, confusion
Stimulants	ECG if cardiac disease
Thioridazine	ECG if cardiac disease
Topiramate	Bicarbonate
Tricyclic antidepressants	ECG if cardiac disease
Valbenazine	ECG if cardiac disease
Valproic acid	VPA level, LFTs, CBC for platelets, pregnancy test, ammonia if confusion
Venlafaxine	Periodic BP
Ziprasidone	ECG if cardiac disease

[1] Some guidelines recommend monitoring glucose and lipids with all SGAs

[2] HLA-B*1502 is a gene
Asians, especially the H

[3] Duloxetine should not
prescribing information

[4] The serum creatinine i
results include the estir
laboratory-evaluation/